UNIVERSITY OF DERBY

Exploring the Roles of Impulsivity and Self-Compassion as Risk Factors for Analgesic Addiction.

Mayoor Dhokia

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Preface and Acknowledgements

The structure of this thesis is such that each section is delivered as a single chapter. The opening chapter, a literature review (Chapter 1), was conducted to survey the scientific landscape surrounding key themes of this research. This helped to identify gaps in scientific knowledge and provided impetus for all studies which comprise this thesis. Chapter 2 provides details on the measures used throughout this study which can also be used as a source of reference. Each study (Chapter 3, 5 and 6) includes a chapter on the following: introduction material, methodology, participants results from the study and a discussion section purporting to relevant findings from the study itself. Chapter 4 builds towards a rationale for the use of CMT as a therapeutic intervention for painkiller dependence. This piece of research concludes in Chapter 7 by providing a general discussion and directions for future research. References are provided in Chapter 8. This work is also accompanied by an Appendix

I would like to dedicate the completion of this thesis to a curious 9-year-old boy who gained excitement and fascination with the world around him. A boy who gained greater pleasure in breaking his toys just to see how they worked, than playing with the toy intact. This boy's name is Mayoor.

I would first like to thank all the participants who took part in this study without whom none of this would have been possible. This thesis is a culmination of a joyous working relationship with my supervisor, Prof. James Elander, to whom I am eternally grateful for having faith in me and providing continual support throughout this journey of exploration and has generously paved the way for my development as an aspiring research scientist. I offer great appreciation and gratitude to Dr. Keith Clements for his detailed insights and also to Prof. Paul Gilbert for support, materials and stimulating conversation. I would also like to thank my Viva Voce examiners, particularly to Dr. Frances Maratos for her unreserved patience and inspiring comments throughout.

Lastly, many thanks to my constant, Pratima Dhokia.

"If I have seen further it is by standing on the shoulders of Giants"

Isaac Newton

Abstract

Addiction to analgesics remains a global problem among those with chronic pain while prevention strategies remain limited. This thesis aimed to investigate and reduce the effects of psychological risk factors towards painkiller dependence. These included impulsivity and meta-cognitive factors [Self-hate (HS), Self-inadequacy (IS) and Self-reassurance (RS)]. The meta-cognitive factors are sub-scales within the "Forms of Self-criticising/Self-attacking" self-report measure often used in researching Self-compassion. Compassion is regarded as being warm and understanding towards ourselves during suffering or feeling inadequate, rather than responding harshly with self-criticism. Impulsivity, the tendency to choose smaller-but-sooner rewards in lieu of larger-but later rewards, is a well-known risk factor for developing drug dependence but has not been fully investigated for its role towards painkiller dependence. Additionally, the meta-cognitive risk factors have not been investigated for their role towards painkiller dependence or their relationship with impulsivity. A novel facet of all three studies was that they were all delivered via a bespoke web-platform.

Study 1, a cross-sectional study of one group of participants (N=259) aimed to (1) explore the prevalence of painkiller dependence within participants who had chronic pain; (2) elucidate the role of cognitive and behavioural aspects of impulsivity towards painkiller dependence and (3) to investigate the role of IS, HS and RS towards painkiller dependence. Notable significant positive correlations were found between painkiller dependence and daily prescription painkiller consumption; Pain Intensity; Pain Frequency (PF); IS; HS and facets of impulsivity. Regression analysis highlighted low scores for Delay Discounting (DD) and high scores on Lack of Perseverance, NU and IS predicted higher levels of painkiller dependence. Three significant interaction terms (PF x IS; HS; RS) allowed for a moderation analysis to address Aim 3. This showed that IS, RS and HS acted as moderators for PF on Painkiller dependence. Results indicate impulsivity, IS, and HS to be risk factors for painkiller dependence.

Study 2 was a pilot randomised controlled trial (RCT) aimed to assess acceptability and feasibility of a web-platform that delivered a Compassionate Mind Training (CMT) intervention to those with chronic pain. Participants were randomised into one of two groups (CMT vs. Relaxation). CMT group participants engaged with a

psycho-education video library and a CMT intervention. RM group participants listened to theory-neutral relaxation music and did not engage with CMT related activities. All participants completed the study with no attrition. All feedback questions pertaining to acceptability and feasibility were above the threshold value of 5. Analysis of participant feedback led to two major additions to the web-platform: A dynamic colour-coded timetable and a personal Pain Diary. These new features were applied to Study 3 which was a large-scale version of Study 2.

Study 3, an RCT aimed to (1) reduce severity of identified risk factors for painkiller dependence (as found in Study 1) by increasing Self-reassurance and (2) seek associations between variables which reduced/increased in CMT group participants. Participants were randomised into one of two groups (CMT [n=39] vs. Relaxation [*n*=40]) Both groups completed self-report measures and the DD task at three time-points. An Intent-To-Treat analysis was applied to reduce attrition bias. Major outcomes of the study were significant reductions within CMT group participants for: painkiller dependence ($p < .001$)**,** prescription painkiller consumption ($p < .001$). NU ($p < .001$) and Self-hate ($p < .001$). Additionally, Self-reassurance in the CMT group significantly increased ($p = .02$).

To conclude, this piece of research identified and reduced previously unknown risk factors for painkiller dependence. These results may provide benefit for those prescribed painkillers by screening those who may be deemed vulnerable as well as widening our understanding of risk factors for substance dependence.

Table of Contents

List of Figures

List of Tables

Abbreviations

5-HT	Serotonin
5CSRTT	Five Choice Serial Reaction Time Task
ACC	Anterior Cingulate Cortex
ADD	Attention Deficit Disorder
ADHD	Attention Deficit Hyperactivity Disorder
ANOVA	Analysis of Variance
BLA	Basolateral Amygdala
BIS-11	Barratt Impulsivity Scale
CBT	Cognitive Behavior Therapy
CPT	Continuous Performance Task
CMT	Compassionate Mind Training
CFT	Compassion Focused Therapy
CGT	Cambridge Gambling Task
CNS	Central Nervous System
CPT	Continuous Performance Task
CSS	Cascading Style Sheets
DA	Dopamine
DD	Delay Discounting
DERS	Difficulties in Emotion Regulation Scale
DPPC	Daily Prescription Painkiller Consumption
DRL	Differential Reinforcement of Low Rate Procedure
DV	Dependent Variable
EIQ	Eysenck Impulsivity Questionnaire
EIVE	Eysenck Impulsiveness-Venturesomeness-Empathy Questionnaire
FC	Frontal Cortex
FCN	Fixed Consecutive Number procedure
FCSR	Forms of Self-Criticising/Attacking & Self-Reassuring Scale
G-G	Greenhouse-Geisser
HS	Self Hate
IGT	Iowa Gambling Task
ILC	Infralimbic Cortex
IP	Internet Protocol
I-RISA	Impaired Response Inhibition and Salience Attribution
IS	Inadequate Self
IV	Independent Variable
LOPERSEV	Lack of Perseverance
LOPREMED	Lack of Premeditation
LTP	Longer Than Prescribed
MANOVA	Multiple Analysis of Variance
mPFC	Medial Prefrontal Cortex
NAc	Nucleus Accumbens
OFC	Orbitofrontal Cortex
OTC	Over-the-counter
OTCPD	Over the Counter Painkillers consumed per Day
PLC	Prelimbic Cortex
PF	Pain Frequency
PFC	Prefrontal Cortex
PI	Pain Intensity
PU	Positive Urgency
RDA	Recommended Daily Allowance
RGP	Risky Gains Procedure
RGT	Risky Gains Task
SPSS	Statistical Package for the Social Sciences
SRB	Soothing Rhythm Breathing
SS	Sensation Seeking
S-S	Smaller-but-sooner
SST	Stop Signal Task
SUD	Substance Use Disorder
LDQ	Leeds Dependence Questionnaire
L-L	Larger-but-later

MAAS	Mindful Attention and Awareness Scale
MDMA	3,4-methylenedioxy-methamphetamine
NU	Negative Urgency
OXT	Oxytocin
RM	Relaxation music
RS	Reassured Self
SST	Stop Signal Task
STN	Subthalamic Nucleus
SUD	Substance use Disorder
FCN	Fixed Consecutive Number
UPPS-P	Urgency, Premeditation, Perseverance, Sensation Seeking, and Positive Urgency
VS	Ventral Striatum

Chapter 1. Literature Review

This chapter will provide an overview of the relevant literature and empirical evidence on major areas of theory and practice upon which this thesis aims to build upon. Areas of interest include chronic pain, analgesic use, drug dependence, impulsivity (cognitive and behavioural) and compassionate mind training (CMT).

1.1. Chronic Pain

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Chronic pain is pain that persists over a period of time, typically for at least three months Chronic pain can be mild or excruciating, episodic or continuous, merely inconvenient or totally incapacitating (International Association for The Study of Pain, 1986).

The emotional strain of chronic pain can make pain worse. Anxiety, stress, depression, anger and fatigue interact in complex ways with chronic pain and may decrease the body's production of natural painkillers; moreover, such negative feelings may increase the level of substances that amplify sensations of pain, causing a vicious cycle of pain for the person (Jackson et al., 1997). Even the body's most basic defenses may be compromised. There is considerable evidence that unrelenting pain can suppress the immune system (Marchand et al., 2005).

The most common sources of pain stem from headaches, joint pain, pain from injury, and backaches (Fayaz et al., 2016). Other kinds of chronic pain include tendinitis, sinus pain, carpal tunnel syndrome, and pain affecting specific parts of the body, such as the shoulders, pelvis, and neck. Generalised muscle or nerve pain can also develop into a chronic condition. Chronic pain may originate with an initial trauma/injury or infection, or there may be an ongoing cause of pain. Some people suffer chronic pain in the absence of any past injury or evidence of body damage (Rintala et al, 1998).

Table 1 Number of chronic pain sufferers in America

Condition	Number of sufferers	Reference
Chronic pain	100 million	Institute of Medicine of The National Academies (2011)
Diabetes	25.8 million	American Diabetes Association (2015)
Coronary Heart Disease (Heart attacks and chest pain) Stroke	16.3 million 7.0 million	American Heart Association (2011)
Cancer	11.9 million	American Cancer Society (2015)

Chronic pain is known to affect approximately 20% of the European population (Breivik et al., 2006) and is most common in women, the elderly, and individuals from a lower socioeconomic status (Wiesenfeld-Hallin, 2005; Craft, 2007). Estimates of the prevalence of chronic pain vary, but a recent estimate is that 7.8 million people in the UK, 100 million people in America and 1.5 billion people worldwide suffer from chronic pain that has lasted for more than six months (Institute of Medicine of the National Academies Report; 2011). Chronic pain is a condition that has more sufferers than some of the major diseases. Moreover, it appears that the prevalence of chronic pain is rising, with more cases now compared with 40 years ago (Global Industry Analysts; 2011). Further descriptive statistics are provided in Table 1. Smith et al., (2011) report that fewer than 2% of chronic pain patients reported attending a pain management service with the other 98% managed in primary care facilities. Pain management as viewed by said patients was deemed to be "unsatisfactory" (Elliott et al., 2002), partly due to limited evidence for efficient interventions. Chronic pain can be debilitating and persists for many years. The added discomfort of having to travel to such locations does not conjure an appealing prospect.

The general measure to reduce feelings of pain and discomfort is the use of prescription painkillers. Government statistics have shown year-upon-year increases in the consumption of painkillers. For example, within the last ten years alone Australia has more than quadrupled its consumption of common, opioid-based painkillers (codeine, morphine and oxycodone). In 2001 the consumption rate of 22,000,000 doses per annum soared to 106,000,000 doses per annum in 2013. Australia, North America, Western and Central Europe and New Zealand account for more than 95% of global opioid consumption (Berterame et al., 2016).

With the high number of chronic pain sufferers, and addiction, come the associated expenses for treatment, which can cost a nation's economy vast sums of money. Recent European reports state more than €200 billion per annum in Europe and $150 billion per annum in the USA is spent to manage the lives of those with chronic pain (Tracey et al., 2009). A wealth of evidence suggests that recent estimates of the worldwide burden imposed by chronic pain are greatly underestimated (Croft et al., 2010). The World Health Organisation (WHO) forecast that by 2030 the three leading diseases causing strain on society would be coronary heart disease, cerebrovascular disease and unipolar depression (Mathers et al., 2008). Chronic pain is a central co-morbid factor linked with all four entities listed. However, chronic pain itself is far more than a co-morbid factor and is recognized as a condition in itself that can be defined and categorized (International Association for The Study of Pain, 1986; Tracey et al., 2009).

From the statistics presented above, we see that (1) there are a large number of people living with chronic pain; (2) the majority are dissatisfied with the services available to them; (3) patients are consuming large quantities of painkillers with addictive properties; (4) exorbitant amounts of money are spent on pain management and (5) the mortality rate of painkiller consumers is increasing exponentially.

With this is mind we can see that (a) the potential for a painkiller addiction epidemic has indeed become reality and (b) there exists a niche to develop a new intervention for chronic pain sufferers consuming painkillers. In addition to research on the pathophysiology of pain mechanisms, it is imperative to elucidate risk factors allied with the existence and development of painkiller addiction, as this will permit design for therapeutic strategies. Risk factors include socio-demographic, clinical, and biological factors, and recent research has elucidated many of these, with potential clinical relevance. Due to the mind-body connection related with chronic pain, optimal treatment requires addressing psychological factors in addition to physical features of the condition. Psychological studies of those living with chronic pain aim to add another dimension to the treatment program by highlighting risk factors and developing evidence-based therapeutic tools. One significant aspect is the translation of research on cognitive risk factors from animal or small human samples to the general population (Mao et al., 2012). These include, but are not limited to, decision making processes and the tone and content of our internal dialogue. Ergo, should the availability and accessibility of a cost-effective evidence-based therapeutic intervention be made available then this would greatly increase the number of patients who engage with treatment whilst reducing economic burden.

This chapter will review current understanding of cognitive risk factors (impulsivity and self-compassion) associated with potential for painkiller addiction with the expectation of developing an effective therapeutic intervention for management and reduction of painkiller addiction.

1.2. Atypical Painkiller use

Irrespective of our philosophical stance on what pain is, one thing that can be agreed is that pain, for the majority of us, is a great discomfort. Painkillers are drugs that aid in reducing the sensation of pain. The colloquial term “painkiller(s)” refers to a group of drugs called analgesics. Analgesics aim to achieve “analgesia”, or “relief from pain”. The terms “painkiller(s)” and “analgesics” are often used interchangeably. Painkillers can contain opioids as denoted by “*” in Table 2. Opioid-based painkillers are prescribed for moderate to severe pain, predominantly pains with visceral origin, and are used in steps two (Mild pain) and three (Moderate/Severe pain) of the analgesic ladder (World Health Organization, 1996;). The 3-step “analgesic ladder” is a concept whereby (1) mild pain is treated by non-opioid based medication (ibuprofen, naproxen); (2) moderate pain is treated by opiate-based medication (codeine, hydrocodone, oxycodone) and (3) severe pain is treated by stronger opioid analgesics (morphine, fentanyl, hydromorphone). Four broad classes of opioids exist:

I. **Endogenous opioid peptides** (produced in the body: Endorphins, Dynorphins, Enkephalins)
II. **Opium alkaloids** (Morphine, Codeine, Thebaine)
III. **Semi-synthetic opioids** (Heroin, Oxycodone, Hydrocodone, Dihydrocodeine, Hydromorphone, Oxymorphone, Nicomorphine)
IV. **Fully synthetic opioids** (Pethidine or Demerol, Methadone, Fentanyl, Propoxyphene, Pentazocine, Buprenorphine, Butorphanol, Tramadol)

In addition to opioid-based analgesics, many other painkillers also yield a state of analgesia. Three different categories of analgesics exist and are denoted as simple non-opioid analgesics, compound analgesics and opioid analgesics. Table 2 below gives a general overview of these painkillers. Painkillers are available for purchase over-the-counter (OTC) and via prescription from a medically qualified health care professional.

Table 2 General overview of painkillers

	Simple non-opioid analgesics	Compound analgesics	Opioid analgesics
What are they?	The most common form of analgesic, also including Non-steroidal anti-inflammatory Drugs (NSAIDs)	A combination of drugs in one tablet	The strongest type of analgesics
Uses	Mild to moderate pain or alongside stronger painkillers	Mild to moderate pain or alongside NSAIDs	Moderate to severe pain or alongside NSAIDs
Availability	Pharmacies and supermarkets. Some NSAIDs are only available on prescription	Milder variants at pharmacies and supermarkets. Stronger variants are only available on prescription	Mostly only on prescription
Examples	Paracetamol, NSAIDs: Aspirin, Ibuprofen	Codeine*, Dihydrocodeine*	Tramadol*, Morphine*, Buprenorphine*, Fentanyl*, Oxycodone*, Methadone*

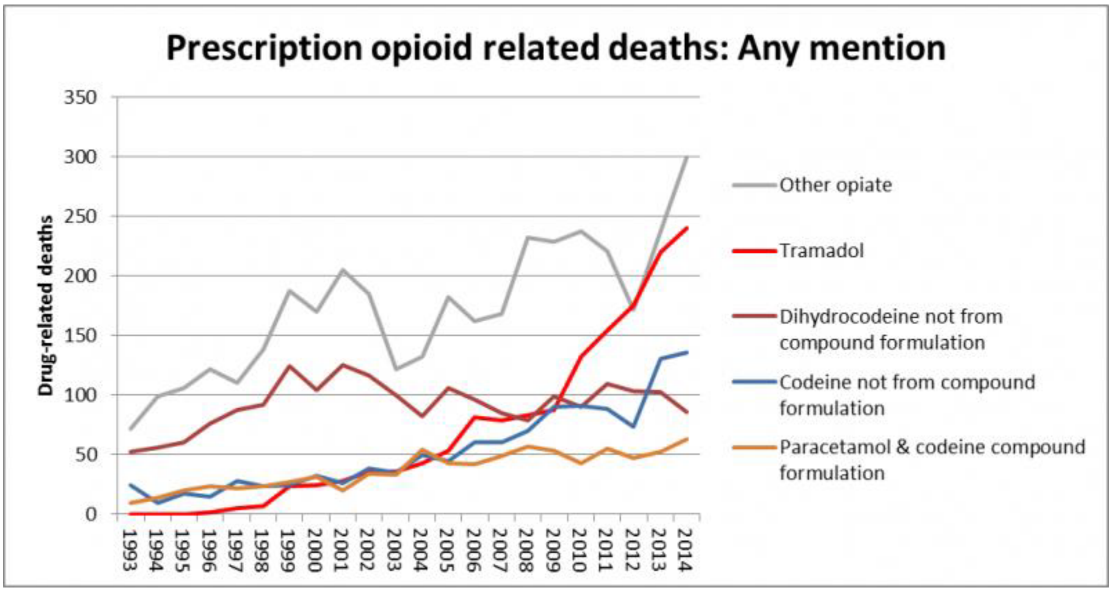
**Contain opioid derived compounds*

The number of patients consuming painkillers is rising drastically out of control. Approximately two million adults age 50 and older (2.1 percent of American adults in that age range) used prescription-type drugs non-medically in the past year (The National Survey on Drug Use and Health (NSDUH) Report, Illicit Drug Use Among Older Adults, 2013). With increasing numbers of people consuming painkillers, the non-medical use is also of concern. Non-medical use of prescription painkillers costs health insurers up to $72.5 billion annually in direct health care costs (Centers for Disease Control and Prevention Analysis, 2011) and in 2009 there were approximately 500,000 emergency department visits in the USA due to poisoning caused by painkillers. The number of deaths due to painkiller overdose in the USA has quadrupled in the past decade (to 14,800 each year, or 40 each day). The misuse of painkillers, using painkillers to relieve pain but in ways other than intended, has grown to become a worldwide health concern. The Centers for Disease Control and Prevention has classified prescription drug abuse as "an epidemic". While there has been a marked decrease in the use of some illegal drugs like cocaine, data from the NSDUH show that nearly one-third (29%) of people in 2009 aged 12 and over who used drugs on their first time began by using a prescription drug for non-medical reasons (The National Survey on Drug Use and Health Report, Illicit Drug Use Among Older Adults, 2013).

Although painkillers have been used with great success, the immense number of people living with chronic pain and consuming powerful painkillers for medical reasons (Goh et al., 2009, Porteous et al., 2005, Proprietary Association for Great Britain Annual Review, 2005), increases the susceptibility for developing tolerance and/or a substance use disorder (SUD; Compton et al., 2006; Lessenger et al., 2008; National Treatment Agency for Substance Misuse, 2011). Prescription painkillers are the second most abused category of drugs in the United States, following marijuana (National Survey on Drug Use and Health Report; 2013).

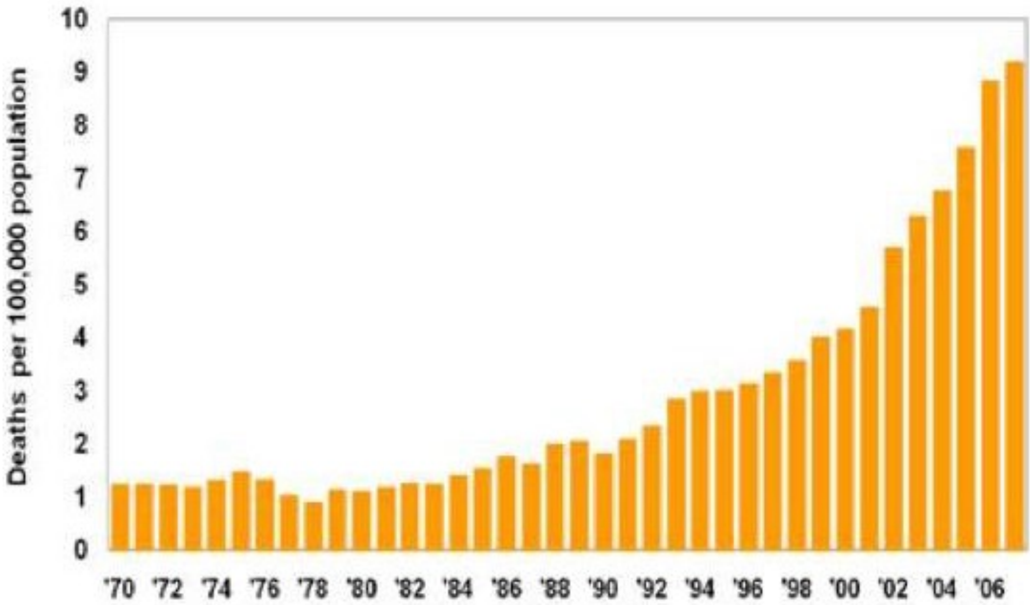
In recent times prescription painkillers have been associated with an increase in opioid related deaths and the trend appears to show a rise in the number of deaths each year. The number of deaths from Tramadol has seen the greatest upsurge from 2009 while deaths from all other prescription opioids also increased each year (Office for National Statistics: Deaths related to drug poisoning in England and Wales. 2014; Fig. 1). Government statistics from the USA also show that the numbers of deaths continue to rise exponentially year upon year (Fig. 2).

Figure 1 Prescription opioid related deaths in the UK (1993-2014)



Source: **Office for National Statistics: Deaths related to drug poisoning in England and Wales. 2014.**

Figure 2 Unintentional deaths due to opioid overdose in USA (1970-2007)



Source: Centers for Disease Control and Prevention, July 2010

It has been postulated that psychological dependence to opioid painkillers does not manifest as a result of pain treatment. The sensation of pain itself was advocated to guard against the possibility of dependence to the medication and this premise was used to bolster the proposition of safe use of opioid painkillers for the management of chronic pain (Kanner & Foley, 1981). Some evidence for this was shown in animal and human studies whereby the opioid induced euphoria was mitigated by pain (Portenoy & Foley, 1986). Conversely, clinical observations and a plethora of empirical research have described challenging behavior ensuing in patients treated with analgesics for chronic pain.

Aberrant painkiller use is a major concern amongst chronic pain patients whereby reports state a 31% prevalence rate of opioid-analgesic misuse (Kahan, et al., 2006). A study by Elander et al., 2014 report almost a quarter of their sample (24%) misused painkillers. Additionally, and despite the small sample size (n=47), Marino et al., 2013 report 11.3% of their sample of participants with chronic low-back pain misused painkillers. Although the majority of chronic pain patients administered opioid-analgesics do not develop a Substance-use Disorder (SUD), the risk towards painkiller dependence has become a major concern for medical professionals (Savage et al., 2003). This has largely been due to (1) medical professionals not being adequately taught how to recognize the signs of addiction; (2) cross-fertilization of medical terms regarding addiction, abuse and dependence and (3) a lack of research into the psychological factors to complement the physiological research on addiction.

Psychological risk factors such as impulsivity have been shown to contribute to an elevated propensity towards painkiller misuse (Marino et al., 2013; Martel et al., 2014; Vest et al., 2016) and therefore warrant further investigation. Self-compassion as a risk factor for painkiller addiction has yet to be explored. With current interventions for the disorder being limited in their effectiveness, such research is crucial for the development of more successful treatment and prevention strategies (Nestler et al., 2003).

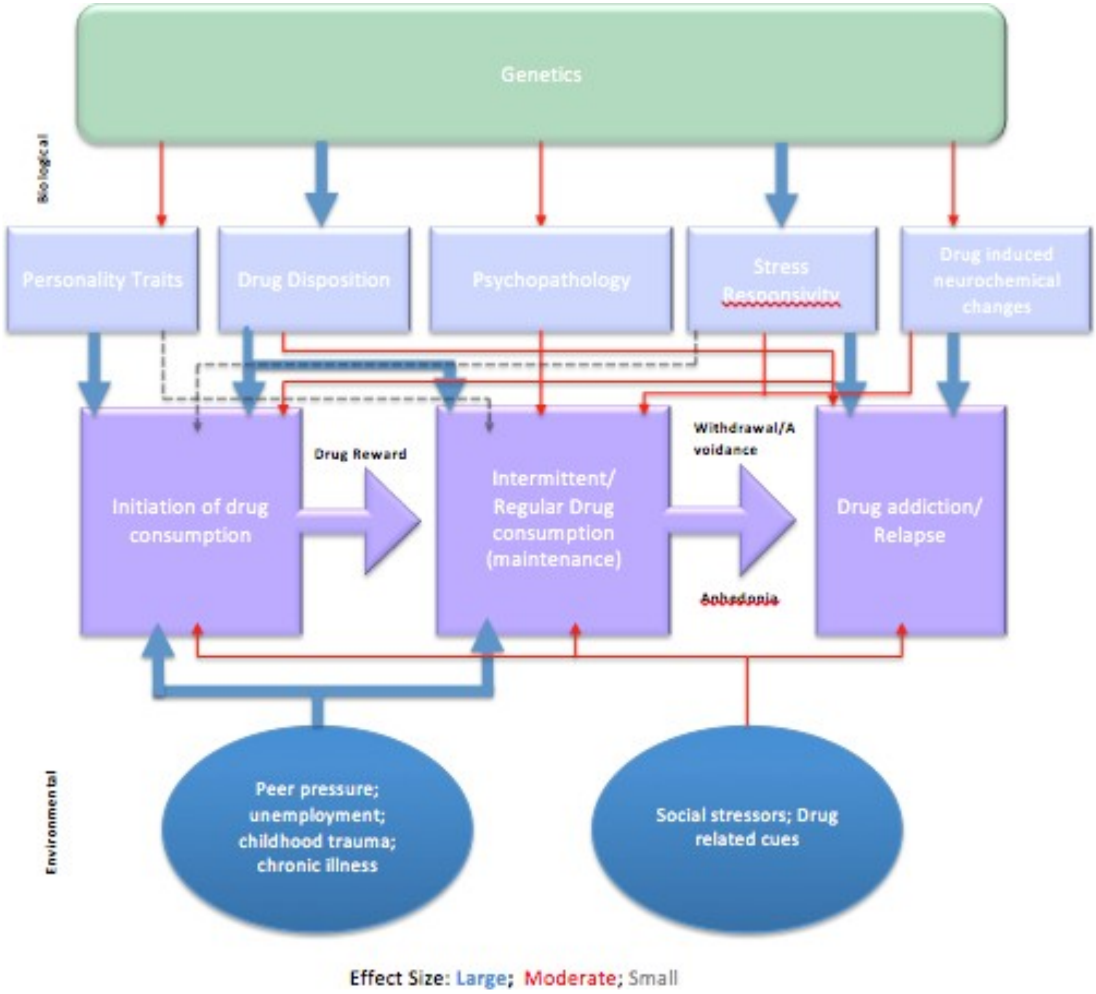
1.2.1. Stages of addiction

Addiction to painkillers does not develop overnight but in stages. The majority of addiction models propose a 3-step model (Figure 3). Addiction relating to all drugs including painkillers begins by (1) initiation of painkiller consumption which progresses to (2) intermittent/regular consumption of painkillers, also known as the maintenance phase, and finally (3) Addiction. The process can be cyclical if punctuated by a phase of relapse/cessation which are accompanied by withdrawal symptoms

(Kreek et al., 2005). Twin studies have shown that while genes function as a risk factor for addiction, our environment and personality traits also play a significant role (Tsuang et al., 1999). Personality traits such as risk-taking (Brand et al., 2008) and dysfunctional impulse control are thought to influence the initiation and maintenance phase (Fig. 3; Verdejo-Garcia, et al., 2007a; 2007b; 2007c). Although the reasons to initiate opiate consumption in the chronic pain patient and the street drug abuser are vastly, possessing an impulsive personality may act as a risk factor for consuming painkillers beyond safe boundaries i.e. consuming more painkillers than the RDA (Recommended Daily Allowance) or continuing to consume painkillers for longer than the prescribing period (LTP).

This can be hypothesized to occur within those in possession of opioid analgesics whereby the impulse to consume more than the recommended dose of painkillers is not adequately curtailed. The progression from sporadic use (abuse) to addiction/dependence is regulated by physiological and psychological entities (Nestler, 2013). Other biological systems dysregulated by chronic drug consumption are involved in craving, withdrawal symptomatology and possibly towards the development of a chronic anhedonic state that promotes relapse.

Figure 3 Stages of addiction and risk factors (Adapted from Nestler, 2013)



1.2.2. Conceptualisation: Addiction, Abuse, Misuse and Dependence

Inconsistencies in terminology have greatly hampered efforts to define and quantify opioid addiction. The terms *drug dependence* and *drug addiction* are often used interchangeably throughout the scientific community; however, this reasoning brings misperception and bewilderment, predominantly to the motivational causes of Substance Use Disorder (SUD).

Drug *addiction* is viewed as a disorder of the brains reward system (Ruffle et al., 2014; Olsen, 2011) characterised by compulsive engagement with rewarding stimuli despite negative consequences (Nestler, 2013; Taylor et al., 2013). Addiction is also regarded as a disease process that promotes such behaviours. A key property of addiction is that addictive stimuli are positively reinforcing (Malenka et al., 2009) and so raise the probability that an individual will continue with repeated exposure to that stimulus

(American Society for Addiction Medicine, 2012). In the case of prescription painkillers, the relief of pain they provide and the surge of Dopamine (DA; neurotransmitter substance) both act as positive reinforcers. The terms addiction and dependence are often used interchangeably. Addiction often summarised as a disorder of the brain characterised by compulsive engagement in rewarding stimuli despite adverse consequences.

Drug *Abuse* is the use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others. It is often stated to occur outside of sociocultural norms. Ergo, the motivation to consume the drug could possibly be preferred in comparison to other motivators. The origin(s) of substance abuse and addiction can be of similar derivation but are usually distinct. Addiction demands activation of motivational and neural reward systems by drugs whereas drug/substance abuse usually does not. Instead it involves psychosocial factors with minor effect on neural pathways. An example of drug abuse fueled by psychosocial factors is anabolic steroid abuse (Perez-Lopez et al., 2004). Leading researchers argue impulsivity to be a risk-factor for drug abuse (Moeller et al., 2001a) and in recent years the second highest number of deaths from any substance abused were from opioid use disorder (Global Burden of Disease Study, 2013). Drug abuse may often lead to drug addiction, drug dependence or both.

Drug misuse, a term often used incorrectly, is stated by the World Health Organisation as the "*Use of a substance for a purpose not consistent with legal or medical guidelines, as in the non-medical use of prescription medications. The term is preferred by some to abuse in the belief that it is less judgmental*" (Lexicon of alcohol and drug terms published by the World Health Organization, 2019). It is also denoted using a drug in a way that was not intended (e.g. crushing pills into powder form to increase absorption of active compounds). The rate of prescription analgesic misuse has quickly superseded illegal drug use in the United States. The National Institute of Drug Abuse reports that 7 million people were consuming prescription analgesics for nonmedical use in 2010. Among 12th graders, nonmedical prescription drug use is now second only to cannabis (PDMP Center of Excellence. 2010–2013.) it has been said that "Nearly 1 in 12 high school seniors reported nonmedical use of Vicodin; 1 in 20 reported such use of OxyContin (NIDA, December 2011.). Both of these drugs contain opioids.

It can also be applied when an individual continues to consume prescription painkiller when the original medically diagnosed condition has subsided. Furthermore, it can also be applied when an individual who is prescribed painkillers consumes more than the recommended daily allowance (RDA) and/or for longer than the prescribing period.

Drug *Dependence*, unlike addiction and abuse, pertains to the individual being dependent, or reliant, upon a drug to perform normal physiological functioning (Praveen et al., 2012). Dependence is unmasked by blocking access to drug consumption, which results in withdrawal symptomatology, a cardinal feature of dependence (Malenka et al., 2009). All drugs, including opiate painkillers, yield their own characteristic withdrawal symptoms when consumption is abruptly halted. Withdrawal symptoms for opiates are typified by visceral and physiological maladies, e.g. irregular heart rhythm, diarrhea and nausea. Psychological maladies would include, but are not limited to, anxiety, anger, depression, negative thinking patterns and paranoia.

The DSM-V clinical guidelines (American Psychiatric Association. Diagnostic and statistical manual of mental disorders - 5th ed., 2013) have combined substance abuse and substance dependence to form the term Substance Use Disorder. Each drug (excluding caffeine) has its own section in the manual. Opioid dependence is now defined by meeting at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.

5. Recurrent opioid use resulting in a failure to fulfil major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of an opioid.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal).
12. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

The criteria (A and B) for opioid withdrawal set out in the DSM-V is as follows:

A. Presence of either of the following:

1. Cessation of (or reduction in) opioid use that has been heavy and prolonged (i.e., several weeks or longer).
2. Administration of an opioid antagonist after a period of opioid use.

B. Three (or more) of the following developing within minutes to several days after Criterion A:

1. Dysphoric mood.
2. Nausea or vomiting.
3. Muscle aches.
4. Lacrimation or rhinorrhea.
5. Pupillary dilation, piloerection, or sweating.
6. Diarrhea.

7. Yawning.
8. Fever.
9. Insomnia.

Substance dependence can often be stated as an adaptive state accompanying a withdrawal syndrome upon cessation of repeated exposure to a stimulus (e.g., drug consumption).

Both addiction and psychological dependence occur via a form of operant condition known as psychological reinforcement (Olsen, 2011) however they occur through different forms of reinforcement whereby addiction is mediated through positive reinforcement and psychological dependence is mediated by negative reinforcement i.e. avoidance of negative withdrawal symptoms (Nestler, 2013). Painkillers themselves, increase the frequency of neuronal firing of dopaminergic neurons. The increased frequency of action potentials results in greater release of DA into the synaptic cleft. Thus, increasing the effects of DA when the neurotransmitter binds to receptors in the post-synaptic neuron. The painkiller consumer experiences the enhanced DA activity as positive affect, relief from pain and a heightened sense of euphoria. When the pharmacological action terminates (i.e., the opiates are eliminated from the nervous system), the painkiller consumer is likely to develop elevated motivation to repeat this experience and with regular and repeated exposure to a drug related stimulus comes psychological dependence (Hanson et al., 2011; Robinson & Berridge, 1993; Berridge & Robinson, 1998).

1.2.3. Psychological Dependence and Physical Dependence

Many substances are known to generate psychological dependence without generating an exceptionally powerful motivation to circumvent abstinence and vice – versa (Hanson et al., 2011). Caffeine offers the allure of achieving a stimulating consequence that involves general arousal supplemented with slight boost in positive mood. As the ardent coffee drinker normally chooses not to forego their ritualistic activities with caffeine, many consciously desist in situations where the cost might be too high or when access is denied. The resultant abstinence has both psychological (lowered mood) and physical (e.g., mild headache) withdrawal symptoms, however the motivation to subside this phase is significantly less than the intensity manifested by highly addictive drugs such as nicotine (Piasecki et al., 1997), methamphetamine

(Lende et al., 2007) and opiates (Van Ree, 1999). It is also well established that physical dependence often manifests exclusive of addiction, as with SSRIs (Selective Serotonin Reuptake Inhibitors; Senay et al., 2003) and addiction can arise exclusive of significant physical dependence (e.g., marijuana).

In a similar vein, psychological dependence is known to arise exclusive of addiction (e.g., caffeine), however it remains to be elucidated as to whether addiction ever occurs exclusive of psychological dependence (West & Brown, 2013). Naturally substance abuse may or may not be supplemented by addiction and substance dependence. In addition, there exists persuasive data that physical dependence is not the prime cause of addiction although it can be a significant contributor towards a general motivation for sustained substance use (Bozarth, 1989, 1990,1994).

Many factors influence initial drug *use*. Personality, peer pressure, stress (physical, physiological and psychological) all contribute to the early stages of substance abuse (Fig. 3). These factors become less important as substance use continues and the individual frequently experiences the potent pharmacological effects of the drug. When the pharmacological action of a drug dominates the individual's behaviour and the normal psychological and social control of behaviour is no longer effective, the addiction is fully developed. This "loss of control" is a common feature of drug addiction and reflects its devastating nature. Furthermore, certain susceptible individuals may become addicted to their pain-relief medication. For these reasons the psychological risk factors need to be explored.

To summate thus far, *drug addiction* refers to the motivational intensity of substance use; *drug abuse* refers to the consumption of a substance without precise orientation to motivational intensity; *drug misuse* refers to drug consumption in ways other than originally intended; and *drug dependence* refers to the necessity of using a substance to sustain usual psychological and/or physiological functioning without allusion to the motivational intensity of the substance use or if such activities go against societal norms. These four terms have specific and different definitions although there are many apparent scenarios whereby all three apply to a particular substance-use predicament such that one may be dependent upon a drug which they abuse because they are addicted and so all three can loosely be classified under the umbrella term of *aberrant substance use* (West & Brown, 2013). The graded severity of psychological dependence to opiates can be captured using self-report measures such as the Leeds Dependence Questionnaire (Raistrick et al., 1994).

1.2.4. Theories of Substance Dependence

The conceptualisation, knowledge and resulting theories on substance dependence have witnessed a swift evolution. Irrespective of this, an exact and universally accepted definition of the disorder remains unfinished work. Prior work attempted to include both tolerance and withdrawal as hallmarks of drug dependence (Kalant, 1987) and focused heavily on physical aspects of dependence. However, tolerance and withdrawal are well established to occur irrespective of presenting with typical addictive behaviours (O'Brien & Volkow, 2006), which has led to redefining the concept with the inclusion of psychological and behavioural aspects of drug dependence. Behaviours associated with dependence usually involve compulsive patterns of drug-seeking and drug consuming behaviours despite the user having knowledge of impending negative outcomes (Robinson & Berridge, 2003; West, 2006). It is imperative to note that casual drug use does not always necessarily escalate to an addicted state. Dependence to drugs manifests after a convergence of interactions, which include the drugs pharmacological effects, social cues, environmental cues and neurobiological entities (Meaney et al., 2002).

1.2.4.1. Pleasure Seeking Theory of Substance Dependence

Previous theoretical accounts of addiction concentrated on the desires to experience a positive affective state that results with drug consumption as the major process underlying addiction (Markou et al., 1993). The characteristic property of addictive drugs to yield euphoric sensations via activation of neural reward pathways has been central to the majority of popular theories and research in an attempt to further comprehend addiction. The most commonly abused drugs such as alcohol, cocaine, opioids, nicotine, marijuana and amphetamine have specific initial targets, they all have a shared ability to activate and augment extracellular concentrations of DA in the nucleus accumbens (NAc) and related regions of the mesolimibic-mesocortical DA pathway. This particular pathway is believed to be critical for acute reinforcing actions (Robbins and Everitt, 1996; Nestler, 2005). It has been contended that experiencing the rewarding properties of a drug provides an impetus for repeated use of the addictive drug (Di Chiara & Imperato, 1988a; 1998b; Di Chiara et al., 2004). Although it seems plausible to suggest that initial drug use may be associated with euphoric and gratifying effects, and that in some cases addicted users abuse drugs exclusively to attain the positive effects, the theory does not justify for the persistence of drug abuse when the pleasurable effects are minimal or even absent e.g. when tolerance builds from repetitive use of alcohol, cocaine or heroin (Lamb et al., 1991; Robinson and Berridge, 1993).

Successive theories have rather focused on “avoidance of aversive withdrawal symptoms” in an effort to comprehend and include the behavioural and neurobiological facets concerning drug dependence and addiction. Termination of drug use after continued use results in withdrawal symptomatology. These symptoms are characteristics of the drug consumed and can be both physical and psychological (Hughes et al., 1984; 1991). Prolonged drug consumption leads to an array of neuroadaptations within the DA nexus as an attempt to maintain a homeostatic environment due to hyperactivation caused by drug use (Koob & Le Moal, 2001). Hypoactivation within the DA is also well known (Dackis & O'Brien 2005) and is thought to be tied to the experience of withdrawal (Altman et al., 1996). As withdrawal symptoms are usually negative, their avoidance is thought to be a major incentive to continue drug seeking and drug consumption. However, this account of addiction does not fully explain relapse which can occur for months or years after cessation and even when all physical symptoms have become extinct (Robinson & Berridge, 1993).

1.2.4.2. Neurobiological Theories of Substance Dependence

The rise in researchers adopting a neurobiological and psychological perspective has been the result of previous theories not being able to fully account for the entire complexity of addiction. The incentive-sensitisation theory (Robinson & Berridge, 1993) aims to address some of this. A major proponent of the theory is that the DA and NAc neural systems become sensitised upon chronic drug use. The consequence is an increased firing rate of neurons and subsequent release of neurotransmitter substances when the drug is consumed as well as when drug related stimuli are presented (Robinson & Berridge, 2003). These systems are not analogous to systems that produce feelings of pleasure and withdrawal but are said to mediate the incentive salience or the "wanting" of reward (Robinson & Berridge, 2000). Upon repeated drug consumption, the incentive value of the drug becomes associated with drug related cues/stimuli making them progressively more "wanted". This in turn leads to powerful cravings and eventually compulsive drug seeking and drug consuming behaviours. The resulting neuroplasticity that takes place during this process, has been shown to remain resolute long after cessation of drug consumption in both animal and human studies (Strakowski et al., 1996; Castner & Goldman-Rakic 1999). The perpetual sensitization makes previously dependent users vulnerable to relapse at any time after drug consumption has ceased (Robinson & Berridge, 2000; 2003). Although the theory stipulates a theoretical explanation for compulsive drug use, craving and relapse observed in opiate use disorders, it does not fully account for loss of control over behaviours which are often seen within this unique populace (Goldstein & Volkow, 2002). Such behaviours include failure to remain abstinent despite severe negative consequences (e.g. injecting risks). The inability to accurately choose between small rewards given immediately (injecting Heroin) and large rewards given later (good health) is a facet of impulsivity and an important concept related to addiction as we shall see in section 1.3 (See Fig. 4).

1.2.4.3. Cognitive Theories of Substance Dependence

Cognitive theories on addiction take impulsivity into account by attempting to explain drug dependence in relation to self-regulation. Unlike impulsivity, self-regulation is regarded as taking "*planful action designed to change the course of one's behavior*" (Miller & Brown, 1991), the "executive (i.e. non-automatic) capacity to plan, guide and monitor one's behavior flexibly, according to changing circumstances (Diaz & Fruhauf, 1991). Self-regulation requires planning and accommodating social and physical factors in addition to one's goals and then acting accordingly. Substance dependence is viewed as diminished self-regulation and a consequence of excessive reliance on external sources (e.g. drugs) in order to maintain psychological and physical stability. More importantly, we see that self-regulation is almost a polar opposite of impulsivity.

1.2.4.4. Personality Theories of Substance Dependence

Another group of theorists on addiction argue that certain individuals are more prone to developing a substance use disorder through a so-called "addictive personality". Hans Eysenck discusses this in the *psychological resource model* (Eysenck, 1997). Eysenck presents a model containing three dimensions of personality: P (psychoticism), N (neuroticism) and E (Extraversion) (Eysenck & Eysenck, 1985). The dimension of P is described as a propensity for functional psychosis that lies within a spectrum ranging from "altruistic" to "schizophrenic" and some traits of this personality type include egocentricity, aggression and impulsivity. The dimension of N equates to a propensity for emotional dysregulation and traits include moodiness, anxiety and irritability. Studies have shown that the association between extraversion and drug dependence to be inconsistent and unreliable, however numerous studies have uncovered a convincing association between drug dependence and high scores on N and P (Francis, 1996). Results from these studies suggest that individuals prone to negative affect (high N scores) and/or those who are more aggressive and impulsive (high P scores) are more likely to have problems with substance use. As these are correlational studies it becomes challenging to ascertain the nature of the relationship between drug dependence and personality types, as it is possible that drug consumption itself may have led to impulsive tendencies and irritable mood. Nonetheless there exists a relationship between drug dependence, impulsivity and negative affect.

Supporters of the Rational Choice Theory to explain addiction attempt to explain why individuals participate in self-destructive behaviours (Elster & Skog, 1999). A core proponent of drug dependence is that individuals have impaired control over drug consumption. The American Psychiatric Association (2013) exemplify this as an individual who consumes opiates for longer than the prescribed period or someone who consumes opiates in quantities greater than the recommended daily allowance (RDA). Depending on the context, this difficulty may be enlarged – for example a former heroin addict who has not injected for some time may walk past an area where he/she used to purchase heroin and decide to purchase heroin. Some would argue that this embodies "weakness of will" or that drug addiction is simply acting out "against one's own better judgment" (Davidson, 1985; Pears, 1984). This group of theorist's states drug dependent individuals have at least two choices, both of which are evaluated in regard to their consequences in the future. Individuals realise that one option is superior yet choose the other option. For example, a painkiller addict may have decided to stop consumption and yet accept painkillers from someone, despite knowing at the time that they should not. The difficulty with this stance is knowing whether the individual had knowledge *at the time of acceptance* that choosing to consume the painkiller(s) was the least favored option. Opposing this view, some theorists claim that drug dependent individuals do make rational choices regarding their decision to continue drug use. These theories attempt to show rational individuals become knowingly trapped in a consumption pattern and once they realise that their current lifestyle is actually suboptimal, still continue to act in the same way (Skog, 1999). Many have tried to explain this paradox and have focused on the drug-dependent individuals' inability to consider the immediate rewards associated with drug consumption, weighed against the long-term benefits of abstinence. The term "cognitive myopia" has often been applied to such individuals (Hernstein & Prelec, 1992). Other views on the matter suggest that although individuals can consider a range of future benefits. Present and future benefits have different weightings, with greater weight attached to rewards dispensed in the present moment (Ainslie, 1992; Becker & Murphy, 1988). The preference for the smaller-but-sooner (S-S) reward is said to be the impulsive choice and is known as Delay Discounting (DD; Cherek et al., 1994). The rate at which rewards are discounted and the general preference of an individual for S-S rewards or larger-but-later (L-L) rewards can be empirically tested using the DD behavioral measure. Many studies have described individuals with a strong preference for S-S rewards to be significantly more susceptible to drug dependence than those with a strong preference for L-L rewards (Ohmura et al., 2005; Odum et al., 2006; Petry et al., 1998; 1999; 2003) and contemporary research has begun to investigate impulsivity in an effort to further elucidate the role of DD in opioid dependence (Madden et al., 1997; 1999; Odum et al., 2000).

The prefrontal cortex (PFC) is regarded as the seat of impulsivity and a large body of evidence from neuroimaging studies have shown long term drug abusers to have atypical structure and function within the PFC, specifically the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC; Franklin et al., 2002; Goldstein & Volkow, 2002; Rose et al., 2003). It has been declared that dysfunctional activity within the PFC is strongly correlated with drug abuse and subsequent loss of control when drug initiation and maintenance of addiction is concerned (Jentsh & Taylor 1999, Ersche et al., 2010). This trio of neural regions (PFC, OFC and ACC) are well established in regulating decision-making processes, regulating affective behavior and gauging reward value of stimuli. The ACC is known to exert inhibitory control over behaviour and is unique in that it acts as an emotional switch as well as a logic gate (Aron et al., 2004). This suggests that certain individuals could have a greater propensity to seek and consume painkillers depending on their current emotional state (Francis, 1996) particularly if one scores highly on neuroticism (emotional dysregulation) and psychoticism (aggression, impulsive). Contributing research has shown addiction to be a state of impaired response inhibition and salience attribution (I-RISA). The proposed I-RISA model (Goldstein & Volkow, 2002) assumes that addiction is related to elevated salience of drug rewards and associated stimuli, diminished salience of alternative natural reinforcers and *debilitated inhibitory control* towards responding to drug related stimuli. Thus, neurobiological data complements the theories above in ascribing impulsivity and negative affect as risk factors for drug dependence.

In a similar vein, researchers have tried to describe the essence of addiction as being “compulsive”. The premise being that loss of control over drug consumption and persistent drug seeking behaviours are mediated by an impaired PFC which gives rise to dysfunctional inhibitory behaviours (Lubman et al., 2004). There remains one aspect yet to be accounted for, the question of whether an atypical PFC network truly equates to a vulnerability marker for the development of addiction, or whether it is a consequence of drug consumption (Olmstead 2006). Regardless of this, the successive work of researchers has managed to widen our knowledge base by including impulsivity and negative affect as risk factors for addiction. This has spurred an increase in attention from researchers worldwide to study and further understand this multifaceted construct and its relationship with substance dependence. What also remains to be discovered is what role, if any; impulsivity plays in the dependence to opioid analgesics.

1.3. Impulsivity: A Multidimensional Concept

Impulsivity can be observed throughout the life stages. Children may exhibit this in the form of taking a toy from a sibling to satisfy their immediate desire foregoing the punishing consequence of a nearby parent. Adolescents show impulsive tendencies, perhaps through the self- gratification of spending student loan funds on anything but their tuition fees. Adults too show impulsive tendencies. The prospect of mounting credit card debts and high-interest loans are an all too familiar scenario for the unfortunate many. In this predicament, impulsivity is regarded as decisions which are performed quickly with little thought on an optimal and rational strategy for future consequences.

Impulsivity has a significant role in "adding colour to everyday life" (Evenden, 1998a; 1999a;). Although reaching a consensual definition of impulsivity has been cumbersome, we witness it in everyday day life in the form of purchasing things on a whim or consuming that glazed doughnut left in the staff canteen. Impulsivity is a multifaceted psychological construct commonly defined in terms of deficient inhibition of behaviours and impaired decision-making. The definition of impulsivity is continually widening as new research is brought to light. Impulsivity includes engaging in behaviours without sufficient foresight and prematurely responding to stimuli which may be detrimental or result in adverse consequences (Moeller et al., 2001b; 2002; 2007). Impulsivity includes cognitive and behavioral portions of the initiation of behaviour that reveals themselves in various environments. The construct has been defined in a plethora of ways, and many hold the view that it encompasses a variety of factors (Barratt, 1994; Evenden, 1999b).

Accepted uses of the term allude to (1) disinhibited rapid-response impulsivity (i.e., responding without sufficiently assessing the situation and/or context) (Swann, et al., 2001; 2004); (2) responding without consideration of, or regard for, consequences (Sims, 1988);(3) having an inability to delay reward (Monterosso & Ainslie, 1999); (4) the inability to sustain attention (Dickman, 1993); (5) as part of the personality dimension of extraversion, (Eysenck, 1983); (6) a tendency to engage in risky behaviours (Eysenck, 1993), and (7) the seeking of novel sensations (Zuckerman et al., 1978). Researchers have gone as far as to describe impulsivity as an act of behaviour which is “spur of the moment” and having inadequate attention (Barrett & Patton 1983), the tendency to partake in hasty processing of information which can be predisposed to error (Dickman, 1990) and a strong inclination towards immediate rewards over delayed rewards (Logue et al., 1988). As we piece together this myriad of definitions it becomes evident that impulsivity is more a multifaceted concept than a singular stand-alone behaviour. Impulsive behaviour is a manifestation of various interacting occurrences that are facilitated by distinct neurobiological apparatus (Hollander & Stein 1995).

In an effort to integrate the range of characteristics of impulsivity within its definition, Moeller et al., (2001b) view impulsivity as "a predisposition toward rapid, unplanned reactions to internal or external stimuli without regard to the negative consequences of these reactions to the impulsive individual or to others". Impulsivity has been seen both in normal personality traits and also within dysfunctional behaviours (Stein et al., 1993). These include, but are not limited to, conduct disorder and its adult variant antisocial personality disorder, borderline personality disorder (Barratt et al., 1997; Casillas & Clark, 2002), mania (Swann et al., 2001) and attention deficit/hyperactivity disorder (Solanto et al., 2001; Salbach et al., 2002). A rich body of literature has shown that elevated levels of impulsivity are associated with drug dependence (Allen et al., 1998; Krishnan-Sarin et al., 2007; Jentsch & Taylor, 1999; Soloff, et al., 2000) and opioid use disorder (Lejuez et al., 2005). Data has also revealed self-reported impulsivity to be higher in those with substance abuse disorders in comparison to controls (Soloff et al., 2000). Disorders such as kleptomania, pyromania and pathological gambling have been classified within the DSM-V as 'impulsive control disorders'. Elevated levels of impulsivity in early life has some predictive powers towards early onset substance abuse disorders in later life (Clark et al., 1999; Cloninger et al., 1988; Robins & Price, 1991).

Self-report measures have long been favored as a tool to capture the essence of impulsive personality. Measures such as the Barrat Impulsivity Scale (Patton et al., 1995), the Eysenck Personality Questionnaire (Eysenck & Eysenck, 1978) and more recently the UPPS-P (Negative Urgency, Lack of Premeditation, Lack of Perseverance, Sensation Seeking, Positive Urgency; Whitesyde & Lynham, 2006). Such questionnaires ask participants to report on their impulsive decision-making and the way they plan a task. A combination of attention failure (Robbins, 2002), a markedly reduced ability to inhibit a response (Winstanley et al., 2005) and reduced ability to gauge probable negative long-term consequences (Ainslie, 1975) are capture by self-report measures and have thus allowed health care professionals to demarcate several impulse control disorders based on failure to control one's impulsive tendencies. These include, but are not limited to, kleptomania, pathological gambling, trichotillomania and substance abuse; American Psychiatric Association, 2000). Many of the hallmarks of impulsivity have been shown to precede and predict drug consumption in rodents (Dalley et al., 2007). A plethora of studies show that inability to delay reward is strongly associated with increased risk for substance misuse and abuse (Petry, 2001a; Allen et al., 1998; Jentsch & Taylor, 1999; Swann et al., 2004). It has too been shown that the rate at which delayed values are devalued are predictive of treatment outcomes in rehabilitative settings (Yoon et al., 2007). It has however, been hypothesised by other authors that the devaluation of delayed outcomes are positively associated with variables such as life expectancy and socioeconomic status (Wailson & Daly, 1997). In such circumstances one may adhere to the "live for the moment" attitude as the optimal strategy for maximal gains. Behavioural researchers have highlighted little evidence of reinforcement contingencies that may imbue a type of delay tolerance i.e. an ability to wait for a reward (Mazur & Logue, 1978). This calls for the urgent need of a more thorough understanding of impulsivity, specific conceptualisation of impulsivity and the need for an evidence-based therapeutic intervention to reduce impulsivity.

It is evident that "impulsivity" encompasses a broad spectrum of behaviours that likely amalgamate various neural architecture and thus would be susceptible to various manipulations from various drugs of abuse. Despite this knowledge, it is yet to be established which facets of impulsivity play the most prominent role towards the path of SUD. Impulsive choice (Fig. 4) has been shown to correlate robustly with the wide range of SUD (Bickel et al., 2006; Kirby et al., 1999; Madden et al., 1997 & 1999; Odum & Bauman, 2010; Petry & Cassarella, 1999; Reynolds et al., 2004; Richards et al., 1999; Vuchinich & Simpson, 1998, Swann et al., 2002) but has not been applied towards the investigation of addiction to painkillers.

When considering impulsive decision making from an evolutionary perspective, it would appear counterproductive and against the grain of natural selection to choose the S-S reward. This is because choosing a smaller reward in lieu of a larger reward would not result in maximising gains. However, impulsivity has remained a key determinant of decision making throughout the animal kingdom as organisms that opts for a smaller but immediate food item, mate or hiding place in favor of a superior but delayed alternative may realise that the superior food was consumed by a competitor, the mate was unavailable or the hiding place no longer available. To paint an overall picture, the only certain feature of an environment is uncertainty.

1.3.1. Substance Abuse and Impulsivity

Impulsivity is a hallmark risk factor for substance abuse disorders. According to the diagnostic criteria of the DSM-V (American Psychiatric Association, 2013) the disorder can be defined as a dysfunction of impulsive control. Substance abuse can be conceptualized as a problem of impulsivity in that firstly drug dependent individuals frequently display a failure in the ability to refrain from inappropriate drug seeking and taking behaviour, continuing to administer the drug despite repeated efforts to abstain. Furthermore, they display an incapacity to wait, a change in the perception of time, and predominately select the more immediate drug rewards or the relief of drug withdrawal over various pro-social, often larger delayed rewards associated with a drug free lifestyle (Madden et al., 1997).

A growing body of data shows that opiate addicts may be less compromised in general neuropsychological functioning than alcohol or stimulant abusers (Brand et al., 2008; Rogers & Robbins, 2001). However, aptitude on measures of cognitive impulsivity is equally diminished amongst opiate users in contrast to other abusers of other drugs (Ersche et al., 2006; Verdejo-Garcia & Perez-Garcia, 2007). Data has been collated to show diminished response inhibition on the Stroop interference score (Mintzer & Stitzer, 2002; Verdejo-Garcia et al., 2007a), although a contemporary study in relatively pure heroin users did not support this view (Fishbein et al., 2007). On measures of cognitive impulsivity, opiate users showed reduced reflection and higher error rates (Clark et al., 2006; Lee & Pau, 2002), and impaired performance on measures of decision-making including the Iowa Gambling Test (IGT; Petry et al., 1998; Pirastu et al., 2006; Verdejo-Garcia et al., 2007b) and the Cambridge Gamble Task (Ersche et al., 2006).

Fishbein et al., (2007) performed neuropsychological tests within a group of relatively pure Russian heroin users. A battery of tests showed increased risk-taking (Cambridge Risk Task); deficits in executive function (Tower of London) and memory (Delayed Match to Sample, Paired Associates Learning). Characteristics of these heroin users was quantitatively analogous to the characteristics gathered from a sample relatively pure alcohol users. Heroin users also presented with robust effects on DD tasks. Of interest there was found to be a steeper discounting of both suppositional and real delayed monetary rewards (Bickel & Marsch, 2001; Kirby & Petry, 1994 & 2004; Kirby et al., 1999; Madden et al., 1999). This elevated discount rate has shown reasonable correlations with self-reported trait impulsivity (Kirby & Petry, 2004; Madden et al., 1997).

To exemplify, one study examining those who inject heroin found that those who were currently injecting had greater DD rates than former injectors (Bretteville-Jensen, 1999). Methadone use has been also been shown to impair response inhibition and decision-making (Ersche et al., 2006; Verdejo-Garcia et al., 2005). This would suggest that opiate-derived drugs and impulsivity have a strong synergistic relationship about one another. However, heroin-related deficits in cognitive inhibition seem to persist beyond the window of acute drug effects; i.e. at least 3 weeks of abstinence (Fishbein et al., 2007). Much of the literature has been unsuccessful in providing associations between dosage and/or duration of opiate use alongside measures of impulsivity (Clark et al., 2006; Rogers et al., 1999a; Kirby & Petry, 2004). Ecological validity of delay-discounting scores have been associated with manifestations in real-life risky choices such as needle sharing (Odum et al., 2000) and risky sexual behaviour (Lejuez et al., 2005). The rate of DD may be sensitive to current drug use status and the following studies will aim to include a drug-use history. The DD task has yet to be applied to those aberrantly using opiate-derived analgesics specifically OTC Painkillers and prescription painkillers.

The fact that impulsiveness is a prominent feature within substance abuse disorders has increasingly led research to focus on the possible role of the construct in the initiation, maintenance and relapse of the disorder. There are two broad approaches to human research exploring the relationship between impulsivity and substance abuse. They differ in techniques utilised to assess impulsivity using either (i) self-report personality questionnaires or (ii) behavioural state measures. The three studies in this piece of research will use both self-report measures and the Delay Discounting paradigm as a behavioural measure for impulsivity (Reynold et al., 2005). Delay discounting is the preference for a smaller-but-sooner (S-S) reward in lieu of a larger-but later (L-L) reward. This was exemplified by the child participants in the famous Stanford Marshmallow Study (Mischel, 1972) who opted to eat the marshmallow before the experimenter returned (S-S / impulsive preference). In this study, the experimenter would place a single marshmallow in front of a child and was instructed that they could eat the single marshmallow immediately if they wanted (S-S reward) or they could wait for the experimenter to return at a later point in time (approximately 15 minutes later), and if they did wait without consuming the first marshmallow then the child would be given two marshmallows (L-L reward). While it has been argued that the Marshmallow Study is a test of delayed gratification and not DD, there are many impulsivity/delay-related similarities between these measures, and the majority of researchers who publish within the relevant literatures treat the two procedures as though they are equivalent (Evenden & Ryan, 1996; Green, Fry, & Myerson, 1994; Johnson & Bickel, 2002; Mischel, Shoda, & Rodriguez, 1989; Schweitzer & Sulzer-Azaroff, 1995).

1.3.1.1. Quantifying Impulsivity

Facets of impulsivity can be quantified in a multitude of ways. Direct observation of naturally occurring behaviors in predefined scenarios is the most common method. In addition to this, questioning participants about their tendencies within specific situations further complements behavioral paradigms. The task of devising a laboratory task which correlates efficiently with what is deemed impulsive behavior in the natural environment has faced difficulties. The construction of such tasks would be highly relevant and useful towards a deeper comprehension of early-onset substance abuse. A task in which participants engage with to delineate impulsivity is a far more robust a measure as it does not rely on introspection or self-inquisition. Such behavioral measures permit the prospect to simultaneously gather neurophysiological, pharmacological and imaging assessments (e.g. functional magnetic resonance imaging), which in turn promote a deeper interpretation of the underlying neurobiological parameters of impulsivity.

In comparison to behavioral measures, impulsivity as quantified using self-report questionnaires highlights a propensity to performing a specific custom in different circumstances over time, such that it reveals impulsivity as a trait. Two of the most widely documented self-report questionnaires are the Eysenck Impulsiveness Scale (EIS; Eysenck, Easting, & Pearson, 1984) and the Barratt Impulsiveness Scale (BIS-11; Patton, Stanford, & Barratt, 1995). The former covers two factors: Impulsivity, which is supplementary to failure of considering consequences and lack of response inhibition, and Venturesomeness, which is more likened to risky behaviors or sensation seeking. Marsh et al have shown that women with higher scores on the Eysenck Impulsiveness Scale make more commission-errors (CE) on the Immediate Memory Task/Delayed Memory Task (IMT/DMT) than do women with lower scores (Marsh et al., 2002). In addition, impulsive CE on the IMT/DMT are associated with higher scores on the BIS-11 (Dougherty et al., 1999; Swann et al., 2002), however one study did not find a significant correlation in adolescents (Dougherty et al., 2003). Gauging impulsivity via self-report measures may be good for descriptive purposes but self-report measures but, as discussed below, are susceptible to false-positives. However, self-report measures are useful for screening or pre-selecting participants.

1.3.1.2. Impulsivity: Trait Approaches

To explore impulsiveness in drug dependent populations the self-report measures are most commonly used. These include the Barrat Impulsivity Scale (BIS), Eysenck Impulsivity Questionnaire (EIQ), and the Eysenck Impulsiveness-Venturesomeness-Empathy Questionnaire (EIVE), and the UPPS-P.

The BIS (Barratt, 1985) measures impulsive tendencies via three subscales:

1. Non-planning (lack of future orientation).
2. Cognitive impulsiveness (fleeting thought patterns and impatient

tendencies).

3. Motor impulsivity (acting with lack of foresight).

Researchers that have used this scale have highlighted that substance abusers have elevated scores when compared to matched controls (Patton, Stanford and Barratt,1995). A wide array in the substances of abuse also attest to this conclusion e.g. cocaine (Moeller et al., 2002; Coffey et al., 2003), opioids (Kirby et al., 1999), alcohol (Bjork et al., 2004) and nicotine (Mitchell, 1999). Data analysis has also revealed that higher scores correlate positively with greater severity of addiction. Skinner et al., (2004) showed that the more cigarettes an individual smoked on a daily basis, the greater their score on the BIS. Similar results were seen when examining the frequency of past alcohol consumption (Fishbein & Reuland, 1994), daily cocaine use (Moeller et al., 2001a) and scores on the addiction severity index in poly-substance abusers (Reilly et al., 2000).

The popularity of the BIS has also been shown to have predictive prowess when drug rehabilitation is of concern. Cigarette smokers with elevated scores have been shown to relapse faster than those with lower scores after a one-day smoking cessation intervention (Doran et al., 2004). Those dependent on cocaine show a similar pattern when a twelve-week treatment was implemented (Moeller et al., 2001a).

A well-documented feature of the BIS is its ability to distinguish between schizophrenic patients who live with or without a substance use disorder (Blanchard et al., 2001). Process addictions such as pathological gambling have shown higher scores when compared to non-abusing gamblers (Petry, 2001b).

An adapted subscale from the Eysenck Personality Questionnaire (Eysenck & Eysenck, 1978) known as the EIQ has shown elevated scores of trait impulsivity in substance abusers in comparison to matched controls (Golding and Cornish, 1987). Amongst dependent individuals consuming alcohol, cocaine and opiates higher scores were observed in comparison to matched controls (Madden et al., 1997; Conrod, Pihl, Stewart and Dongier, 2000; Petry, 2001a). The EIQ is also able to distinguish between smokers (Mitchell, 1999), non-smokers and ex-smokers (Bickel et al., 1999) on levels of impulsivity, with smokers being significantly more impulsive.

The IVE questionnaire (Eysenck's Impulsivity, Venturesomeness and Empathy Questionnaire; Eysenck & Eysenck, 1978) measures impulsive tendencies across a spectrum of three subscales: venturesomeness, impulsivity and empathy. The scale represents a trend amongst other scales in that it captures proclivity towards lack of foresight, rapid decision-making processes and motor impulsivity. Research utilising this scale has shown polydrug abusers are associated with greater scores in comparison to matched controls (Butler and Montgomery, 2004). Data obtained has painted a picture to show that the opioid dependent individuals show higher scores on the impulsivity scales when compared to matched controls (Kirby et al., 1999). The same results were seen when crack cocaine using individuals were used (Lejeuz et al., 2005). When *severity of substance use* was investigated, it was shown to correlate with the impulsivity score in those who consume MDMA (Parrot et al., 2000), caffeine (Jones & Lejuez, 2005) and methamphetamine (Simons et al., 2005).

An interesting finding from the use of the IVE is that it has shown an additive effect on impulsivity in those with existing psychopathologies such as pathological gambling (Petry, 2001b) and antisocial personality disorder (Petry, 2002). This additive effect was highlighted by a study showing women with comorbid-bulimia nervosa with alcohol dependence scored higher on scales of impulsivity than participants with bulimia but were not alcohol dependent (Kane et al., 2004). It is due to these findings that such populations are often excluded from studies so that data is not skewed.

The UPPS-P Impulsive Behavior Scale (Lynam et al., 2006; Whiteside & Lynam, 2001; 2003; 2005) is another widely used self-report measure to capture 5 facets of impulsivity. A plethora of evidence exists showing that UPPS-P scores are elevated in SUD populations in comparison to drug-naïve controls. These self-report measures evaluate a broad spectrum of dispositional features of the individual such as how the individual would typically behave in a specific circumstance, or to what degree the individual agrees or disagrees with specific statements.

The different dimensions of the UPPS-P have been meaningfully associated with several dysfunctional traits and psychopathological disorders. Negative urgency has in particular been associated with cigarette craving, severity of stimulant addiction, behavioural addiction symptoms (compulsive buying, pathological gambling, cyber-addiction), dimensional elevations on bulimic tendencies, risky sex, suicidal ideations and risk of intimate partner violence (Anestis et al., 2007; Billieux et al., 2007; 2010; 2012; Curcio et al., 2011, Deckman et al., 2011; Derefinkn et al., 2011; Klonsky et al., 2010; Verdejo-Garcia et al., 2007). Negative urgency, in combination with lack of premeditation, has also been associated with borderline and cocaine dependence diagnoses (Tragesser et al., 2009). Positive urgency has been associated with hazardous drinking, risky sex, recreational drug use and pathological gambling (Verdejo-Garcia et al., 2010; Zapolski et al., 2009). Lack of perseverance has been associated (in combination with urgency and lack of premeditation) with insomnia, intrusive thoughts proneness, ADHD, and weight fluctuations in eating disorders (Gay et al., 2011; Miller et al.,2010; Mobbs et al., 2008; Schmidt et al., 2010). Finally, sensation seeking has been specifically associated with drug and alcohol use, gambling, delinquent acts, instrumental aggression and antisocial traits (Smith et al., 2007; Whiteside & Lynam, 2003). A rationale for using the UPPS-P in studies 1-3 is given in section 2.2.

In order to provide a balanced critique, it should be stated that there are some limitations within the framework of SUD populations. First, most self-report measures do not clearly differentiate between existing characteristics of the individual that may have become permanent features since inception of drug-use from those characteristics that preceded onset of drug-use. One would usually assume that an elevated score on any of the self-report measures is indicative of a stable characteristic of the individual, the methodology is inept in highlighting this effect with any empiricism. Second, self-report measures are subject to subterfuge via biases in social desirability and demand characteristics and that may, unsurprisingly, differ between control and SUD samples. Third, impulsivity may directly impede completion of the questionnaires themselves, such that impulsive individuals may give less attention and deliberation to questions than non-impulsive individuals. Fourth, introspective ratings presume that individuals have adequate insight to rate their personality with precision.

The relationship between opiate use and impulsivity has amassed much attention in recent years (Ersche et al., 2006; Verdejo-Garcia & Perez-Garcia, 2007). On self-report measures, heroin users have shown increased impulsivity scores on both the BIS-11 and Eysenck scales (Kirby et al., 1999; Madden et al., 1997). The UPPS-P scale has shown heightened impulsivity in cocaine users, cigarette smokers and in pathological gamblers (Albein-Urios et al., 2011; Billieux et al., 2007). Heroin abusers also score lower on personality measures of future time perspective, suggesting diminished ability to plan ahead or a greater focus on immediate as compared to delayed rewards (Petry et al., 1998).

A common conclusion drawn from self-report measures of impulsivity are that scores from substance abusers are higher than those with matched controls. Although useful indicators of cognitive processes, self-report questionnaires are limited by the subjects' insight and view of the self (Moeller et al., 2001a). Individuals may also not want to disclose personal information about themselves and thus may provide an answer which they deem to be more socially acceptable. Ergo, self-report measures are subject to subterfuge. Such studies are therefore not ripe enough to *fully* explain the relationship between impulsivity and substance dependence and so should be supplemented with behavioural measures of impulsivity (i.e. Delay Discounting). The measurements obtained are of trait impulsivity, which most agree to be a stable trait. It is then possible that elevated scores observed were present throughout the individual's life and thus provide a greater propensity for an individual to engage in drug consumption which inevitably leads to drug dependence. It could also be viewed that impulsivity is not the cause; but the consequence of drug consumption in that chronic consumption could lead to structural changes within neural architecture responsible for impulsive tendencies. Supporting evidence for the former was shown by Allen et al., (1998) who described a continued elevation of trait impulsivity following cessation of abuse in previous substance abusers.

1.3.1.3. Impulsivity: Behavioural Approaches

Behavioural measures of impulsivity aim to delineate two portions of the impulsive construct with the aim of quantifying individual self-governing components and provide a distinct functional characterisation of the construct (White et al., 1994; Kindlon et al., 1995; Ho et al., 1999; McDonald et al., 2003; Reynolds et al., 2006; Winstanley et al., 2005; Dom et al., 2007).

One arm of the researcher's arsenal is to conduct laboratory measures with the aim of capturing impulsivity as a failure of inhibitory control. The go no-go paradigm is a well-researched task that captures this form of impulsivity (Gomez et al., 2007). Another established component to quantify impulsive behaviour is to capture the preference for a S-S reward over a L-L reward, even in a predicament where the immediate reward is less valuable than that of the delayed reward. A strong preference for S-S being the impulsive choice. The DD task aims to capture participants preferences for either S-S or L-L rewards (Cherek et al., 1997).

1.3.1.3.1. Behavioral measures of impulsive choice

The limitations with self-report measures have spawned great interest in developing objective measures of impulsivity using behavioral measures that quantify impulsivity in terms of reaction times, accuracy and the ability to make beneficial choice (Dougherty et al., 2003, 2005; Evenden, 1999b; Moeller et al., 2001a; 2001b; Reynolds, 2006).

Figure 4 Fractions of impulsivity and their respective behavioural measures

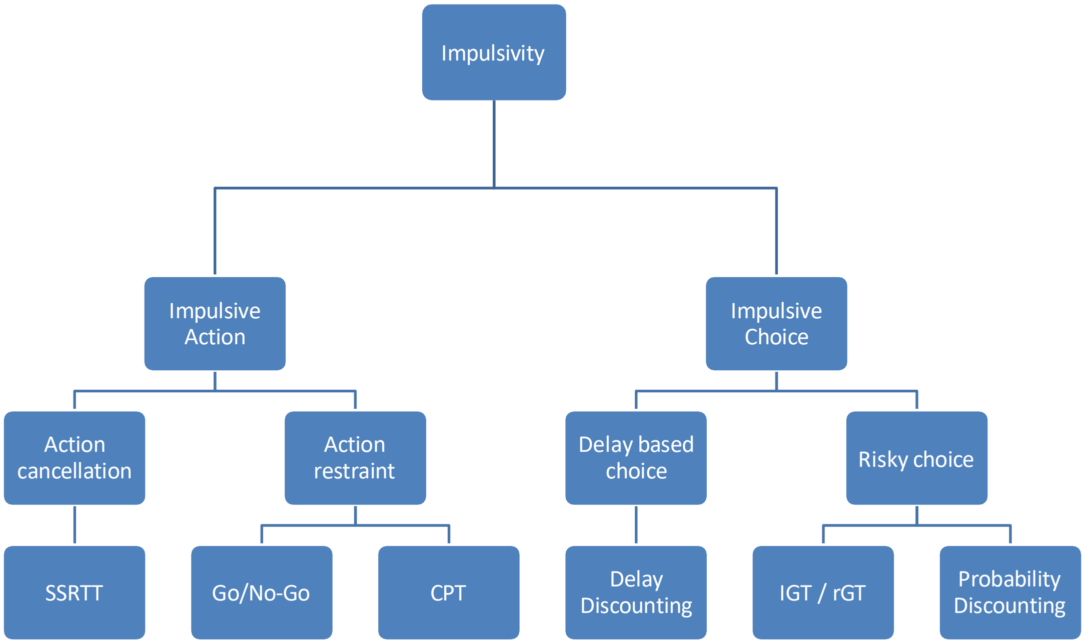


Figure 4 depicts the two most established categories of impulsivity upon which behavioral measures can be applied to quantify impulsivity. Impulsive Action (Motor Impulsivity): contingent upon the suppression of an automatic (pre-potent) response. Examples include but not limited to the Stop Signal Reaction Time Test (SSRTT), the go/No-go test, the Stroop test, and measures of commission errors on Continuous Performance Tests (CPT) (Logan et al., 1997). Impulsive Choice (Cognitive Impulsivity), an expansive term referring to impulsive decision-making. Elevated levels of cognitive impulsivity have been shown to lead to aberrant decision-making on delay-discounting tasks (Bechara, 2003; Knoch & Fehr, 2008).

Another stream of impulsive choices includes those choices contingent on risk. Cardinal measures include the Iowa Gambling Task (IGT) (Bechara et al., 1994), the Risky Gains Procedure (RGP; Paulus et al., 2003), the Cambridge Gamble Task (CGT) and Risky Gains Task (RGT) (Rogers et al., 1999a; 1999b). Here impulsivity is be quantified by opting for a highly rewarding preference irrespective of obvious potential for detrimental consequences – a hallmark of substance misuse and abuse.

Although scores on these tasks may not specify impulsive tendencies (Busemeyer & Stout, 2002), there are significant links between the literature on impulsivity and decision-making within the substance-use dependent (SUD) population.

1.3.1.3.2. Behavioural Measures of Inhibitory Control

Logan et al., (1997) describe behavioural inhibition to be an inability to appropriately withhold or terminate thoughts and actions. As described above, this is a core component of addictive behaviours and is observed when there is a loss of control over compulsions towards drug seeking and drug consuming behaviours (Jentsch & Taylor, 1999; Goldstein & Volkow, 2002). The resulting predicament faced by individuals who are unable to control such behaviours is a continual failure to abstain from drug consumption.

The most widely documented behaviour task used to quantify inhibitory control is the go/no-go paradigm in which subjects are required to inhibit pre-potent responses (Newman & Kosson, 1986). Participants learn via trial and error or respond as quickly as possible to a discriminative stimulus e.g. a particular letter on the screen, a light or sound tone. An appropriate response to a "Go" signal is usually rewarded and is often a small monetary reward, points or a social reward. When animal subjects are used, food is usually given to fasted animals. At specific time points, participants are required to inhibit a response when the "Go" signal is not shown and instead a "No-go" signal is displayed. When human subjects are utilised, dependent on the variant of the paradigm being used, an incorrect response during a "no-go" being displayed results in either no reinforcement or a penalty e.g. loss or reduction of reward.

Comparably, both asymmetrical and symmetrically reinforced go/no-go paradigms have been developed with the use of animals. In the latter of the models, successful inhibition of responding, in addition to correct go responding during No-go trials, is also reinforced (e. g. Harrison et al., 1999). Across all variants of the task that have been developed, inappropriately responding during the absence of a 'Go signal', is argued to be a valid index of degree of impulsiveness (Newman & Kosson, 1986). These inappropriate responses are commonly known as errors of commission or false alarms.

Another well-researched methodology towards elucidating behavioural inhibition is the stop signal task (SST) (Logan et al., 1997). The SST is shaped from the theory that behaviour inhibition is a result of two systems i.e. activation and inhibition of behaviour (Fowles, 1987). The theory posits that hyper-stimulation of the activation system in conjunction with a hypo-stimulation of the inhibitory system results in loss of control over behaviour. The SST captures inhibitory control by assessing the overall effect of the activational and inhibitory systems via measurements of the individual's aptitude for inhibiting a pre-potent motoric reaction.

Participants are instructed to respond to a go signal as quickly as possible however, a predetermined number of trials of the go signals are preceded by a stop signal. This can be in the form of a light or a tone. When the stop signal is presented, the participant is instructed to inhibit any previously initiated response. The go signal is dependably presented across the majority of trials, this produces a pre-potency to respond. A delay between the two signals differs between tasks (10-300ms). The requisite for a lengthened dormancy between the go and no-go signal in order to efficiently inhibit a response correlates significantly with the frequency of failures to suppress a response and so consequently is related with weak inhibitory control (Logan et al., 1997). Lengthier reaction times to inhibit responses are thought to be symptomatic of a debilitated inhibitory system.

The SST can be applied to non-human subjects whereby test subjects are expected to respond to a stimulus (auditory or visual). Analogous to the human version, a no-go signal is delivered at random intervals after the go signal has been presented. As with human test subjects, impulsivity is measured as the time needed to inhibit a response. The longer the reaction time the greater the level of impulsivity (Eagle & Robbins, 2003).

The continuous performance task (CPT) is yet another behavioural measure that is chiefly used in human test subjects but has been applied to animal models and it is known as the five-choice serial reaction time task (5CSRTT; Carli et al., 1983). Although this measure is used to assay impulsiveness, it has been argued that the CPT is chiefly a measure of sustained attention. Participants are instructed to respond as quickly as possible to a series of rapidly presented targets (<500ms) and to briefly presented targets (Rosvold et al., 1956; Dougherty et al., 1999). As with the SST, a response is deemed to be impulsive when there is a failure to suppress response to a non-specified target and it is known as a false alarm. To be rewarded, animals are to respond correctly by nose poking in one of five apertures when an illuminated signal is presented above the aperture. Impulsivity is said to be observed by the number of times an animal performs a premature or inappropriate nose poke into an aperture. Inappropriate responses, analogous to false alarms, are usually met with a punishment, usually in the form of a time out period the 5CSRTT captures impulsiveness and is also a measure of sustained and divided attention (Robbins, 2002).

Another behavioural measure often used in animal test subjects is the operant model known as differential reinforcement of low rate procedure (DRL) which is used to gauge the level of inhibitory responding (van den Broek et al., 1987). Test subjects are rewarded when the required behaviour occurs during a fixed time interval e.g. in a DRL 60”, reinforcement is dependent on a withholding a response for a minimum of 60 seconds. Should an impulsive untimely response occur, no reward is given, and a time out period occurs. The paradigm is not without reproach as many contend several factors, other than inhibitory control, can sway outcomes e.g. motor performance (Evenden, 1998b) and timing ability (Wiley et al., 2000).

1.3.1.3.3. The Delay Discounting Paradigm

Preference for S-S rewards over L-L rewards is argued to be a robust behavioural index of impulsivity (Rachlin & Green, 1972; Ainslie, 1974). In contrast 'self-control' is regarded as the opposite preference where the ability to wait for the L-L reward is demonstrated by an individual. From this perspective impulsive behaviour is readily observed in drug abusers in that they frequently select the immediate reinforcing effects of drugs (S-S reward) over the long term social and health benefits associated with a drug free life style such as a career or family life (L-L rewards; Madden et al., 1997). These findings are amenable to quantification, replication and are generalisable.

The application of the DD task has been administered to various populations suffering SUD whereby a significantly extensive body of evidence shows that users of opioids, alcohol, cocaine, methamphetamine, and tobacco discount by delay significantly greater than matched non-using controls (Bickel et al., 2006; Green & Myerson, 2004; Reynolds, 2006; Yi et al., 2010).

Those with SUD have been known to act impulsively by opting for a S-S reward, such as drug acquisition, over a L-L reward such as good health or financial security. Delay discounting, a cognitive phenomenon, presents the deterioration of subjective value of a reward as a function of postponed delay to that given reward (Rachlin & Green, 1972). This finding has been generalised to many populations however an ever-increasing body of evidence highlight those with SUD repeatedly show steeper DD rates than non-SUD controls. (Bickel et al., 2006; Kirby, Petry, & Bickel, 1999; Madden et al., 1997; Odum & Bauman, 2010; Petry & Cassarella, 1999; Reynolds, et al., 2004; Richards et al., 1999; Vuchinich & Simpson, 1998). The importance of these studies suggest that a thorough comprehension of DD would likely give clues towards predicting those prone to addiction and aid prevention and therapeutic interventions for those with SUD.

As described above one investigative stratagem for elucidating impulsive decision-making in humans (and non-humans) has been to employ the DD paradigm (Bickel & Marsh, 2001). Based on behavioural economics DD refers to the fact that the subjective value of an outcome depreciates when it is delayed (Green et al., 1994). Although the psychological assessment of DD originated from nonhuman-animal research (Chung & Ilermstein, 1967; Rachlin & Green, 1972; Ainslie, 1974), a number of procedures have been developed to assess delay aversion in human subjects. Typically measures of DD are based on psychophysical choice procedures (Mazur, 1987; Richards et al., 1997).

The DD paradigm initiates when a human participant is required to make a choice between two possible reward outcomes. This can be in the form of two place cards on a computer screen denoted as “A” and “B”. Choosing a card delivers a reward followed by a time-out period. Arbitrarily, card A will deliver a £5 reward followed by a 5 second time out (S-S) while card B will deliver a £15 reward followed by a 15 second time out period (L-L) with the former option being the impulsive choice.

An alternative version of the DD paradigm permits for the quantification of the rate of discounting of the larger delayed reward in relation to time. This can be realised by altering the time delay of rewards throughout each trial to permit determination of the value of rewards at which reversal of reward preference occurs. In the "adjusted amount procedures" (Richards et al., 1997; Mitchell, 1999) test subjects are presented with two reward choices: one is a large but delayed reward, and the other is a small immediate reward. The magnitude in delay is adjusted each trial (starting with a long delay and moving towards a shorter delay) until the preference between choosing the large/delayed reward and immediate/small reward are approximately equal. The stage at which *equal preference* is given to obtaining a small/immediate reward or a large/delayed reward is referred to as the "*point of indifference*". Throughout both tasks the point of indifference can be determined across several delays that can then be plotted graphically to deduce the rate at which the subjective value of the reward decreases over time.

There are two mathematically derived models which have been fundamental to quantification of DD (Ainslie, 1975; 1992). First, the exponential model, forecasts the subjective value of the delayed reward and was found to be discounted exponentially when tested with participants i.e. for equal increments in delay of the reward, there is an equal proportion of decreased reward value (Kirby, 1997).

(1) $$V= A_kD$$

In the *exponential function* (1) V is signified as the current subjective value of a delayed reward, known as the "point of indifference", A is the value of the delayed reward, k is an empirically-derived constant proportional to the degree of DD and D is the duration of delay of the reward. It is contended that the larger the degree of discounting equates to a greater display of impulsivity.

The second model contends that delayed reward is discounted in a *hyperbolic* manner such that the devaluation of delayed rewards is proportional to their delay (Ainslie, 1992). For each unit of time that comprises the delay of delivery, the reward's current value decreases by a progressively smaller quantity (2).

$$V = A / (I + kD) \tag{2}$$

Mainstream research comparing both models however has suggested that the *hyperbolic function* may be a more realistic representation for the discounting of delayed reward in both animals and humans (Kirby, 1997; Richards et al., 1999; Mazur, 2001). An alternative analysis is to measure the area under the curve as an additional measure of aversion to delay (Ohmura et al., 2005).

Most DD tasks presented to participants are in the form of questions and the outcomes are "hypothetical" and take the form of money, drugs, food or health outcomes (Madden et al., 1997; Odum et al., 2000; Chapman et al., 2001). The advantage of hypothetical outcomes is that they allow for the study of receiving large rewards (£1,000) and longer delays (8 months) which would otherwise be very cumbersome to imitate with "real" rewards and delays. A second advantage is that hypothetical rewards circumvent the ethical responsibility of rewarding participants with real drugs or dispensing real money to those with SUD (Petry 2001b). Some studies have allowed the participant to choose the outcome they preferred (e.g. food, money or drugs) in just one randomly selected trial from all other hypothetical rewards made to reduce study limitations and increase validity (Kirby, 1997).

Temporal discounting theory of impulsivity are the basis of animal models created to quantify impulsivity. Despite there being many flavours of the delayed reward paradigms, all models require an animal, usually a rat, to choose between an S-S reward and a L-L reward. The original model used a two-armed maze with one arm dispensing two food pellets immediately and the other arm dispensing ten pellets after the animal is delayed for a predefined amount of time (Thiebot et al., 1985). Greater preference for the S-S reward is said to be evidence for impulsivity. The model was advanced by automating each delay of reward, so a delay function could be plotted (Mazur, 1987; Evenden & Ryan, 1996; Richards et al., 1999). The model paradigm has variants known as "adjusting" or "systematic" procedures. Adjusting paradigms require trained test subjects to make a choice between one of two levers. One lever dispenses a single pellet of food immediately (S-S reward) while the other lever delivers more than one pellet after a predefined delay (L-L reward). The delay to delivery of the L-L reward is controlled by the experimenter and is systematically amplified during successive trials (Evenden & Ryan, 1996). An index of impulsive choice is calculated by the per cent choice of delayed rewards across varying delays. The "adjusting" paradigm the quantity of the S-S reward or delay to delivery of the L-L reward is adjusted according to the animal's previous choice (Mazur, 1987; Richards et al., 1999) and continues across trials until a point of indifference is reached. This point of indifference indexes the tolerance to delayed reward, the smaller the magnitude of immediate reward or shorter the adjusted delay at this point the more impulsive the animal is deemed to be. Adjusting models differ marginally from systematic delayed rewards measures, in that they measure the degree to which a participant values the standard alternative rather than which alternative reward is preferred.

1.3.1.3.4. Differentiating Delay Discounting and Delay of Gratification

It appears prudent to make explicit the differences between DD, and a popular area of study in developmental psychology, "delay of gratification." It is tempting to take results from the latter area as indicative of processes in the former area, but this is not necessarily appropriate.

Mischel's classic "delay of gratification" paradigm (e.g., Mischel, et al., 1972; Mischel, et al., 1989) looks very similar to the DD paradigm. In Mischel's research, preschool-aged children were asked to wait alone in a room until their experimenter returned. They were informed that if they waited for the experimenter to return on her own, they would receive a larger reward (e.g., two cookies), but if they summoned her back early, they would receive a smaller reward (e.g., one cookie). Mischel and colleagues investigated many variables that caused or correlated with longer waiting times.

Many of the features of delay of gratification studies and DD studies are very similar, including the use of S-S and L-L rewards. However, there are important distinctions to be made. Delay discounting research is concerned with how people *make* choices, while delay of gratification research is concerned with how people *sustain* choices. In DD studies, the participant is not required to make a continuous exertion of self-control, since the choice s/he makes is binding; there is no opportunity to switch from the L-L to the S-S during the delay period.

Reynolds and Schiffbauer (2005) detail some empirical differences between DD and delay of gratification. The first difference is the developmental onset. Delay-dependent discounting is not seen until 9 or 10 years of age, while sensitivity to delay time was observed in Mischel's preschool delay of gratification studies. Additionally, serotonin (5HT) lesions in rats impaired delay of gratification behavior but not discounting behaviour (Winstanley et al., 2004b). So, while the two paradigms may be similar enough for delay of gratification findings to inform DD explanations to some extent, they are sufficiently different to require sincere caution when doing so.

Research that has adopted behavioural tasks in the attempt to define further the relationship between impulsivity and drug dependence can generally be categorized into those that have (i) compared levels of impulsivity in current substance abusers and non-substance abusers, (ii) compared amongst abusers levels of impulsivity across different pattern of substance misuse, (iii) examined the effects of acute drug deprivation on impulsivity and (iv) examined impulsivity as a predictor of drug abuse. Each of these categories will be reviewed incorporating findings from research that has focused upon both licit and illicit drug use.

1.3.2. Comparison of Levels of Impulsivity in Substance Abusers and Non-substance Abusers

A wealth of evidence has shown that those with SUD (licit and illicit) show elevated sensitivity to delayed rewards when compared with matched controls that are not abusing substances. Research has shown that those dependent on opioids have steeper discounting curves than matched controls when hypothetical money is used as a reward (Madden et al., 1999). One example to highlight the severity of difference in discounting was shown whereby to reduce the subjective value of $1000 by 60%, required a delay of one year for heroin abusers, while the equivalent delay was five years for matched controls (Madden et al., 1999).

The DD paradigm was used to show heightened intolerance to delayed rewards in heroin abusers who were given the opportunity to win one of their reward choices they chose during the experiment (Kirby et al., 1999). Similar findings were shown in cocaine abusers (Moeller et al., 2002; Coffey et al; 2003). Petry (2003) added to our understanding by showing that heroin and cocaine abusers discounted delayed reward at a faster rate than matched controls irrespective of the outcomes. This piece of research also made a finding that discounting of delayed reward was consistently greater than matched controls regardless of the reward e.g. health, food or freedom.

Common views revealed by these discoveries are that they initiate explanatory clues towards the high-risk behaviours shown by those with SUD. Those with SUD are more likely to commit illegal acts in order to feed a drug habit and more like to engage in poor drug-hygiene e.g. sharing and/or re-using injecting paraphernalia. Common illegal acts committed by those with SUD include theft/burglary in order to feed drug habits and are thought to be due to their consequences (e.g. prison sentence) being delayed in time and are therefore highly discounted (Petry, 2003).

Elevated discounting of delayed reward is not unique to those with a SUD for illicit drugs, similar behaviours are seen in those with a SUD for licit drugs such as painkillers (Dhokia et al., 2014), cigarettes (Bickel et al., 1999) and alcohol (Richards et al., 1999).

Although studies have shown alcoholics to demonstrate significantly higher discounting of delayed monetary rewards than matched controls, these results could not be replicated in further research that assessed discounting rates of heroin, cocaine and alcohol abusers (Kirby & Petry, 2004). Those abusing cocaine and heroin had similar DD rates and were significantly steeper in comparison to alcoholics and matched controls. Interestingly, the findings showed that alcoholics and matched controls had similar rates of DD. This finding was argued to be due to self-selection bias of participants whereby less impulsive participants would be more likely to volunteer for the study ergo were not representative of the general alcoholic population (Kirby & Petry, 2004).

When investigating the cigarette smoking populations, many research groups have found robust differences between smokers and non-smokers. Smokers have shown greater inclination for choosing the S-S reward in lieu of the L-L reward when compared to matched non-smoking participants (Bickel et al., 2001; Mitchell 1999; Reynolds et al., 2004; Reynolds et al., 2006a). The observed effect is consistent even when there is disparity in the reward sizes, during the deliberation of both losses and gain and also when choosing between various commodities such as health and food as possible rewards (Odum et al., 2002). Furthermore, a study by Spillane et al., (2010) found significant differences on all sub-scales of the UPPS-P when comparing current smokers with non-smokers whereby current-smokers scored higher on all subscales.

There exists the reasoning that significant differences in impulsive decision-making surface only when comparing highly dependent cigarette smokers to mildly addicted tobacco smokers. This line of thought stems from the fact that the above two studies where no difference was found had employed a population of smokers where the average number of cigarettes smoked per day was between 7 and 14. However, in studies where significant differences were found, the participants could be classified as either "heavy" or "light" smokers where heavy smokers consumed a minimum of 20 cigarettes per day (Bickel et al., 1999; Mitchell 1999; Reynolds et al., 2004; Reynolds 2006a).

An important finding which has been replicated many times is that drug abusing populations discount their hypothetical drug of choice more steeply than monetary rewards even when the quantity of the hypothetical drug reward has been calibrated to be the equivalent of the monetary reward e.g. for a cocaine abuser: 1g of cocaine vs. £50 cash. The finding has been demonstrated amongst many drugs of abuse including smokers (Bickel et al., 1999; Baker et al., 2003; Johnson et al., 2007), alcoholics (Petry 2001a), cocaine (Coffey et al., 2003) and heroin abusers (Madden et al., 1997; 1999). Suggested reasoning for these observations is that obtaining the drug itself in lieu of cash offers the addicted individual immediate avoidance of unpleasant and aversive symptoms and prevents onset of withdrawal (Madden et al., 1997; Bickel et al., 1999; Petry 2001).

Solnick et al., 1980 state that humans will be more inclined to make an impulsive choice should this lead to avoidance of aversive consequences in comparison to pleasurable consequences. However, this does not agree with findings that show light smokers and social drinkers that show steeper DD rates who did not show signs of withdrawal (Johnson et al., 2007; Petry 2001).

The heightened discounting of consumable drug rewards in comparison to monetary rewards could be better explained by the reasoning that drugs themselves are primary consumable reinforcers which are usually found to be discounted to a much more than conditioned, non-consumable reinforces such as a monetary reward. It has been shown that primary consumable reinforcers (food and alcohol) were discounted evenly in a non-SUD sample population but were discounted more than monetary rewards (Odum & Rainaud, 2003). A likely explanation to this is that foods and drugs are seen to be a perishable commodity that could be non-consumable over time thus diminishing their future value. Irrespective of the mechanism involved, the steeper discounting of drug rewards is relative to the individual and in comparison, to the other reward outcome and is a common observation in both licit and illicit drug abusers. One major criticism to the methodology is that participants make choices for hypothetical rewards and also do not experience the delay associated with its delivery.

Early literature reviews shared the view that hypothetical rewards may serve to underestimate the rate of discounting (Kirby 1997). However, there has been a growing consensus that the use of hypothetical rewards and actual rewards are quantitatively analogous (Johnson & Bickel 2002; Madden et al., 2003; 2004; Lagorio & Madden 2005; Johnson et al., 2007). Over many studies in humans and animals, the hyperbolic function has accounted for the discounting of hypothetical reward outcomes with reliable accuracy (Mazur 1987, Richards et al., 1997) and can therefore offer a valid methodology to assess levels of DD.

1.3.3. Comparison of Levels of Impulsivity Across Different Patterns of Substance Misuse Amongst Abusers

Many studies, as outlined above, have evaluated the connection between impulsivity and the intensity and extent of drug abuse. The mainstream of research has been attentive upon diverse patterns of drinking and smoking behaviour and, sadly, little can be said about the role of impulsivity towards painkiller consumption and painkiller dependence. As opiate-analgesics are often an appropriate course of treatment for chronic pain, a better understanding the role of impulsivity in the development of opiate-analgesic addiction may elucidate risk factors in individuals. Identifying such risk factors may then lead to strategies of preventing dependence.

Studies have compared DD rates amongst light and heavy drinkers and between light and problem drinkers within the student population. Results led to the conclusion that heavy and problem drinkers scored higher on impulsive choice than light drinkers (Vuchnich & Simpson 1998). The highest measures of DD scores were found within the problem drinkers which lent support to the notion of dose dependent type relationship with impulsive decision making. These finding have since been replicated in adolescent light and heavy drinkers where a marked steepness in DD curves was observed in those who consumed the most alcohol (Field et al., 2007). Studies conducted within those dependent on alcohol have been conducted and results showed that those with early onset alcoholism had higher levels of discounting of delayed hypothetical rewards when compared with late onset alcoholics (Dom et al., 2007). The absence of significant correlation exhibited concerning years of abuse or dependence and rate of discounting steered to authors to conclude that their revelations hinted that elevated impulsive choice could pose as risk factor in the development of early onset alcoholism.

Less reliable results have been revealed between social smokers (also known as 'chippers') and heavy smokers. Chippers are those who smoke cigarettes on a regular basis yet do not become addicted to nicotine/tobacco. In a study where participants experienced both real-time rewards and delayed rewards, individuals whom smoked more than 40 cigarettes per week exhibited significantly greater rates of discounting of monetary rewards when compared to both matched control non-smokers and lighter smokers who consumed less than 40 per week (Heyman & Gibb, 2006). In addition, the lighter smokers did not differ from controls. The lighter smokers in a study conducted by Johnson et al., (2007) were no different to heavy smokers where both smoker groups presenting significantly higher levels of discounting of delay of monetary rewards in comparison to non-smokers. The irregularity in results yet again may be accredited to the vague taxonomy of what is deemed a "light smoker". Those who smoked less than 10 cigarettes per day were classified as "light smokers" in the Johnson et al., (2007) study. This allowed them to smoke 70 cigarettes per given week, which is substantially more than the categorisation for light smokers in Hyman and Gibb's study (less than 30 per day).

The nonexistence of heightened impulsiveness in chipper smokers has been shown elsewhere when comparing heavy and occasional smokers on a possible measure of disinhibition, the Continuous Performance Task (CPT; Yakir et al., 2007). Heavy smokers in the study made significantly more errors in the task than both control and chippers. An interesting finding to come from this study was that chippers showed a significantly greater aptitude in withholding prepotent responses than control subjects (Yakir et al., 2007). The CPT primarily assesses attention and so the positive effects witnessed for the light smokers may be due to nicotine's ability to enhance attentional and attentive properties when consumed in low and infrequent doses (Fan et al., 2002; Hahn & Stolerman, 2002).

As mentioned above, evidence for the lack of relationship between light smoking and disinhibition has been exhibited by, the go/no-go task, a model predominantly applied to quantify inhibitory control. Adopting this behavioural measure authors were unable to find performance disparity between non-smokers and light smokers (Doran et al., 2004). A wealth of evidence is available to support that impulsivity differentiates between smokers and non-smokers but there also exists some data to suggest impulsivity differentiates within smokers. This was shown by seminal studies highlighting positive correlations between self-reported cigarette consumption and their delay-discounting scores (Spinella et al., 2002; Reynolds et al., 2004; Ohmura et al., 2005; Johnson et al., 2007).

To summate thus far, research has included current and past abusers and there is some suggestion that elevated scores on impulsivity and DD can be reduced. Moreover, it is likely there exists a critical period of abstinence, specific to the drug of abuse, before an observable decline in DD scores is seen.

An additional analysis of findings could be that having low levels of impulsivity facilitate abstinence. No definite inferences can be drawn concerning the relationship between disinhibition and abstinence from drug abuse due to the rarity of studies that included an active and an abstinent drug group. However, studies that have compared users in both early and later stages of abstinence to non-drug users have demonstrated consistent poorer levels of inhibitory control. This suggests that chronic drug consumption could equate to an alteration in inhibitory control that endures subsequent to termination of drug abuse. Equally, the data could suggest that suboptimal behavioural control predates drug consumption and constitutes a vulnerability marker towards the development of an addiction. Research that quantifies the fractions of the impulsive spectrum longitudinally, prior to, during and after drug abuse will allow us to draw a more accurate conclusion on the temporal association between impulsivity and drug dependence.

1.3.4. Examination of the Effects of Acute Withdrawal on Impulsivity

There exists a small collection of studies that aim to elucidate the effect of acute drug withdrawal or deprivation on impulsive choice and lesser still on the inhibitory control. It has been shown that opioid dependent participants maintained on buprenorphine had varying levels of impulsivity dependent on whether they were deprived of the drug. When these individuals were in a deprived condition, they discounted both heroin and monetary rewards significantly more than when they were in an opioid sated state (Giordano et al., 2002). Results also echoed previous research whereby the drug of choice, Heroin in this instance, was discounted to the greatest degree during both deprived and sated states with discounting rates observed to be three times more rapid than delayed monetary rewards.

Analogous results have also been drawn for temporarily deprived smokers (Field et al., 2006). Smokers who had not smoked for a period of 13 hours were seen to discount both delayed hypothetical money and cigarettes significantly more than when they performed the task after 5 minutes of deprivation. Once more we see that the drug of abuse shows the steeper discounting rate. A study that showed an inconsistency, conducted by Mitchell et al., 2004, showed smokers deprived of nicotine for 24 hours did not differ significantly from non-deprived smokers in terms of discounting hypothetical monetary reward. However, there was an increase in discounting for cigarettes when participants were acutely deprived which led authors to argue that there was a heighted preference for cigarettes rather than there being an intolerance to delay. The disparity in research outcomes can be partly attributed to both the lack of power (*n*=11) in Mitchell's study, and the variants of DD tasks employed across studies.

The amplified levels of impulsive choice during early withdrawal may play a vital part in the maintenance and relapse of drug dependence. Shortfalls in self-control during early abstinence may equate to a greater probability of dependent individuals choosing the instant rewarding effects of the drug, or relief of withdrawal, as the larger delayed rewards linked with a drug free lifestyle will be discounted to a greater magnitude during this stage. Ergo, commitments to abstain may fail while drug consumption continues.

Intriguingly enough, 41% of a sample of cocaine and alcohol dependent individuals provided “impulsive action”, or loss of control as a reason to why they felt that they relapsed while only 7% reported cravings as a reason for relapse (Miller and Gold, 1994).

It is imperative that future research seeks to elucidate the role of impulsivity during acute withdrawal in hope that it may widen our knowledge of cessation failures amongst those with SUD. While contemporary data is starting to reveal the prominence of impulsivity in relapse and thus validating the need for both behavioural and pharmacological interventions to target impulsivity for the treatment of substance dependence. A study in which alcohol dependent individuals were seen to relapse quicker if they had deficits in inhibitory control (Noel et al., 2002) exemplifies this need. Similarly, the magnitude of impulsive choices made on a CPT task was shown to be significantly greater in adolescents who were unsuccessful in abstaining from smoking during a fourteen-week smoking cessation plan (Krishnan-Sarin et al., 2007).

Data on the effect of acute deprivation on impulsivity if compared alongside data assessing enduring abstinence propose that perchance a biphasic relationship between abstinence and impulsivity may occur, at least in the case with impulsive choice behaviour (Reynolds, 2006b). Initial abstinence from the drug and early onset withdrawal may result in an escalation of impulsivity, and theoretically at a greater risk of relapse. Impulsivity may begin to decrease with continued abstinence (Bickel et al., 1999; Petry et al., 2001). Such conclusions cannot yet be drawn pending research that assesses temporal fluctuations of impulsivity in a longitudinal study that commences at initial withdrawal and continues through to long-term abstinence within subjects.

1.3.5. Examination of Impulsivity as a Predictor of Drug Abuse and Dependence

Data to suggest that impulsivity may predispose individuals to substance abuse remains sparse. A notable study that assessed predictors of cigarette smoking in adolescents concluded that sensitivity to delayed gratification may be more of a risk factor but not a predictor for future smoking, however baseline DD values were significantly greater in current smokers. This encouraged the theory that possibly impulsivity is amplified by smoking (Audrian-McGovem et al., 2004).

Tarter et al., 2003 explored the role of disinhibition and highlighted that although the magnitude of inhibitory control at ages 10-12 did not influence drug consumption at aged 16, it was possible to predict development of SUD in adolescents aged 19. Data from this study suggests that while disinhibition may play a minor role towards initiation of drug consumption it can significantly forecast future progressive drug consumption once a drug has been consumed. Similarly, empirical evidence shows that compromised executive functioning in childhood, including a weakened ability to inhibit responding, was a valid predictor of substance misuse in later life (Aytyaclar et al., 1999). More so, smoking, cannabis consumption and the range of other drugs consumed were predicted.

Data from animal studies show support that impulsivity may predispose onset of SUD. In an adjusted amount DD paradigm, and also in a 5CSRTT, baseline levels of sensitivity to a delayed reward and the magnitude of anticipatory responding predicted the extent of cocaine self-administration in rats (Perry et al., 2005; Dalley et al., 2007). A positive correlation was observed between the level of impulsivity and the rate of self-administration on both behavioural measures.

Comparably, animals displaying high intolerance to delayed reward consumed significantly more freely available ethanol than both medium and low-level impulsive groups (Poulos et al., 1995). Moreover, mice that demonstrated impulsive responding on an appetitive signalled nose poke task, a paradigm comparable to the 5CSRTT, also drank more ethanol (Bowers & Wehner, 2001). Taken together, these outcomes hint trait impulsivity may precede and act as predisposing feature towards substance misuse and perhaps SUD.

The existing literature, albeit somewhat limited with regard to opioids and painkiller use, suggests that impulsivity is an important risk factor when considering the onset of an opioid use disorder. Examining the relationship between impulsivity and opiate-analgesic misuse risk in a chronic pain population provides a unique opportunity to examine such a risk factor. Results from both animal models and human studies regard impulsivity to be a risk factor for the cause, as well as a consequence of substance use disorders (Bornovalova et al., 2005; Conrod et al., 2000; Dick et al., 2010; Ersche et al., 2010). Furthermore, a large body of evidence has shown that impulsivity is associated with opioid-use disorders (Madden et al., 1997; 1999). Studies employing animal models show that morphine use leads to increased impulsivity in the rat (Kieres et al., 2004; Patti et al., 2009). Studies in humans have also observed that opiate-dependent individuals display higher levels of impulsivity compared to controls (Kirby et al., 1999; Nielsen et al., 2012; Robles et al., 2011).

The complications in applying behavioural tasks in longitudinal research in addition to the limited knowledge concerning the stability of performance in such tasks has meant that research in this area is yet to fully flourish (Mitchell, 2004). The most accepted argument to suggest impulsivity is a risk factor for SUD comes indirectly from studies using children diagnosed with impulse control problems (e.g. ADHD; conduct disorder) which carry a significantly higher probability that they will abuse both licit and illicit substances (Biederman et al., 1997; Moss & Lynch, 2001; Molina & Pelham, 2003). If one ponders on the evidence presented thus far, it is highly plausible that elevated impulsivity may act as predisposing factor towards drug dependence and therefore emphasizes great importance for future prevention approaches to manage both impulsive choices and disinhibited behaviour.

1.4. Neurophysiological mechanisms of impulsivity and its relation to drug dependence

An abundance of research has focused upon revealing the neural mechanisms underlying impulsivity. In the following sections both the neurochemical and neuroanatomical evidence will be reviewed and how these mechanisms may modulate the heightened impulsivity associated with drug dependence additionally explored.

1.4.1. Neuroanatomical Basis of Impulsivity

The great majority of research outcomes investigating the neuroanatomical basis of impulsivity have focused on the frontal cortices (FC). An abundance of data exists to support the notion that structures in the prefrontal cortex, an area involved in planning, is a key neural substrate of impulsivity while substructures are responsible for finer aspects of impulsivity (Aron et al., 2004). This neural region is involved in various stages of addiction (Everitt et al., 1999; Jentsch and Taylor, 1999; Kalvias and Volkow, 2005).

Studies carried out on the human participants with existing lesions (infarction, hemorrhage with no evidence of diffuse axonal injury, or resection of a benign tumor with no detectable evidence of diffuse brain pathology) in the medial prefrontal cortex (mPFC) show a significant increase in inability to perform adequately on the no/no-go task (Picton et al., 2007), a finding that echoed earlier studies carried out in non-human primates (Iversen and Mishkin, 1970). Lesions to neighbouring neural regions such as the anterior cingulate cortex (ACC), prelimbic cortex (PLC), infralimbic cortex (ILC) also show greater disinhibition manifesting as premature responding in rats tested on the 5CSRTT (Chudasama and Muir, 2001, Passetti et al., 2002; 2003; Christiakou et al., 2004; Chudasama et al., 2004). The role of 5-HT (Serotonin), in the PFC, is once again made prominent when it was shown to modulate baseline inhibitory responding. Rats that displayed greater levels of premature responses had correlating increasing levels of (5-HT; Dalley et al., 2002).

Lesions to a subregion of the PFC known as the orbitofrontal cortex (OFC) were shown to result in both elevated disinhibited responses and preservative responding in rats tested on the 5CSRTT (Chudasama et al., 2003). Lesions to the OFC in non-human primates was shown to lead to an increase in the number of commission errors in the go/no-go task (Iversen & Mishkin, 1970; Butter et al., 1973).

Excitotoxic lesions to the ACC and the mPFC did not affect impulsive choice that was indicative of augmented sensitivity to delayed reward to which the authors concluded that these neural areas of the PFC contribute more towards inhibitory control than impulsive decision making (Cardinal et al., 2001). However, the OFC, another sub-region of the PFC, does seem to donate effort towards impulsive decision-making. Mixed outcomes have been observed in rats with lesions to the OFC whereby both an increase (Kheramin et al., 2002; 2004; Mobini et al., 2002) and decrease (Winstanley et al., 2004a) in the choice of the smaller immediate reward in systematic delayed reward paradigms. Although differences in outcomes can be ascribed to methodological disparities across studies (e.g. time point of lesion is made), empirical evidence of choice preference has established that vicissitudes in impulsivity can be accredited to variations in sensitivity of both magnitude of reward and delay due to damage to the OFC (Kheramin et al., 2002; 2004).

As mentioned above, anomalies in PFC subregions is regarded as a significantly important neurobiological mechanism responsible for progress towards addiction which could be due to suboptimal self-control (Jentsch & Taylor, 1999; Goldstein and Volkow, 2002; Lubman et al., 2004). This is exemplified by imaging studies showing a reduction in gray matter density within the aforementioned neural subregions in polysubstance cocaine, methamphetamine, alcohol and nicotine abusers (Pfefferbaurn et al., 1997; Liu et al., 1998; Franklin et al., 2002; Brody et al., 2004).

Furthermore craving, bingeing and drug intoxification, are linked with activation of the OFC and the ACC across addicts of varying drugs of abuse, whilst hypoactivity of the OFC and ACC are linked with long term withdrawal believed to be related the downregulation of D2 receptors (Brody et al., 2002; Goldstein and Volkow 2002; Rose et al., 2003; Neuhaus et al., 2006). A seminal study by Paulus et al., 2007 showed that hypoactivity of the dorsolateral PFC and parietal cortex to predict relapse in methamphetamine users.

Neuropsychological measures also add to the wall of evidence for impaired OFC function being a risk factor for an addiction whereby high performance on such tests is dependent on a healthy functioning of the PFC. The Bechara Gambling Task (BGT) is one such neuropsychological test that evaluates sensitivity to decision making of future rewards. Impaired performance was attributed to use of cocaine when cocaine abusers were compared to non-using controls. Similar results were observed in methamphetamine and alcohol abusers. Performance scores for these population of drug abusers were similar to scores obtained by those with bilateral lesions to the OFC (Bechara et al., 2001; Bechara and Damasio, 2002). The causal relationship has been implied between performance on the BGT and length of chronic abuse whereby poor task performance, as indicated by greater dysfunction of the OFC, was seen to correlate positively with the years of amphetamine abuse (Rogers et al., 1999b).

To summate, there is a large body of empirical evidence to suggest both regions of the Ventral Striatum (VS) and FC govern and regulate impulsive behaviour. Subregions of these neural areas seem to be differentially associated with inhibitory control and impulsive decision making, with the OFC and the NAc to be the only structures that control comparably the two forms of impulsivity. Inhibitory control appears to be regulated by the ACC and mPFC while the Subthalamic Nucleus (STN) has shown differential roles in the control of disinhibition and impulsive decision-making. Again, both regions are key areas when addiction is concerned whereby chronic drug abuse being linked to neural adaptations in the ACC and mPFC (Koob et al., 1998; Goldstein and Volkow, 2002).

Ergo, anomalies within these sub-regions of the FC are highly probable to underlie the heightened impulsivity seen with addiction. A causal relationship between these neurological mechanisms and impulsivity and or addiction, however, cannot be verified as of yet, leaving the direction of the relationship between these variables to be yet fully elucidated.

It is highly likely that the neurobiological alterations linked with drug abuse in these neural areas (Koob et al., 1998) may result in loss of control over drug consumption and insensitivity to delayed consequences equating to persistent drug seeking, consuming, and relapsing behaviour. Rather, these neurobiological irregularities may appear to highlight a susceptibility to drug abuse, a theory sustained by Dalley and colleagues (2007).

1.4.2. Neurochemical Basis of Impulsivity

The neurotransmitter substances involved in impulsive behaviour are aplenty. Two of the most prominent neurotransmitter substances, Serotonin and Dopamine, are discussed in detail below.

1.4.2.1. The Role of Serotonin

Of the major theories surrounding neurobiological influences on impulsivity, the mediating role of Serotonin (5-HT) has been highlighted in the bulk of these. Serotonin has been argued to have an inverse relationship with impulsive behaviour (Logue, 1988). Precedence for the role of 5-HT in impulsive behaviour stems from seminal studies on violent behaviour and on suicide (Asberg et al., 1976), who posit that when concentrations of 5-HT decrease, there could be greater scope for impulsive behaviour to manifest. The author also states that the concentration of 5-HT found in the cerebrospinal fluid (CSF) was significantly lower in aggressive individuals, but only when the aggression was of an impulsive nature. Comparable data include violent suicide attempters (Coccaro, 1989), children with conduct disorders (Stoff et al., 1987) and healthy individuals with significantly higher trait impulsivity scores.

Additional data is offered by findings in non-human primates that suggest aggression and impaired impulsive control is related with low levels of 5-HT (Westergaard et al., 1999). Studies that aim to influence the activity of 5-HT provide some evidence for its role in impulsive behaviour. The majority of these come from animal models of delayed reward, which show perturbations in the 5-HT pathways to be associated with variations in impulsive behaviour in rats (Ho et al., 2002).

Depleting 5-HT in the forebrain of rats led to a greater preference for smaller immediate rewards when compared to sham lesioned rats (Bizot et al., 1999). Again, in T-maze, the lesion did not affect judgment between the magnitudes of the two reward outcomes. Such data are consistent to those of Thiebot (1992) where impulsive decision-making was increased when 5-HT was reduced. Complementary results have also been observed when an operant paradigm is used. Reduced concentrations of 5-HT and its metabolite 5-HTAA, induced by 5,7 dihydroxytryptamine (5 ,7-DHT), amplified preference for the smaller immediate reward in comparison to the sham-lesioned controls (Ho et al., 1998; Mobini et al., 2000a). Additionally, it has been hypothesised that the heightened impulsive choices observed are due to a heightened sensitivity to delay as opposed to alterations in sensitivity to reward magnitude (Mobini et al., 2000b). Equally, by enhancing 5-HT function, by either enhancing its release (d-Fenfluramine) or by selectively blocking its reuptake (fluvoxamine, fluoxetine, clomipramine) it has been established that an increased preference for the delayed larger reward in the T-maze procedure in rats is most likely to occur (Bizot et al., 1988; Poulos et al., 1996).

Contemporary data suggests that a reduction in impulsivity is observed in pigeons who underwent an adjusted delay paradigm following a 17-day period of SSRI's: fluoxetine, paroxetine and citalopram (Wolff & Leander, 2002). Complimentary data also supports this notion in that increasing 5-HT in the medial frontal cortices and in the cingulate cortices equated to a reduction in the number of impulsive choices made in animals that were considered hugely sensitive to delayed gratification at baseline (Adriani et al., 2004).

Research outcomes have not always been consistent. The elevated impulsivity observed upon administration of 5,7-DHT has been known to produce only a short-term effect (Bizot et al., 1999) while later studies showed global 5-HT (Serotonin; a neurotransmitter substance) depletion to revise impulsive choice (Winstanley et al., 2005).

The variety of anomalies existing between research outcomes may be accounted for by methodological differences and by use of the various DD paradigms. Where research showed a lack of effect via 5-HT depletion the DD paradigm used was a “systematic” DD task (Winstanley et al., 2003; 2004a). Where research showed a significant elevation in DD the “adjusting” DD paradigm was used (Wogar et al., 1993; Mobini et al., 2000a; 2000b).

Global reduction in 5-HT has also been known to affect behavioural disinhibition in rodents who show increased impulsive responses on the go/no-go task (Harrison, Everitt & Robbins, 1999) and in DRL (Wogar, et al., 1992; 1993), FCN procedures (Evenden, 1998b) and the 5CSRTT (Harrison et al., 1997a; 1997b; Winstanley et al., 2004a).

While timing behaviour may account for greater premature responses following 5-HT disruption in the DRL procedure, this same conclusion cannot be applied to impaired control of response in the go/no-go task. This is due to explicit visual exteroceptive cues that indicate explicitly when to respond and when to withhold a response thus there being no need to estimate timing and allowing for a stronger conclusion to be drawn regarding 5-HT and response disinhibition (Harrison et al., 1999). Yet more evidence is available for the role of 5-HT in the modulation of response inhibition whereby a decrease in premature responses are seen in rodents following pharmacological procedures that enhance quantal release of 5-HT. Administration of Fluoxetine, an SSRI, led to a reduction in the number of premature responses in a DRL task (Richards et al., 1995) whilst Imipramine, a monoamine reuptake inhibitor, resulted in a reduction in the number of impulsive responses in the FCN procedure (Evenden, 1998a; Evenden, 1998b). The latter finding equated to the plausibility that stimulation of noradrenergic and dopaminergic pathways in addition to serotonergic pathways may play a central role in this fraction of impulsivity.

By manipulating the diet to endorse rapid tryptophan depletion (RTD) it has become possible to study 5-HT reduction in humans (Williams et al., 1999). Reduced levels of 5-HT have been shown to lead to decreased inhibitory control on a variety of behavioural tasks such as the go/no-go, SST and CPT in healthy males and in participants who have a family history of alcohol addiction (Crean, et al., 2002; Walderhaug et al., 2002; Walderhaug et al., 2005). No significant effects have been published regarding RTD on impulsive decision making using a hypothetical DD paradigm (Crean et al., 2002). Thus, upon 5-HT depletion a consistent increase in disinhibition has been shown relative to the effects seen on impulsive decision making. This could form support for the theory that these two components of impulsivity are possibly, at the neurobiological level, dissociable (Evenden, 1999a), whereby the serotonergic system plays a cardinal role towards modulating inhibitory control.

While no effect of serotonergic manipulation was detected in human participants, this could have been due to the hypothetical version of the task being less sensitive to acute state changes in impulsivity induced by RTD. As mentioned above, tasks involving humans such as the EDT where rewards and their delay to delivery are experienced in real time are seen to show greater sensitivity to the acute effects of drugs more than hypothetical DD paradigms (Reynolds et al., 2006b). Manipulations of 5-HT may lead to greater effects on impulsive choice in such paradigms and should be explored further. Data that has focused on SSRI's have shown changes in behavioural inhibition and in sensitivity to delayed gratification. The resulting effects are multifaceted and hint that 5-HT may modulate specific portions of impulsive behaviour via the mediation of 5-HT's receptor subtypes.

1.4.2.2. The Role of Dopamine

Studies exploring the pharmacological role of neurotransmitters have also covered the position of Dopamine (DA) in impulsive behaviours. The powerful dopamine antagonist d-Amphetamine has been the most widely used compound to assess the effect of elevated levels of DA. Acute doses have yielded mixed results in both human and animal studies whereby increases (Charrier and Thiebot, 1996; Evenden and Ryan, 1996; Cardinal et al., 2000; Isles et al., 2003; Helms et al., 2006) and decreases (Richards et al., 1999a; 1997; Cardinal et al., 2000; Wade et al., 2000; de Wit et al., 2002; Winstanley et al., 2003; van Gaalen et al., 2006) in impulsivity have been concluded. When methamphetamine is administered chronically to mimic real-life patterns of use it has been shown to promote choice of the immediate smaller reward in rodents (Richards et al., 1999a). The opposing revelations from these studies following acute administration of amphetamines were due to several methodological differences e.g. differences in reward outcomes, concentration of amphetamine (Isles et al., 2003) and whether or not there was a reward predicting cue during the delay to delivery of the L-L reward (Cardinal et al., 2000).

Confirmation of an association between disinhibition and DA has been provided. Administration of low to moderate doses of d-Amphetamine in humans results in elevated levels of synaptic DA which in turn led to significant increases in inhibitory control on the go/no-go task and SST paradigm. The effect itself was however only limited to participants with lower than average baseline levels of inhibitory control (de Wit et al., 2000; 2002). Similar outcomes have been observed in animal studies utilising low doses (0.25mg/kg and 0.5mg/kg) of d-Amphetamine in a SST designed for rats (Feola et al., 2000). Conflicting data has been provided when higher doses are used in rodents tested on the DD paradigm show test subjects to have an opposite effect on inhibitory control (Isles et al., 2003). Furthermore, significantly higher impulsive responding observed in the DRL (Wiley, Compton and Golden, 2000), FCN (Evenden 1998a; 1998b), asymmetrical go/no-go (Ridley et al., 1980) and 5CSRTT procedures (Cole and Robbins, 1987; Harrison et al., 1997; Van Gaalen et al., 2006) have been demonstrated. The ability of amphetamine to modulate levels of both forms of impulsivity has however been shown to be partially reliant on serotonergic neurotransmission.

In a further study, although an opposite increase in premature responding in 5CSRTT was shown following amphetamines administration, 5-HT neurotransmission was crucial for the manifestation of amphetamines effects (Harrison et al., 1997). Taken together, this suggest that both behavioural inhibition and sensitivity to delayed reward are regulated through complex interactions between the DA and 5-HT systems.

Only a handful of studies have attempted to research the neurochemical basis of impulsive choice at the DA receptor level.

Upon administration of the D2 antagonist Raclopride and the D1/D2 antagonist Flupenthixol (Cardinal et al., 2000; Wade et al., 2000), but not D1 antagonist SCH23390 (Wade et al., 2000), it was observed there to be a greater penchant for the S-S reward, supporting the prominent role of the D2 receptor in the intolerance to delayed reward. Later research showed that in a systematic DD paradigm, impulsivity was increased upon administration of D1 antagonist SCH23390 whilst treatment with the D2 antagonist Eticlopride had no effect (van Gaalen et al., 2006). Yet again, the contrasting roles found of the DA receptors in the modulation of impulsive choice may be accounted for by differences in methodology e.g. adjusting verses systematic delayed reward task.

The role of the D3 receptor has been explored and is thought to play a role in the modulation of delay aversion. An escalation in the number of S-S choices made was observed when upon a low dose administration of the D3 agonist 7-0H-DPAT (van den Bergh et al., 2006).

Receptors D1 and D2 play a role in modulating motoric impulsivity. In direct disparity to the effects of the D1 receptor antagonist SCH23390 in an adjusting amount DD procedure, the antagonist has been shown to decrease premature responding in the 5CSRTT (Hahn, Shoaib and Stolerman, 2002; van Gaalen et al., 2006) while activation of the receptor following high doses the D1 agonist SKF38393 increased premature responding (Pezze et al., 2007). Furthermore, pre-treatment with the D1 antagonist led to a reversal of increased premature responding on the task following treatment with cocaine, nicotine and amphetamine (van Gaalen et al., 2006) and in 5-HT depleted animals led to a reduction in the elevated levels of impulsivity (Harrison et al., 1997).

Evidence from human studies also showed no significant observable changes in stop signal reaction time upon treatment with L-DOPA in children diagnosed with ADHD (Overtoorn et al., 2003). These results suggest that while DA may not play a central role in the aptitude to halt an already initiated response and switch to an alternative behaviour, it may play a vital mediatory role affecting the capability to wait and withhold inappropriate impulsive responding as measured in the FCN and 5CSRTT.

What is evident from the research is that modulation of DA affects impulsive choice as well as disinhibition in terms of the ability to wait and withhold inappropriate and premature responding. Furthermore, DA's influence over impulsivity seems to be contingent on the complex interplay with the serotonergic neural architecture (Harrsion et al., 1997; Winstanley, 2003).

At the receptor level, major importance has been placed on the function of the D1 and D2 receptors and some minor importance has been placed on the D3 receptor. The receptors themselves seem to have distinct roles in that D1 and D2 receptors have contrasting roles towards modulating impulsive choice and thus lends support to the notion that impulsivity is a multifaceted construct.

DA, being a key neurotransmitter substance on the central nervous system (CNS), plays a pivotal role in drug addiction and it is plausible that DA plays a cardinal role in the interplay between impulsivity and addiction. The majority of drugs, with benzodiazepines being an exception, act on the CNS to increase DA concentrations to supraphysiological levels. This elevated release of DA in the mesolimbic system is regarded to be a responsible for the rewarding properties of drugs of abuse (Koob et al., 1994; Di Chiara, 1998; Koob & Le Moal, 2001).

When a substance of abuse if administered, DA levels increase in both addicted and non-addicted study participants, therefore it cannot be concluded that DA alone is responsible for a comprehensive understanding of addiction (Volkow et al., 1997a; Volkow et al., 2002). Instead, it is thought to be the rise in DA followed by DA depletion and the role of the mesolimbic and mesocortical circuits is what triggers the process of addiction (Goldstein and Volkow 2002; Volkow et al., 2002). States of withdrawal and abstinence from the preferred drug of abuse are associated with low levels of DA (Lingford-Hughes and Nutt, 2003) as evidenced by neuroimaging studies which highlight a 50% reduction in DA neuronal activity in detoxified cocaine addicts in comparison to controls (Volkow et al., 1997b).

The D1, D2, and D3 receptors that are involved in the modulation of impulsivity play a significant role towards the addiction of a plethora of commonly abused substances including cocaine, heroin, methamphetamine nicotine and ethanol (Comings & Blum, 2000; Thanos et al., 2001; Volkow et al., 2002; Heidbreder et al., 2004; 2005; Nader et al., 2006; Schmidt, Anderson and Pierce, 2006; Schmidt and Pierce, 2006; Vengeliene et al., 2006). More precisely, activation of the D1 receptors in the Nucleus Accumbens (NAc) shell endorses reinstatement of cocaine seeking behaviour in rats (Schmidt et al., 2006; Schmidt & Pierce, 2006), while antagonism of this receptor (by SCH23390) decreases the reinforcing properties of cocaine (Barli and Pierce, 2005). Intriguingly, activation of the D1 receptor as previously discussed increases premature responding in the 5CSRT (Pezze et al., 2007), whilst blockade of the receptor attenuated the heightened impulsive responding following treatment with cocaine, amphetamine and nicotine (van Gaalen et al., 2006).

Data suggests that D1 receptor activation is most likely to mediate the reduced inhibitory control exhibited by those with SUD. The D1 receptor may also appear to have potential value in terms of being a target for therapeutic treatment of pathological impulsiveness as seen in aforementioned individuals. The D2 receptor has also found some acclaim in the realms of drug addiction research such that the density of this receptor is significantly lower in the striatum of opiate, alcohol and cocaine abusers (Volkow et al., 1996; 1997b; 2001; Wang et al., 1997). It is also accepted that the abnormal down-regulation of the D2 receptor is known to occur in the months that follow abstinence (Volkow et al., 1993; 1997b). The D2 receptor has also been known to have a position in both inhibitor control and sensitivity to delayed reward, manipulation sin the D2 receptor bioavailability may be a common abnormality which links drug dependence and impulsivity across a wide variety of commonly abused drugs. Furthermore, data suggests that the persistent down-regulation of the D2 receptor that follows abstinence (Petry, 2001b; Kirby and Petry, 2004; Hoffman, 2006), may account for the dysfunctional impulsive control observed in addicts, particularly cocaine abusers (Kirby & Petry, 2004; Heil et al., 2006).

Although the evidence presented thus far is encouraging there does exist a limitation in that they do not reveal whether a dysfunction in DA and D2 receptors, associated with modulation of both addictive and impulsive behaviours, is a resultant effect of chronic drug abuse encouraging elevated impulsivity detected or is it instead a dormant risk factor for drug abuse which would place impulsive individuals at greater risk for drug addiction.

Evidence from the field of neurobiology has shown a connection between DA, addiction and impulsivity whereby high impulsive rats, as assessed on the 5CSRTT, were shown to have a significant reduction in D2 receptor density in the NAc which in turn rendered them more susceptible to greater rates of cocaine self-administration (Dalley et al., 2007). Results gave support to previous research in which D2 receptor deficient mice and non-human primates with lower levels of D2 receptors both showed greater levels of cocaine self-administration (Caine et al., 2002; Nader et al., 2006). Genetic studies in humans have provided evidence in polysubstance abusers of nicotine and opiates to have variations in D2 receptors which were later found to be linked to the D2 Taq 1A and B1 allele (Smith et al., 1992; Comings and Blum, 2000; Xu et al., 2004; Gelernter et al., 2006). These discoveries lend great support to the theory that low D2 receptor density manifests as a predisposition or vulnerability marker for drug addiction, possibly via deficient inhibitory control.

Taken together this may suggest that elevated levels of D2 receptors may act as a protective buffer against drug abuse by fostering greater self-control (Volkow et al., 2002). Interestingly, the transfection of D2 receptor gene into the NAc was shown to reduce alcohol consumption in rats (Thanos et al., 2001). One should take care not to assume a unidirectional relationship occurs between DA, impulsivity and addiction as it is possible that chronic drug consumption can impair a pre-existing dysfunctional DA system which gives rise to loss of control and the compulsion to consume drugs as is well observed in individuals with a SUD.

Moreover, it is yet to be known whether a reduction in D2 availability has a genetic underpinning which gives rise to elevated sensitivity to delayed gratification. Finally, the D3 receptor is now beginning to receive more attention from the academic community on its role towards impulsivity and drug addiction. The D3 receptor is chiefly found in the mesolimbic structures, specifically in the accumbens and has been implicated in a variety of addictive processes and behaviours e.g. antagonism of D3 leads to a reduction in nicotine induced conditioned place preference and locomotor activity (Pak et al., 2006), alcohol seeking behaviour (Vengelinc et al., 2006) and self-administration of cocaine in rodents (Xi et al., 2006).

Although research is incomplete regarding the responsibility of this receptor in impulsivity recent evidence suggests that stimulation of the receptor by the agonist 7-0H-DPAT resulted in heightened impulsive choice in a DR paradigm (van den Bergh et al., 2006). D3 receptor antagonism may therefore provide us with a promising novel pharmacological approach to treatment that could significantly reduce a number of addictive behaviours including sensitivity to delayed reward.

1.4.2.3. The Role of Oxytocin

The hypothalamic neuropeptide Oxytocin (OXT) nicknamed the “cuddle chemical,” the “hug hormone,” and the “love drug.” OXT plays an integral role in a plethora of social and stress-related behaviors including social interaction, maternal behavior, as well as reducing anxiety (Neumann, 2007). Prior research on OXT s mostly focused on female reproduction (Pederson & Prange, 1979). However, more recent discoveries posit that OXT has a significant role in prosocial behaviors such as attachment (Carter, 1998) and social behaviours (Ferguson et al., 2000). Further studies have discovered that both central and peripheral administration of OXT produces anxiolytic (anxiety reduction) and anti-stress effects in animal models (Ring et al., 2006; Landgraf & Neumann, 2004).

The role of OXT in areas concerned with social relationships is aplenty, however its role governing impulsive decision-making and behaviour remains to be explored further. Two recent studies provide promising results which show OXT role in impulsivity. Demirci et al., 2016 provided us with a study where 40 male school-aged children diagnosed with ADHD had blood serum levels measured for OXT and compared with age-matched healthy controls. Both groups completed a self-report measure of impulsivity (BIS-11). Results showed the impulsivity scores were significantly higher and serum oxytocin levels were significantly lower in the ADHD group (52.5±18.1 and 37.62±9.0, respectively, $p< .001$). Additionally, serum OXT levels showed a negative correlation with impulsivity and attention subscale scores of BIS-11 in the ADHD group (i.e. low levels of OXT are correlated with high scores of impulsivity. A second noteworthy piece of research was conducted by Plessow et al., 2016. In this double-blind, placebo-controlled crossover pilot study 10 healthy overweight/obese men were administered 24 IU intranasal OXT. After a fifteen minutes delay of being administered receiving OXT or placebo, participants completed the go-/no-go paradigm, a widely used task to assess strategy and ability to suppress behavioral impulses. After receiving OXT, subjects showed increased reaction times (RTs) in the task compared to the placebo condition and fewer errors under OXT compared to placebo. These results indicate that after a single dose of OXT, subjects proactively exert control over their behavior, increasing RT in the go task, which, in turn, reduces impulsiveness.

A growing body of evidence has started to highlight the significant role for OXT in drug addiction (Sarnyai & Kovács, 2014). Some studies have stated that recreational drugs stimulate the OXT system (Dumont et al., 2009) and that social bonding and drug addiction may share a common neural pathway (Liu et al., 2011; Young et al., 2011). This notion is additionally reinforced by results that state drug and alcohol dependent individuals typically display poor decision-making. abilities (Dawe et al., 2004). Of greater relevance to this study and in regard to psychological dependence to painkillers, OXT administration was shown to decrease analgesic tolerance and withdrawal (Kovacs et al., 1985; Sarnyai & Kovacs, 1994).

Central OXT infusions impaired methamphetamine-induced conditioned place preference and stress-induced reinstatement (Qi et al., 2009). Moreover, OXT decreased both methamphetamine and cocaine-seeking behaviours upon self-administration of OXT (Carson et al., 2010; Cox et al., 2013; Zhou et al., 2014). Combined, these findings imply that OXT could be a potential candidate as a therapeutic target for psychological dependence (McGregor & Bowen, 2012). Thus, an evidence-based therapy that can increase levels of OXT may be of benefit for those suspected of having psychological dependence to painkillers. One such therapy is Compassionate Mind Training (CMT). CMT aims to increase compassion and increased levels of compassion may stimulate the soothe system which is thought to be sub-served by the neurohormone OXT (Gilbert, 2010). CMT is a branch of Compassion Focused Therapy (CFT). The theory behind CFT will be explored below.

1.5. Self-compassion: Theoretical foundations and empirical support

This section will explore theoretical and empirical aspects of self-compassion, self-criticism and reassurance.

Research efforts in the western world have begun to study self-compassion, a construct borrowed from Buddhist philosophy (Neff, 2003a, Gilbert, 2009), and its utility in psychological practice. Early empirical evidence has shown that those scoring high on self-compassion also score high on other associated variables such as social connectedness, greater health and wellbeing, higher emotional intelligence, greater life satisfaction and are happier, less anxious and lower feelings of shame, guilt and burnout. (Barnard & Curry, 2011; Gilbert et al., 2007; Neff et al., 2007; Williams et al., 2008).

An ever-growing evidence base has shown strong correlations between self-compassion and psychological well-being (Neff et al., 2003; 2007) which has spawned another area of investigation which questions if self-compassion can be increased and if so, then what the mechanism might be and whether high self-compassion may also result in a reduction in clinically significant scores of psychopathologies. Researchers and clinicians alike have shown keen interest in the development of interventions (e.g. Compassionate Mind Training) which aim to increase self-compassion and focusing on specific aspects of existing therapies which have an emphasis on facets of self-compassion (e.g. Acceptance & Commitment Therapy; Mentalisation Based Therapy; (Kirby et al., 2017). This section aims to conceptualise and define self-compassion and distinguish it from other constructs of "*Self*" whilst reviewing empirical work on other psychological constructs related to self-compassion. Variables with strong associations between self-compassion and well-being would highlight the need for interventions which increase self-compassion.

1.5.1. Historical Roots

Research efforts have provided a wealth of empirical evidence examining empathy and “compassion for others” and similarly exploration of *self*-compassion is expanding at a rapid rate. Buddhist literature states that a requirement for compassion is the desire to ease the distress in oneself as well as in others (Neff, 2003a; Neff, 2003b) while the Tibetan word “tsewa”, which translates as “compassion” does not distinguish between compassion for oneself or for others. Therefore, some western research efforts are constructing a theoretical and empirical understanding of self-compassion.

1.5.2. Conceptualisation and components of Compassion

The efforts of many researchers have aimed to define Self-compassion. The sections below will explore the two leading conceptualisations of compassion as proposed by Dr. Kristin Neff and Prof. Paul Gilbert respectively.

To being with, Kristin Neff (2003a) has defined self-compassion as a construct of three major bipolar-components which are all related to each other and are manifested during times of pain and distress. The three components being (1) kindness to oneself and understanding of oneself in lieu of being self-critical, (2) viewing one’s imperfections as part of a common human condition instead of being an isolated experience to that individual, and (3) having a mindful outlook to one’s pain and distress instead of evading the distressing situation or catastrophizing (Neff, 2003b).

Terms of use should also be clarified at this stage. Self-criticism in this study is composed of self-hate and self-Inadequacy. The concept of self-reassurance is also prominent throughout this thesis. Self-criticism and self-reassurance are discrete entities and are not regarded to be positive and negative poles of a single construct. Self-reassurance is distinct from self-compassion, however “*even if self-compassion and self-reassurance have been described as different constructs, they are both ways of relating to oneself with care and concern in the context of personal short comings, failures, and life struggles*.” (Petrocchi et al., 2019; Pg. 2). Similar views are held by Hermanto & Zuroff (2015, Pg. 1) use the terms self-compassion and self-reassurance interchangeably and state "*Self-compassion and self-reassurance are ways of relating to oneself with care and concern in the context of personal inadequacies, failures, and difficult life struggles.*" This piece of research will adhere to the conceptualisation of Compassion by Paul Gilbert who defines self-reassurance as *"…the ability to be kind, caring, and supportive to oneself in the face of setbacks*" Gilbert et al., (2004, Pg. 3). The following section below will elaborate on the three bi-polar components (Sections 1.5.3. – 1.5.5.).

1.5.3. Self-kindness and Self-judgement

Both Gilbert et al., (2005) and Neff (2003a) agree that self-kindness encompasses empathy, warmth and sensitivity to all facets of oneself and one's actions, feelings, thoughts and behaviours. Those considered to be self-kind see their worth as unconditional (Rogers, 1961, Maslow, 1968). Despite life's setbacks, self-kindness incorporates affirming that one is deserving of happiness, compassion, joy and affection.

Juxtaposed to this is self-judgement which comprises hostility to oneself and an internal dialogue flavoured with self-criticism (Neff, 2003a). Self-judgemental individuals tend to discard their own feelings, impulses, desires and thoughts as well as their self-worth (Brown, 1998). These individuals often state that such feelings "feel natural" and so may be unaware or "acclimatised" and find it difficult to change to new ways of thinking, feeling and relating to themselves (Brown, 1998). It has been said that increasing self-kindness is a process of increasing self-awareness of judgements towards oneself and the damaging effect it can have (Gilbert & Irons, 2005). Thus, the journey towards self-kindness involves first cultivation of awareness towards self-judgement (Gilbert & Irons, 2005).

1.5.4. Common Humanity and Isolation

Philosophical treatise from the Buddhist culture state we are all connected in some way and to consider oneself as distinct from this connection is illusory. We all long for connectedness. (Brown, 1998). Common humanity is essentially the recognition of this connection and more so a reminder during times of pain, disdain and despair. It also involves forgiving oneself and accepting of the limitations of being human and the imperfections that entail (Neff, 2003a). In reality, the majority of people during times of despair will feel isolation. This is particularly true for those living with chronic pain as there are accompanying mobility issues often associated with the condition (Mort & Philip, 2014). Again, this is also true for those facing substance use disorders as addiction often has taboos imposed by the culture and society the individual lives in (Hammersley et al., 2002). Thus, those who deem themselves to be failures or shameful will usually withdraw and isolate themselves. This can be physical isolation or isolating certain negative thoughts from themselves and end up with feelings of struggle, inadequacy or hate (Dinger et al., 2014).

1.5.5. Mindfulness and Over-identification/Avoidance

Mindfulness has become ever popular and fashionable in recent times since its spread to the western hemisphere where it has been transformed into audio tapes, YouTube videos, mobile apps and celebrity endorsement. Mindfulness pertains to applying an acute awareness whilst focusing the attention towards accepting the present moment (Shapiro et al., 2005). Mindfulness includes cognitive attention and blends this with warmth to that present experience (Kabat-Zinn, 2003). The practise also requests one to observe and label one's thoughts and emotions rather than reacting to them, thus one is observing and sorting one's feelings in that present moment. Mindfulness is thought to aid in reaching a richer experience and gain insight from the present moment without the distracting thoughts of self-judgment or anxieties relating to events other than those of the present moment (Neff, 2003a).

Over-identification and avoidance are two ways in which mindfulness is said to be hindered. Over-identification according to Gilbert et al., (2006) and Neff et al., (2009) involves the rumination of limitations within oneself and can lead to tunnel vision which halts experiencing the present moment. Those who often engage in over-identification tend to augment and amplify the impact and consequences of a failure (Shapiro et al., 2007). Similarly, avoidance of negative experiences which lead to distress tend to deepen and exaggerate the associated negative affect aroused through times of perceived failure (Kabat-Zinn, 2003) and the effects can be chronic (Germer, 2009).

1.5.6. The Self-compassion Scale

These 6 components (Self-kindness, Self-judgement, Common humanity, Isolation, Mindfulness, Over-identification/Avoidance) form subscales in the self-report measure devised by Neff (The Self-Compassion Scale (SCS)). The SCS has shown to have good reliability and internal consistency of both the total scale and the subscales within a student population (Neff, 2003; Neff et al., 2008). Finally, the convergent validity of the SCS total score has been linked to measures of neuroticism, rumination and self-esteem which are regarded as being theoretically related constructs. Results from a study conducted in a student sample showed strong positive correlations with observed self-esteem and a significant negative relationship with neuroticism and rumination (Neff, 2003; Neff et al., 2007).

The SCS does not, however, come without criticism. Confirmatory factor analysis (CFA) has been used by researchers to test the SCS's factor structure which have shown differing opinions. A particular study confirmed the six-factor structure with a higher-order factor of self-compassion when tested in a student population (Garcia-Campayo et al., 2014). However, other research groups have tried to replicate the six-factor structure but failed to demonstrate evidence for a higher-order factor within community samples which concludes that the six subscales cannot be totalled and equated as a score for overall self-compassion (Petrocci et al., 2014). Furthermore, a recent study (Williams et al., 2014) stated that none of the models could be replicated in a sample of those diagnosed with depression or from within a sample derived from the local community. This research group also employed a CFA test on a single factor model where each of the six items were loaded into an overall factor of self-compassion and still failed to find a statistically significant fit.

1.5.7. Components of self-compassion and their relationships

Research efforts exploring the relations between components of self-compassion remain sparse. Neff (2003b) proposes some formulation to this but even this remains relatively succinct. Neff fails to clarify whether the three bi-polar components are inherently or definitively associated with each other or whether they stimulate, create, moderate or modulate each other. At a minimum, they enhance each other. More so, the precise combination of these three bi-polar facets of self-compassion, according to Neff, which aim to be distinct from other views of self-compassion will be discussed below (Neff 2003a, 2003b).

The immediate question which arises is whether an individual(s) can be self-compassionate should one of the three facets (self-kindness, mindfulness, common humanity) be absent or merely lacking in strength (underdeveloped). It seems plausible that all three components work together when compassion is directed within (to oneself) or outward (to others) as this often requires being in a state of pain, having an awareness of that pain whilst not avoiding it and possessing a state-of-mind which aims to relieve oneself of the pain (Kabat-Zinn et al., 1985; Costa & Pinto-Gouveia, 2011). For this reason, it becomes a challenge to view, and explore, the constellation of self-compassion as having mutually exclusive components. While one can intuitively see how the three bipolar components can facilitate each other much more empirical research is needed to examine such relations. One possibility is via factor analysis (Lawley & Maxwell, 1962) whereby one could ascertain whether self-compassion is a higher order factor comprised of all three first level factors. Should this be the case then the next step would be to query if the various factors provide equal contribution to the higher order factor with regards to factor loadings. Furthermore, research studies employing this concept of self-compassion could employ an intervention in order to ascertain whether increasing one factor (e.g. common humanity) will also cause an increase in the other factors. This methodology would aim to address current concerns and in turn further our understanding on conceptualising self-compassion.

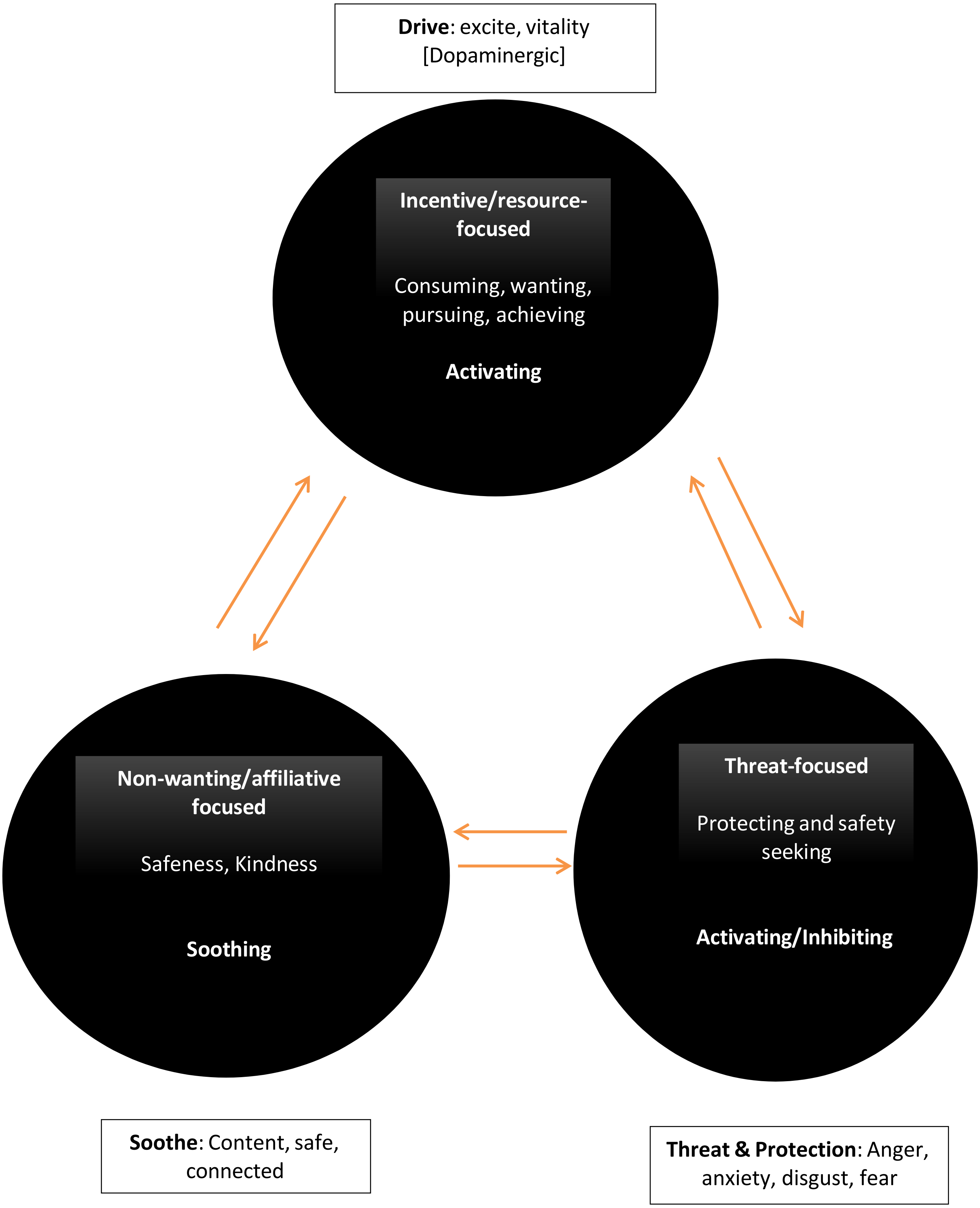
Definitions of self-compassion, however, vary. The self-esteem cognitive therapists McKay & Fanning (1992) view self-compassion as understanding, acceptance and forgiveness. From a social psychology and Buddhist tradition, Neff (2003a; 2003b) sees compassion as consisting of three bi-polar constructs related to kindness, common humanity and mindfulness. Kindness involves understanding one's difficulties and being kind and warm in the face of failure or set-backs rather than harshly judgemental and self-critical. Common humanity involves seeing one's experiences as part of the human condition rather than as personal, isolating and shaming; mindful acceptance involves mindful awareness and acceptance of painful thoughts and feelings rather than trying to force them away or deny them. Compassion-focused therapy focuses on the skills and components of compassion which are discussed below (Gilbert, 2010).

1.5.8. The origins of CFT and CMT

CFT and CMT were initially produced from consistent observations (Gilbert, 2009, pg. 199). Initially, clients who expressed high degrees of shame, guilt and/or self-criticism were observed to have great difficulty in being kind to themselves. They also had difficulty with expressing self-compassion and had a significantly lower repertoire of thoughts which would constitute self-reassurance in times of distress and pain. Additionally, it is well established that abuse, neglect and various traumas can give rise to shame and self-criticism later in life (Andrews, 1998). Those who have had the misfortune to have experienced the aforementioned trauma during early stages of development are shown to have higher sensitivities to threat and rejection and are more prone to having a self-critical internal dialogue with themselves in times of distress and "they experience their external and internal worlds as easily turning hostile" (Gilbert., 2009).

A pivotal finding from early clinical observations was that many clients who expressed high levels of shame, guilt and self-criticism were able to understand the logic of the CMT exercises and the logic imbued by the clinician but had difficulty in accessing and generating feelings of safeness and warmth towards themselves and/or to others i.e. they had difficulty accessing the "Soothe System" (Gilbert et al., 2005). In order to help clients feel less self-critical and more self-reassured, Gilbert et al., (2005, 2006, 2009) sought to unravel the neurophysiological circuitry underpinning this affect system and produced "The Three Circles Model" as shown in Figure 5 below.

Figure 5 The Three Circles Model



The three circles model (Figure 5; adapted from Gilbert, 2009) is a depiction of how our emotional systems allow us to feel reassurance, warmth and safety. Neurophysiological studies examining emotional systems (Panskepp, 1998) have shown that it is possible to differentiate at least three distinct, but synergistic, emotion regulation systems and protective systems. The sections below will outline the three systems which constitute the three circles model.

1.5.8.1. Circle 1: The Threat and Protection System

The neurophysiological underpinnings of the threat and protection system, which exists in all living beings, has begun to be well characterised through advances in modern research techniques (LeDoux 1998). The primary aim of this system is to translate threats into emotions (e.g. anxiety and fear). These feelings then prepare us for action towards the perceived threat/threatening situation. Such actions can include fight, submission or flight (Gilbert, 2001). The recruitment of serotonergic synapses plays a prominent role in this system and both pre- and post-synaptic neurons have been known to recruit more receptors in times of threat and show sensitisation to threats (Osinsky et al., 2008). This also permits for a system that is malleable or 'plastic'. It is thought that early life events such as childhood trauma, abuse or neglect may lead to this hypersensitisation of the system. Behaviourally this may lead to the development of coping strategies which are switched on automatically (Caspi, 2006).

Some coping strategies can cause individuals to become submissive and hyperaware of social status, power and rank within their surroundings and may see themselves as mediocre or sub-standard. In social contexts this can cause one to feel heightened anxiety and a greater propensity to engage in "people pleasing" behaviours (Gilbert 2005, 2007). These behaviours, which may appear to be beneficial to the individual, have actually shown to lead to low self-esteem, lowered motivation towards the pursuit of goals and prone to anxiety (Gilbert, 2009). These strategies can augment the way in which an individual views and manoeuvres within the social landscape.

The trained CFT practitioner aims to formulate by examining the client's functional symptoms and the problems associated with their coping mechanisms. The practitioner will however stress to the client that their pathology is through no fault of their own but will explain the pitfalls of their coping strategies (Gilbert, 2010). It is from this position that compassion can begin to emerge as clients reduce the frequency of their self-condemning and self-critical thoughts. Only then is the client able to practise the application of new coping mechanisms and/or think of new ways to cope better with existing feelings by developing a new relationship with their thoughts (Gilbert 2002; 2005; 2009).

1.5.8.2. Circle 2: The Drive System

The pursuit of nutrition, nesting areas and mating partners, to name a few, are required by almost all living animals and it is their emotional systems which aid greatly in these tasks (Mellor, 2012). This emotional system is also activated when humans attain their favourite foods, attain a preferred mating partner and even the consumption of drugs (e.g. nicotine, alcohol, opiates). This system aims to navigate us towards our desires and goals in life (Depue, 2005) and is linked with feelings of excitement, joy and pleasure. These fleeting feelings of choosing small rewards in lieu of larger rewards obtained later in time is a hallmark feature of impulsivity (Madden et al., 1997) and in Buddhist teachings these feelings of pleasure will give us feelings of temporary pleasure but not ultimate happiness (Zsolnai, 2011).

The Threat/Protection system and the Drive system are thought to interact and coregulate each other through complex patterns of neurochemical activation and deactivation. Some individuals may have an overactive Threat detection system which may lead to feelings of anxiety (Gilbert, 2001; Le Doux, 1998; Panksepp, 2010).

Those who are motivated to choose immediate rewards and chase social status with the aim of appeasing feelings of subordination and/or self-inadequacy may feel strong desires to constantly demonstrate and express self-worth within their social environments. Such a cycle of thoughts, feelings and behaviours are thought to be manifested by the drive system (Depue & Morrone-Strupinsky, 2005) and are fuelled by the expectations of the society within with the individual resides (Pani, 2000). This can include influences from friends, family members and more recently, social media (Meshi et al., 2015). In the context of chronic pain, many sufferers claim to feel isolation and lack of purpose in their lives .These new feelings are usually distinctly different to feelings they had prior to diagnosis, particularly with those who are home-bound (Wolf & Davis, 2014). Such a situation gives less opportunity for one to achieve their desires and goals and in CFT the therapist explores these goals and what may happen if set-backs occur. The therapist will then categorise these thoughts as either self-critical (self-hate, self-condemning or self-inadequacy) or as self-compassionate (self-reassuring thoughts, talking to oneself with warmth). It is the “tone” and texture of these thoughts which is important (Kupeli et al., 2013; Gilbert., 2009).

1.5.8.3. Circle 3: The Soothe System

Where both the drive system and the soothe system produce positive affect, they produce a distinctly separate repertoire of emotions. The soothe system produces feelings associated with contentment which gives rise to a sense of peace, comfort and security (Gilbert, 2010). A state of content achieved by activation of the soothe system, according to Gilbert (2009), is activation of a system that mediates well-being; possibly via Oxytocinergic and/or Opiatergic neuronal pathways and should not be regarded as merely hypo-activity of the drive system.

Principles of CFT borrowed from the research of Attachment Theory (Bowlby, 1969) reason the soothe system to be fashioned from behaviours given to us from a primary care giver (cooing, stroking, skin-to-skin contact) which have a soothing effect on the recipient’s neural architecture.

These interpersonal interactions have been well studied and documented to highlight the role of the autonomic nervous system which has adapted in ways that facilitate such interactions themselves and to produce a soothing and content feeling within both organisms (Porges, 2007; Gilbert 1989, 2007, 2009). The principal neurotransmitter substance of the soothe system is thought to be Oxytocin (See section 1.4.2.3.).

1.5.9. Conceptualisation and Formulation of Self-Compassion according to Gilbert

Gilbert (2010) conceptualises compassion in evolutionary terms, stating that compassion is an evolved motivational system intended to control negative affect, where compassion is seen to have originated from similar origins that primates evolved to form attachment bonds and engage in affiliative and supportive behaviours for group survival. He defines compassion as: "*A deep awareness of the suffering of another coupled with the wish to relieve it*" (Gilbert, 2009, p. 13). While the above attributes of self-compassion are principally derived from the works of Neff (2003a), Gilbert (2005; 2009) has also formulated his own unique brand of what compassion is. Gilbert (2005; 2009) regards compassion to be a composed of the following six elements:

1. Sympathy

Possessing sympathy is when an individual is emotionally stimulated by feelings and suffering of others for whom they care about. Within a clinical context, a therapeutic alliance equates to a client being able to experience the clinician as being emotionally integral with themselves in lieu of being affectively disengaged (Decety & Chaminade; 2003).

2. Distress Tolerance

Being able to handle distress is the ability to adequately deal with fluctuations in emotions and the ability to deal with the extremes of these. Those said to possess skills in distress tolerance usually make little attempt to reduce feelings of emotional discomfort. Skills in distress tolerance help one to overcome an emotional crisis and aid us in times of short term and chronic pain (physical and emotional). Distress tolerance is said to be composed of the following attributes:

- Tolerance of uncertainty, or "the tendency to react emotionally, cognitively, or behaviorally to uncertain situations" (Buhr et al., 2002; Page 3).
- Tolerance of ambiguity, or "the perceived tolerance of complicated, foreign, and/or vague situations of stimuli" (Bernstein et al., 2009).

- Tolerance of frustration, or "the perceived capacity to withstand aggravation (e.g. thwarted life goals)” (Leyro et al., 2016).
- Tolerance of negative emotional states, or "the perceived capacity to withstand internal distress” (Simons et al., 2005).
- Tolerance of physical sensations, or "the perceived capacity to withstand uncomfortable physical sensations” (Schmidt et al., 2006).

Recent research findings show that the activation strength of Dopaminergic neurons connecting with the nucleus accumbens, ventral striatum, and prefrontal cortex is related to an individual's predicted value of an immediate reward during a learning task (Ikemoto, 2010). As the firing rate for these neurons increase, individuals predict high values of an immediate reward. Interestingly, these neural regions also play a key role in regulating impulsive behaviours and these connections are weaker in those with SUD. This could implicate that building skills in distress tolerance may aid in recovery from SUD and/or help reduce impulsive decision making (Anestis et al., 2012) and particularly if there is the influence of negative affect. Thus, exploring Negative Urgency (acting impulsively when feelings of negative affect/distress are aroused) would be of great importance and its implications for dependence to painkillers are outlined below (Chapters 3, 5 and 6).

3. Empathy

Possessing empathy is regarded as being appreciative to another person's thoughts, feelings, and situation from their point of view, rather than from one's own. Empathy is thought to assist in prosocial behaviour’s that come from within an individual, rather than being forced, so that one is able to act in a more compassionate manner. While genetic differences give rise to individual differences in the ability to adopt an empathic stance (Knafo, & Uzefovsky, 2013), research suggests it is possible to boost the capacity for empathic understanding (Kramer et al., 1989).

Having empathy is relevant to the focus of this thesis as studies have shown that those deemed as “multiple substance abusers” are more impulsive and less empathic compared to “single substance abusers” and control group participants. There also existed a negative correlation between levels of substance abuse and empathy (McCown, 1988).

4. Non-judgement

This attribute is borrowed from the realms of Buddhist teachings where we learn to experience the present moment "as it is". It is also a key component in Vipassana meditation. It also involves one striving to be less critical, less shaming and non-condemning. This does not mean to say that one's thoughts should be absent from having a preference.

5. Care for well-being

This component entails one to be more caring with the aim of reducing emotional lability, discomfort and pain.

Research findings from Dunkley et al., (2006) showed self-criticism to reduce well-being while increasing risk for depression. Self-compassion and self-reassurance boosts well-being by "giving up harmful behaviours to which one is attached and encouraging oneself to take whatever actions are needed - even if painful or difficult - in order to further one's well-being." (Neff, 2003a, p. 88). Self-compassion is a strong predictor of sound well-being (Neff et al., 2007). Furthermore, a meta-analysis between the relationship between self-compassion and well-being showed self-compassion to be highly correlated with cognitive and psychological well-being than with affective well-being (Zessin et al., 2015).

6. Sensitivity

This component is defined by an individual who demonstrates awareness and is generally in tune with their distress and pain and is also able to label and differentiate their experienced feelings and needs.

These six elements form the basis of Compassion Focused Therapy (CFT) and Compassionate Mind Training (CMT) which was originally devised for populations suffering with high shame, high levels of guilt, aberrant responses to negative affect and self-criticism (Gilbert & Proctor, 2009).

Thus, self-compassion and its components may be defined in more than one way. In CFT, self-compassion is understood in terms of the attributes and skills outlined above (Gilbert 1989, 2005a, 2007, 2009) and form the basis of CFT and CMT in a therapeutic context. The section below outlines the origins of CFT and CMT.

1.5.9.1. Attaining system equilibrium

A further premise of CFT is that the three facets of the three-circle model can become desynchronised or unstable (Gilbert, 2009). The system is thought to become destabilised when the threat/protection system and the drive system enter a state of hyperarousal as is seen in those who score highly on scales of self-criticism. Therefore, bringing about synchronicity, and subsequent stability, between the three facets of the model is a core objective for CFT and CMT (Gilbert, 2010). It is thought that the soothe system in these self-critical individuals becomes difficult to access and activate which may possibly be due to early life experiences which would have stunted its development. These early life experiences include, but are not limited to trauma, neglect and abuse. Theoretical and empirical evidence from Attachment Theory states these individuals mature into adults who express higher than average levels of anxiety and avoidant personality types (Mikulincer 2007). In addition, these individuals have difficulty in feeling soothed and reassured, even when they self-generate thoughts which would usually bring about feelings of calm and content as it is the soothe system that is responsible for these feelings (Gilbert 2005; 2010).

Hypothetical examples of when the three circles model becomes unbalanced, what the effects are and how they can be remedied will now be briefly explored. Hypothetical situation 1: High Threat + High Drive + Low Soothe. This situation leaves individuals driven by the need to avoid risk, improbability or dangerous threats. This leaves them feeling anxious, constantly hyper-alert and emotionally exhausted (burnout). Hypothetical situation 2: High Threat + Low Drive. This leaves the individual in a state of hopeless anxiety. There would be feelings of depression about their anxiety and the negative feelings surrounding inability to escape distress. This is associated with generalised anxiety and depression.

Attempts to subdue our sensitivity to threats are difficult however cultivating resilience and self-reassurance can help us to better manage the threats. The threat/protection and the soothe system have a reciprocal balancing effect (Gilbert, 2010). When individuals acquire and apply skills in self-compassion and CMT, they develop personal resilience; reduce negative perceptions and moderate reactions to threat. Achieving long-term balance between the three circles is about strengthening the soothe system whilst maintaining healthy levels of the threat/protection system and the drive system. Developing the soothe system means to develop a more self-reassuring attitude, being able to self-soothe, accept, acknowledge that "it's not always our fault". Simultaneously, we don't want to ignore threats, nor do we want to lose drive and ambition in life.

It is important to note at this stage that CMT prescribes precise interventions used to activate the affiliative soothe system. The model and theoretical underpinnings behind CMT are based on an evolutionary and neuroscientific background which aims to explain how the repertoires of affiliative emotions have evolved to regulate threat-processing and the attached motivation.

1.5.9.2. The skills of compassion

Gilbert (2009; 2010) provides a skill-set made of six components which aims to produce sensations surrounding inner warmth, compassion and gentleness for the individual and also for others. It is deemed vital that those engaging in CFT/CMT learn to use these skills on themselves as it is commonly revealed that those with high shame, guilt and self-criticism will often employ an aggressive and critical inner voice to try and teach themselves these skills. Therapists trained in CFT/CMT would aim to alter this self-critical tone into a more self-reassuring, calming and soothing tone. This feature of CFT/CMT will be explored later in the thesis and will form an integral part of the online CMT intervention. The section below will outline the six components which, according to Gilbert (2005; 2009) make up the "skills in compassion."

1. Compassionate attention

This skill involves directing one's attention in a manner that aids and benefits our psychological well-being and can involve conjuring up images of compassion in the mind's eye. When in times of struggle with others we tend to look past the positive attributes that person may bring to our lives (Blanton et al., 2001) and so by re-aligning our attention this skill trains us in seeing the situation from a broader and well-adjusted perspective. It is also important that one realigns their attention whilst also injecting feelings of compassion into this realignment process (Gilbert, 2010). Clients will often have their personal strengths and skills highlighted by their CFT practitioner and so it is important that one who is trying to realign their attention becomes aware of these positive attributes as training in this skill also requires one to be mindful of them. They can do this by conjuring up memories which bring feelings of positivity and achievement.

Many therapeutic modalities have similar explanations in that the threat protection system is constantly directing attention to potential negative outcomes, hurdles and barriers in life and so individuals who are hypersensitive to this will benefit by re-aligning their attention on positive outcomes and solutions in hope of freeing themselves from such self-destructive thought patterns (Burkland et al., 2017). This can be achieved by having individuals reframe their thoughts by making a negative response to a scenario into a positive, encouraging and self-reassuring response (Lambert et al., 2012). This concept will also be encouraged to those who engage in the online intervention.

2. Compassionate reasoning

With compassionate reasoning there is an emphasis on knowing that logically understanding the concepts of CFT/CMT is usually insufficient to engage with the therapeutic aspects of CFT/CMT. This statement arose from clinical observations (Gilbert, 2009; 2010) in that clients would often state that "I understand the logic of the exercise, but I still do not feel it."

This skill also facilitates the client in thinking about how we construct our social environments, our working environments and oneself whilst developing a mind capable of balanced reasoning. This statement is not exclusive to CFT/CMT but is evident in other therapeutic modalities (Beck, 1972; Fonagy, 2006).

Thinking about current affective states is important too. Self-critical thoughts are obvious targets of CFT/CMT however it is imperative to understand and recognise the role of possessing a self-critical inner voice and the pitfalls individuals may face when the prospect of changing this inner voice arises. Thus, it is the aim of the CMT intervention to teach the client about the dangers of this self-critical voice and how one can alter this to a more self-reassuring voice by recalibrating one's reasoning (Mayhew & Gilbert, 2008). Again, these skills are taught to participants in the CMT group via psychoeducation videos and interaction with CMT software (Studies 2 and 3; Chapters 5 and 6).

3. Compassionate behaviour

This skill helps the client to reduce feelings of psychological distress and enabling richer development for being more self-compassionate (Gilbert, 2009). It is important to note that the client is not simply taught avoidance strategies, stabilising the threat system or devising new defence mechanisms, rather it is a collaborative approach between client and therapist whereby stimulating positive affect is the aim. The client is encouraged to use a warm, soothing and compassionate tone with themselves; use compassionate imagery, where necessary, and to employ a behaviour (e.g. rationing or keeping the recommended daily allowance of painkillers in a pillbox instead of keeping the whole tub of painkillers nearby) to help alleviate oneself in times of distress (e.g. when cravings for detrimental substances may appear; when in times of experiences severe pain; times of despair). Ideally, compassionate behaviour tasks will be employed to foster feelings of positivity within the individual with the hope of allowing the client to enjoy the experience by helping them become more process-focused and less task-focused (Gilbert, 2010). This can be achieved by having individuals think more about their efforts and place less emphasis on the outcome(s).

This facilitates focusing attention on their efforts, irrespective of the magnitude of their efforts. Reasons for this are that those with high shame, guilt, self-criticism are not naturally inclined to appreciate their efforts (Gilbert & Proctor, 2006). This could be particularly useful for those living with chronic pain where all too often their efforts are not as fruitful as they would have hoped due to mobility issues.

4. Compassionate imagery

Compassionate imagery exercises are similar to method acting and involve the client develop compassionate feelings for themselves. These images can take any shape or form and can include non-human images such as animals or objects found in nature. Imagery has often been used to create compassion (Leighton, 2003; Lee, 2005) in a therapeutic setting where the client is asked to define the attributes of their "ideal compassionate image" such as what they look like, how they sound and their facial expressions. Additionally, clients may be asked to imagine themselves as being highly compassionate and then asked to explore and describe how they feel, their facial expressions and voice tone (Gilbert, 2010).

5. Compassionate feeling

Feeling compassion within oneself is described by Gilbert (2010) as experiencing compassion from others, for others and for the self. These feelings can be produced in many ways. This could include imagining a compassionate image and giving them compassion; behaving in a compassionate way; focusing attention on an experience of compassion; thinking of a time when compassion was given to the client or when the client acted in a compassionate way to another person. Thus, the client could blend skills 1-5 and produce a bespoke skill-set which could be used in times of distress.

6. Compassionate sensation

This skill is regarded as way in which the therapist aids the client to uncover and interact with their feelings within their bodies at times of experiencing compassion This can include feeling compassion for themselves, feeling compassion for others or receiving compassion from others. In combination with skills 1-5, compassionate sensation exercises aid the client in creating and becoming accustomed to feelings of warmth, reassurance and kindness (Gilbert, 2010).

1.5.9.3. Skills of compassion: concluding comments

It is well known that our thoughts and images play a prominent role in guiding our behaviour. Research has shown self-criticism (Self-hate and Self-inadequacy) to be a significant predictor towards addiction (Kelly et al., 2010) and perpetual self-critical thinking is shown to be a trans-diagnostic problem (Speranza et al., 2003). Self-hate is a disliking to oneself and is captured on the *Forms of Self-criticising and Self-reassurance* (FSCSR) self-report measure (Gilbert, 2004; Gilbert & Irons, 2005) by questions such as "I do not like being me." Self-inadequacy is a feeling of inability and is captured on the FSCSR by questions such as ""*I find it difficult to control my anger and frustration at myself.*" The FSCSR will be discussed in detail below (Chapter 2). People deemed to be self-critical have difficulties in accessing a particular affect regulation system which is associated with soothing and a contented form of positive affect (See Fig. 5 above, Three Circles Model; Gilbert, 2009; Gilbert & Irons, 2004; Neff, 2003). This system is stimulated during childhood by social signals of affiliation and care such as physical affection, soothing voice tones and facial expression. These experiences generate feelings of safeness, which are then available to the individual during times of distress (Brewin, 2006).

It is entirely conceivable that living with chronic pain provides fertile conditions for unemployment (Blyth et al., 2001), lack of purpose, social isolation, (Wolf & Davis, 2014), feelings of self-inadequacy and opportunity to consume excess painkillers as shown in study 1. Such conditions could lead towards feelings of self-criticism. Self-criticism is a common automatic response when individuals experience setbacks such as diagnosis of a debilitating health condition. Affective processes direct our behaviour in many ways. When angry, disappointed, isolated, lonely, frustrated, livid or even elated, we often *display* temporal myopia, *behave* brashly and *think* without foresight (Madden et al., 1997). These are also the hallmarks of impulsive behaviour which can potentially lead people to engage in behaviours that give temporary relief but are detrimental in the long run (e.g. substance abuse, or misuse; substance dependence, visceral malfunction, obesity and death). Essentially, self-critical thoughts may lead to impulsive actions with impulsivity being a risk factor for substance abuse and/or drug dependence (Reynolds et al., 2006).

One method to combat self-criticism is via Compassionate Mind Training (CMT; Gilbert, 2005). CMT is an integrated and multimodal strategy with roots in social, evolutionary, developmental and Buddhist psychology, and neuroscience. Gilbert & Proctor (2006, Pg. 359) state "*CMT builds from CBT and DBT approaches of psycho-education, Socratic discussion, guided discovery, learning thought and affect monitoring, recognizing their source, de-centring, acceptance, testing out ideas and behavioural practice.*" CMT incorporates evidence-based approaches for treating mental illness (psychosis, depression, trauma, self-attacking thoughts) by applying powerful change strategies in ways that are designed to help reduce self-criticism and promote self-compassion (Gilbert, 2009). The six skills of compassion outlined above feature heavily in the CMT exercises and the application of these skills were encouraged in the psycho-educations in studies 2 and 3 below. The CMT exercises focused on building compassionate imagery, developing greater awareness of bodily sensations when experiencing compassion and fostering self-reassurance.

CMT aims to quash self-critical thoughts and equips one to think in a balanced way and stimulate positive affect processing so that we are not too emotionally biased in our decision-making processes and resulting behaviours (Gilbert & Irons, 2004). A principal objective of CMT is to facilitate acquisition and development of a healthy relationship with experiences of inner warmth, safeness and soothing, via self-compassion. CMT functions to help people become more attentive, or mindful, to their streams of consciousness. The goal is to alter the relationship with thoughts, rather than change the thoughts themselves and to consciously stimulate the Soothe system by developing inner empathy, understanding, kindness, compassion and warmth (Gilbert, 2005; 2009; 2010).

Longe et al., (2010) performed an fMRI study to elucidate the neural basis of self-criticism and self-reassurance. Results showed that when participants engaged in *self-reassurance*, two neural regions, the Insula and the left Temporal Pole, showed increased activity. Conversely, when participants engaged in *self-critical* thoughts the ACC and the dorsolateral Prefrontal Cortex (dlPFC) showed increased activation. In addition to self-criticism, these neural regions also play significant roles in regulating impulsive behaviours and have prominent roles in the neural circuitry that advance drug dependence. Although Longe et al., investigated self-reassurance, the study showed that neural regions activated during self-criticism are related to neural regions associated with increasing propensity for developing a SUD. Therefore, should self-reassurance reduce self-criticism then this may in turn reduce the likelihood of developing a SUD.

As stated above, those living with chronic pain are in an environment that can readily foster self-critical thoughts. Self-critical thoughts can lead to behaviours deemed as impulsive. Impulsive behaviour is a well-documented risk factor for substance dependence (i.e. painkiller dependence). Studies have showed that the neural regions associated with impulsivity, self-criticism and substance dependence are closely linked. Thus, if it is possible to reduce self-critical thoughts using CMT exercises then it may be possible that a reduction in impulsive behaviours and or/ dependence to painkillers can be achieved.

1.5.10. How CMT may reduce painkiller dependence

CMT is an element of CFT. As a working hypothesis, it can be thought that when one experiences distress, they may resort to the consumption of addictive substances (Machado et al., 2007) which are used to alleviate the distress. This is commonly seen in those who consume drugs; alcohol and cigarettes being typical examples. In those living with chronic pain the consumption of painkillers would be a relevant example. In times of distress (e.g. onset of severe pain), the threat protection system would become active and generate feelings of wanting to protect the individual from pain and keep it safe and pain free (Gilbert, 2005; 2010). In turn this would feed into the drive system and generate feelings of “wanting, pursuing and consumption” targeted towards painkiller consumption in order to alleviate the pain. When the painkillers have been consumed and their effects begin to take place and the individual is pain free then the soothe system may become active and generate feelings of the desired outcome i.e. safe and pain free. This loop of positive reinforcement is clearly detrimental in some individuals as their strategy to become pain free is to continually consume painkillers and so a dependency occurs. Painkillers by their very nature possess addictive compounds and so if one were to continually engage in such behavior then substance dependence will quickly ensue (Nestler, 2001).

Gilbert (2005; 2009) states that the goal of CFT and CMT is to balance the three entities in the three circles model. Therefore, if it were possible to create an alternative way (without the use of painkillers) to directly stimulate the soothe system then the need for excessive painkiller consumption would not be so necessary and dependence would be reduced or eliminated. One such way to stimulate the soothe system is via CMT exercises. These CMT exercises will be employed in the online intervention and are described in detail in a later chapter. Individuals who have a healthy and optimal soothe system are often found to have good skills in self-reassurance (Gilbert, 1992), which is measured using the Forms of Self Criticising and Self-Attacking Scale (FSCSR); discussed in detail in Chapter 2; Gilbert & Irons, 2005). Gilbert states "self-reassurance is the ability to be soothing, encouraging, and supportive to oneself" such as during the onset of pain (Petrocchi, 2018; Pg. 2). Research has also shown the two constructs to be highly correlated (Hermanto & Zuroff, 2016).) Therefore, to quantify the capacity of a participants' ability to self-soothe would be to assess the change in scores of self-reassurance over time (baseline, post-intervention and at follow-up). Similarly, those who have a hyperactive threat/protection system will show to have high scores on Self-hate and/or Self-inadequacy (subscales in the FSCSR scale) and so they too can be quantified. Ideally, interacting with the CMT intervention would aim to balance the three circles by increasing levels of self-reassurance so the soothe system would reduce the effect of the drive and threat/protection system which would lead to increased consumption of painkillers (and possibly dependence).

It is also well documented that high levels of impulsivity are correlated with severity of dependence and consumption of opiates (Rodríguez-Cintas et al., 2016). This relationship will be investigated in Study 1 (Chapter 3). If participants with high levels of impulsivity also have a hyperactive drive system, then one may be more prone to impulsive behaviors and decision making. Therefore, if the soothe system was to become more engaged then this could dampen the drive system should the drive system be responsible for impulsive *action*. At this stage these hypotheses remain as hypotheses and further empirical research will be needed to address the importance of these questions. Additionally, relapse prevention models (Neff et al., 2007; Yarnell et al., 2013) have begun to incorporate third-wave psychotherapeutic models (Acceptance & Commitment Therapy (MacBeth et al., 2012), Mindfulness-Based Cognitive Therapy (Van Dam et al., 2011) and Compassion Focused Therapy/Compassionate Mind Training (Krieger et al., 2013; Gilbert, 2005) as there is now substantial evidence to indicate that those who accept and manage emotional responses to external or internal stressors associated with relapse can generate positive prospects towards behavioural self-regulation such as making *less* impulsive choices which may have negative consequences (Wong et al., 2013; Kroenke et al., 2001). Self-regulation of behaviour change related to health outcomes has been found to be supported by psychoeducation that promotes emotional management and emotional regulation through self-reassuring compassionate abilities (Noorbala et al., 2013). Behavioural approaches in their third wave aim to aid individuals alter the *relationship* with their troublesome thoughts, emotions and bodily feelings in lieu of trying to change or control them, while engaging in adaptive behaviours towards effective and continued behavioural change and well-being (Martin et al., 2006). Of note, CMT aims to aid individuals to better cope with negative self-evaluations, shame and self-criticism (self-hate and self-inadequacy) through the cultivation of compassion and self-reassuring skills. Engaging in CMT inspires one to develop compassionate motivation and engagement with adaptive behaviours with the chief aim of improving well-being (Krieger et al., 2013).

A recent study set to find relationships between self-compassion and the risk of developing a SUD (Phelps et al., 2018). A sample of 477 participants were recruited from social media outlets and classified into three groups (low risk, moderate risk, high risk). Results showed that those in the low risk group had higher mean scores on self-reported self-compassion ($M = 2.86$, $SD = .75$) than the people who were high risk ($M = 2.25$, $SD = .61$; $t(298) = 5.58$ $p < .0001$)). Further analysis using Bivariate Pearson correlations highlighted a strong association between high risk and all self-compassion subscales, as well as low risk and five of the subscales (The Self-compassion Scale;

Neff, 2003; 2015). Study limitations did exist such that the sample size was relatively small, not diverse (mostly Hispanic) so there would be cultural bias introduced (See section 3.15.6. – 3.1.5.6.5.). Authors conclude by stating "raising self-compassion may be a useful addition to substance use disorder prevention and treatment interventions" (Phelps et al., 2018 pg. 438).

As this was a cross-sectional study design it is problematic to establish causality between variables. However, there are advantages to a cross-sectional design (Feldman et al., 1994) which benefit the research process such that they are relatively inexpensive and take little time to conduct, many outcomes and risk factors can be assessed and there is usually no loss to follow-up. Cross-sectional designed studies also provide descriptive statistics with the aim of describing a population, or subgroup of a population, with respect to an outcome (i.e. painkiller dependence) and a set of potential risk factors (See section 3.10.2. – 3.10.6. for potential risk factors in study 1), there is also the benefit of investigating the prevalence of an outcome of interest (i.e. painkiller dependence) within a population at a given time point. For these reasons a cross-sectional design was used in study 1 (Chapter 3).

To conclude, this section has presented theoretical and empirical evidence on the operationalisation of self-compassion. To be explicit, the research efforts contained in this thesis will pertain to the operationalisation of compassion according to Gilbert (Gilbert, 2004; 2005). This was due to the aims of the studies which were to examine the link between the way we talk to ourselves (self-reassured vs. self-critical), impulsivity and painkiller dependence. The tone of our internal dialogue can influence the way we behave, as stated above, which may include impulsive behaviour. Should this be the case then it is well known that impulsivity is a risk factor for developing a SUD (Madden et al., 1997). As the target population are those with chronic pain then they become a population who is at risk for developing a SUD to painkillers, perhaps so if they score high on self-criticism (self-hate and self-inadequacy; activation of the threat/protection and drive system). These can be captured and quantified by the FSCSR scale but more so if they score high on impulsivity. Further details on how CMT can be used as an intervention for reducing painkiller dependence and impulsivity can be found below in Chapter 4.

1.6. Overall summary

The existing literature, albeit somewhat deficient with regard to psychological dependence to painkillers, suggests that impulsivity is a cardinal risk factor when considering the onset of an opioid use disorder. Results from both animal models and human studies regard impulsivity to be a risk factor for the cause, as well as a consequence of substance use disorders (Lejuez et al., 2005; Conrod et al., 2000; Dick et al., 2010; Dolan et al., 2008; Ersche et al., 2010). Furthermore, a large body of evidence shows that impulsivity is associated with opioid-use disorders analogous (Johnson & Bickel 2002; Madden et al., 2004). Impulsivity, a multifaceted construct known to be an important component of personality that has endured evolutionary processes is also a risk factor for a range of psychiatric disorders and substance dependence (Lagorio & Madden 2005; Johnson et al., 2007). A wealth of data suggests that amplified impulsivity, including both heightened sensitivities to delay and substandard inhibitory control are significantly correlated with substance dependence across a spectrum of drugs of abuse suggesting that facets of impulsivity play pivotal roles towards addiction (Madden et al., 1997).

Studies employing animal models show that analgesic consumption leads to increased impulsivity in the rat (Kieres et al., 2004; Pattij et al., 2009). Studies in humans have also observed that opiate-dependent individuals display higher levels of impulsivity compared to controls (Kirby et al., 1999; Nielsen et al., 2012; Robles et al., 2011). Examining the relationship between impulsivity and painkiller dependence within the chronic pain population provides a unique opportunity to examine such a risk factor.

As painkillers are often an appropriate course of treatment for chronic pain, a fuller understanding on the role of self-compassion, self-criticism and impulsivity towards the development of painkiller dependence will aid addiction prevention strategies. Although the expanding body of evidence ties impulsivity to substance dependence, a full comprehension of the complex relationship is yet to be elucidated.

Data derived from self-report measures (e.g. UPPS-P) to differentiate drug abusers from non-abusers adds weight to the theory that individuals with elevated trait impulsivity are at higher risk for developing a SUD (e. g. Swann et al., 2004). This conclusion is based on the principle that such measures are usually deployed to quantifiable long-term behavioural traits. Sadly, however, participants classified as abusers in most studies were not abstinent during the time when the self-report measure was administered (Moeller et al., 2002). Due care must therefore be granted when interpreting these results as there exists the likelihood that elevated scores were in fact due to being in a state of withdrawal or the acute residual effects of the drug(s) itself. Studies that have made use of behavioural measures, viewed to be being more sensitive to subtle changes in impulsivity, have disseminated data to suggest elevated impulsivity could be a result of chronic drug consumption. The level of impulsivity that increases is thought to be linked to factors such as basal level of impulsivity, dose and length of exposure. Leading authors have concluded too that a bi-directional relationship exists between abstinence and impulsive choice. During the initial phase of drug deprivation, there may be an increased sensitivity to delayed gratification while long-term abstinence is observed as a reduction in levels of impulsivity (e. g. Bickel et al., 1999; Petry, 2001b).

Still to be clarified is the notion of whether low levels of impulsivity allow individuals to remain abstinent, and equally whether impulsivity can be reduced after substance dependence (Bickel & Marsch, 2001). The former of these theories have been substantiated by research findings that suggest those with elevated scores on the DD paradigm are at greater risk of future relapse (Krishnan-Sarin et al., 2006).

Enduring dysfunction in inhibitory control however has been linked to difficulties in long-term abstinence (Gourdriaan et al., 2005). These results were shown to occur in models initially implemented to evaluate attention and no direct comparison of current and long-term abstinent abusers were drawn. Irrespective of this, should chronic drug consumption stimulate impulsive responding, then data suggests that regarding inhibitory control such effects may persist for longer subsequent to abstinence. Conversely, it is also plausible to suggest that a dysfunction in behavioural control could pre-exist drug consumption and thus comprise a risk factor for SUD.

Studies that focus on the neurobiological processes that govern impulsivity claim that the adaptations of dopaminergic, serotonergic and oxytocinergic pathways allied to chronic drug abuse act as mediators for elevated impulsivity within this sample of individuals. The neurotransmitters and processes at the core of this relationship are intricate and convoluted. There also exist specific roles of receptor subtypes that mediate both impulsive decision-making and disinhibition. Two well characterised receptors, namely 5-HT_{1A} and D2, adopt cardinal roles and could provide targets for pharmacological therapy (Liu et al., 2004; Dalley et al., 2007).

An expanse of evidence proposes that aberrations in the PFC and VS, areas considered key in addiction, are regulators for the loss of control and sensitivity to delayed gratification in those with a SUD (Jentsch & Taylor, 1999; Cardinal et al., 2001). Particular zones within the aforementioned structures are differentially linked with both facets of impulsivity, thus imparting further evidence for the dissociation at the neural level (Uslaner & Robinson, 2006). Whether or not the anomalies in neurobiology translate to a biological trait vulnerability resulting in elevated impulsivity and consequently a SUD or abnormalities resulting from chronic drug consumption promote disinhibited behaviour and impulsive decision-making resulting in maintenance of drug use is yet to be clarified. To date, evidence is available for both directions (Levy et al., 1993; Dalley et al., 2007).

It remains imperative that future research takes on a prospective design allowing for causal extrapolations to be made surrounding the issues between impulsivity and drug use and drug dependence. Studies that aim to assess and quantify facets of impulsivity both before, during and after chronic drug consumption will permit investigation regarding the magnitude of impulsivity as a risk factor for developing a SUD as well as the effect drug consumption has on impulsivity. In a similar vein, the state of impulsivity from withdrawal through to long-term abstinence should be quantified to reveal the potential role of impulsivity in episodes of relapse and to elucidate whether drug induced changes in impulsivity are perpetual. The after-effect of such research in the field of addiction would be considerable. If impulsivity is unequivocally considered to be a risk factor for the development of a SUD, then individuals can be screened and a preventative stratagem can be implemented. Should it be made resolute that substance abuse augments impulsivity then psychotherapeutic and pharmacological actions can target impulsivity in the hope of leading to an effective intervention for SUD.

Regarding research in humans, longitudinal methodology will permit resolute answers to flourish and clarify the issue of causality between impulsivity and addiction. A pilot study has shown a relationship between DD rates and the likelihood of becoming a smoker. A sizable number of participants were incorporated in the study and were followed from the age of 15 to 21. Results showed that the level of DD was reasonably stable when measured repeatedly over a 3-year period. More intriguing was that those with high DD rates had an elevated probability of becoming a smoker and that taking up smoking did not affect the DD rate. Thus, the DD task presents itself with possessing predictive prowess and highlighting that elevated DD rates being a long-standing pre-existing risk factor able to predict indulgence in cigarette consumption as opposed to it becoming altered as a consequence of smoking tobacco (Audrain-McGovern et al., 2009).

The significance of pre-clinical studies as an endeavour to expose the intricacies of the relationship is of paramount importance, as it will offer the prospect to investigate neurobiological processes governing the relationship between impulsivity and states of drug addiction.

1.7. Hypotheses and Research Questions

The aims of this piece of research is to discover whether facets of cognition (e.g. self-reassurance; impulsive decision-making) act as risk factors for psychological dependence to painkillers. Impulsivity, as explained above has been known to be a risk factor for dependence to a menagerie of addictive substances and processes such as gambling, shoplifting and dangerous driving. It is not yet known whether impulsivity may play a role towards addiction of painkillers; however, it has been shown to heighten susceptibility for addiction to its pharmacological cousin Heroin. Therefore, there is a high degree to plausibility that impulsivity may well be a risk factor for painkiller dependence. Should this be the case then it would be essential to know which facets of impulsivity are responsible.

In addition to cognitive impulsivity, there exists the possibility that behavioural impulsivity may also play a role towards the progression of an addictive state to a substance and so this too should be explored. To answer this query, this study will use a behavioural measure of impulsivity (Delay Discounting Task) to ascertain whether this too would act as a risk factor for dependence to painkillers. Previous research has shown elevated scores on the Delay Discounting Task to be positively correlated with the degree of dependence to a substance.

- The first major hypothesis is that certain facets of impulsivity (cognitive and/or behavioural) will act as progressive risk factors towards psychological dependence to painkillers.

In addition to impulsivity, these studies will be exploring self-critical thought patterns in those living with chronic pain. A large number of the chronic pain population are usually living within the confines of their homes and isolated due to their condition. This provides an environment for developing self-critical thoughts in cases where sufferers may feel disconnected from society, have reduced social interaction and may feel their role in life is not as fulfilling as it once used to be. Over time this may lead to the development of their thoughts being self-critical in nature, which results in low mood (negative affect). Low mood in conjunction with boredom and isolation provides fertile grounds towards dependence of their painkiller medication (Kelly et al., 2010; Longe et al., 2010).

- The second major hypothesis is that self-reassuring thoughts will (a) have strong associations with some facets of impulsivity and also with painkiller dependence, and (b) self-reassurance will decrease the likelihood of painkiller dependence by acting as a protective buffer.

As a concluding research question, these studies aim to clarify how impulsivity and self-critical thoughts may interact to produce a state of painkiller dependence.

The following chapter will outline the measures used throughout this piece of research.

Chapter 2. Measures used throughout Studies 1 to 3

After collecting demographic data (Appendix A) a series of evidence-based self-report measures were administered in all studies. Copies of these can be found in the appropriate appendices.

2.1. Cognitive Impulsivity

Impulsivity was measured using the UPPS-P (Appendix B) self-report measure (Lynam et al., 2006). The 59-item self-report assesses five subscales that are distinct dimensions of impulsivity in adolescents and adults (ages 12-80). The first dimension of the scale, negative urgency (12 items), refers to the tendency to experience strong impulses, frequently under conditions of negative affect. The second dimension, (lack of) premeditation (11 items), refers to the tendency to think and reflect on the consequences of an act before engaging in that act. The third dimension, (lack of) perseverance (10 items), refers to an individual's ability to remain focused on a task that may be boring or difficult. The fourth dimension, sensation seeking (12 items), incorporates two aspects: (1) a tendency to enjoy and pursue activities that are exciting and (2) an openness to trying new experiences that may or may not be dangerous. Finally, Positive urgency (14 items), refers to the tendency to experience strong impulses, frequently under conditions of positive affect. Whiteside & Lynam (2001; 2006) showed that the UPPS-P has good internal consistency, as well as good divergent and external validity. A rationale for using the UPPS-P is given below in section 2.2.

The scale was derived through a factor analytical method that included several widely used impulsivity scales. The five subscales/dimensions of the UPPS-P correspond to the five factors that resulted from exploratory and confirmatory factor analytic methods.

The scale is not considered a measure of trait impulsivity, rather, the scales reflect distinct personality traits that lead to impulsive-type behaviour. Participants are asked to consider acts/incidents during the last 6 months when rating their behaviour and attitudes on a 4-point scale, in which 1-Agree strongly, 2-Agree some, 3-Disagree some, 4-Disagree strongly. Sample items include "I tend to value and follow a rational, "sensible" approach to things."; "I have a reserved and cautious attitude toward life." and "When I am really excited, I tend not to think of the consequences of my actions."

2.2. Rationale for using the UPPS-P self-report measure

Impulsivity has been well established as a risk factor for the development of SUDs (e.g., Littlefield et al., 2012; Guller et al., 2015), as well as the continuation of substance use (e.g., Littlefield et al., 2009).

This piece of research captures impulsive personality using the UPPS-P (Lynam et al., 2007), which assesses impulsive personality through five separate, though related, impulsive personality traits: 1) negative urgency, or a disposition to act rashly in response to negative affect, 2) positive urgency, or a disposition to act rashly in response to positive affect, 3) lack of perseverance, or difficulties seeing tasks through completion, 4) lack of premeditation, or acting before thinking, and 5) sensation seeking, or seeking out novel and/or exciting experiences. The UPPS-P is comprised of 59 questions and scores for overall impulsivity range from 0-236. For each subscale the range of scores are: Negative urgency (0-48), Positive Urgency (0-56), Sensation Seeking (0-48), Lack of Premeditation (0-44) and Lack of Perseverance (0-40). The measure has adequate validity, good internal consistency (greater than or equal to 0.82; Whiteside &Lynam, 2001) and good test-retest reliability (Lynam, 2013). The average item-total correlation of the scale is 0.58. and the psychometric properties for each subscale are also sound (Negative urgency: $\alpha = 0.78$; Lack of Perseverance: $\alpha = 0.79$; Lack of Premeditation: $\alpha = 0.85$; Sensation Seeking: $\alpha = 0.74$; Positive Urgency: $\alpha = 0.85$; α = Cronbach's alpha; Whiteside & Lynam, 2001, Cyders et al., 2014).

It is worth noting that within the scientific literature, each of the five factors within the UPPS-P have been shown to be risk factors for developing a SUD. Negative Urgency moderately to strongly predicts problematic alcohol and substance use (Latzman et al., 2013). Sensation-Seeking has been shown to correlate robustly with increased frequency of substance and alcohol use (Magid & Colder, 2007). Lack of Perseverance has been shown to correlate strongly to problematic alcohol or substance use (Dick et al., 2010; Latzman et al., 2013). Positive Urgency has been shown to relate both to increased frequency and problematic use of alcohol or substances (Cyders & Smith, 2008; Latzman et al., 2013). Lack of Premeditation has been shown to predict increased frequency of alcohol or substance use (Magid & Colder, 2007). Additionally, a meta-analytic review inspecting the five factors and their relationship with substance use disorders concluded that each subscale has a moderate to strong effect size with developing a SUD ranging from 0.1 to 0.3 (Berg et al., 2015). For these reasons the UPPS-P is a robust tool to probe factor(s) which may aid the development of a SUD within a group of participants who are consuming painkillers. Vasileva & Conrod (2019) made comparisons between the most widely used self-report measures for impulsivity and showed that the subscales of the UPPS-P to tessellate best with various addictive substances, as outlined above.

Other popular measures of impulsivity such as the BIS-11 self-report measure (Patton et al., 1995) have shown to reveal mostly motor, non-planning and attentional forms of impulsivity which translate well with defining features of ADHD (Demirci et al., 2016), Oppositional Defiant Disorder and Conduct Disorder (Mathias et al., 2018) but not so well with SUD. Additionally, the Substance Use Risk Profile Scale (SURPS; Woicik et al., 2009) measures impulsivity as a *whole* and does not probe the various facets of impulsivity in the way the UPPS-P does. It has been used widely and is usually used to investigate spontaneous behaviour (e.g. Sensation Seeking) and assess levels of risky behaviour. Much like the BIS-11, it does not consider the role of emotion unlike the UPPS-P (e.g. positive and negative urgency) and has generally been used to investigate similar disorders as the BIS-11 (Robbins, 2018). Finally, the Sensation Seeking Scale (Zuckerman, 1964) has various subscales. While the "*Thrill and Adventure Seeking*" subscale has been shown to correlate well with developing SUD it does not incorporate the role of emotions/affect, unlike the UPPS-P, towards developing SUD and instead focuses on levels of Sensation Seeking itself.

A major strength of the UPPS-P is that the subscales take notice of the influence that positive and negative affect may have on impulsive behaviours. This is important when we are considering the role of self-reassurance/self-criticism which are also tied to the emotions and under their influence. The UPPS-P has also been used extensively to show that facets of impulsivity are linked to developing a SUD including Opiate dependence (Hershberger et al., 2017; Fahmy et al., 2018).

2.3. Pain Frequency and Pain Intensity

Participants stated whether their pain was caused or diagnosed by a medical condition and stated their most common type of pain e.g. Neuralgia, Lower Back Pain, Fibromyalgia, Chronic Migraine, Ankylosing Spondylitis.

Pain Frequency was confirmed by participants who provide a numerical value indicating how many times they felt pain within the past 3 months. The rationale behind this was because chronic pain is deemed to be pain that occurs for at least 3 months. In addition, they stated whether their most common pain existed for "Less than a month", "1-2 months", "2-3 months", "3-4 months", "4-5 months", "5-6 months", "More than 6 months", More than 1 year". The rationale for having these particular options was to give a monthly breakdown of how often pain was experienced and to assess how long people have lived with chronic pain.

Pain Intensity within the last 30 days was calculated as an average of 4 separate ratings ("1. Pain intensity at its worst", "2. Pain intensity on average", "Pain intensity at its least", and "Pain intensity right now"). Each of the four questions had a 10-point scale labelled "0 – No pain" to "10 – Worst pain possible". See Appendix C for the self-report measure used. The options for pain intensity were influenced by a previous study on painkiller dependence (Elander et al., 2014) and on the Brief Pain Inventory (2003).

2.4. Painkiller consumption

Participants reported the frequency of OTC and prescription painkiller consumption in the last 30 days by rating a 17-point response scale labelled "once only", "2-3 times only" "4-5 times only", "6-8 times only", "9-10 times only", "At least 1 per week", "At least 2 per week", "At least 3 per week", "At least 4 per week", "At least 5 per week", "More than 5 per week", "1 every day", "2 every day", "3 every day", "4 every day", "5 every day", "More than 5 every day".

Participants also stated their most commonly consumed OTC and/or prescription painkiller(s) consumed in (a) the last 30 days then stated (b) the amount of active ingredient per tablet and (c) how many tablets they consumed per day on a 14–point scale. Responses included “None”, “1 per day”, “2 per day”, “3 per day”, “4 per day”, “5 per day”, “6 per day”, “7 per day”, “8 per day”, “9 per day”, “10 per day”, “10-15 per day”, “16-20 per day”, “More than 20 per day”.

Painkiller misuse was also determined by asking participants to report how often they consumed their painkillers for (a) longer than the prescribed time period (LTP) and/or (b) consuming more than the Recommended Daily Allowance (RDA). Choosing one response on a 4-point scale provided answers. Responses included “1. Never”, “2. Sometimes”, “3. Usually” and “4. Always”. Misuse here is defined as using medication “for a legitimate medical reason but in higher doses or for a longer period than recommended”. See Appendix D for the self-report measure used.

2.5. Psychological Dependence to Painkillers

The Leeds Dependence Questionnaire (LDQ; Appendix E) quantifies the graded severity of psychological dependence. The 10 item self-report measure is based on ICD-10 and DSM-IV criteria for substance dependence: preoccupation, salience, compulsion to start, planning, maximizing effect, narrowing of repertoire, compulsion to continue, primacy of effect, constancy of state, and cognitive set. The items have a 4-point response scale labelled “Never” (0), “sometimes” (1), “often” (2), and “nearly always” (3). A single score is calculated as a total score across the 10 items (Raistrick et al., 1994).

The LDQ has shown to have validity, internal consistency and test-retest reliability (Raistrick et al., 2014). In the original version of the scale, participants would respond to questions in the context of “drink or drugs.” However, throughout this research (studies 1 and 2) measures were adapted the measure whereby “drink and drugs” will be replaced by “painkillers” (e.g. “do you find yourself thinking about when you will next be able to take painkillers?”).

2.6. Rationale for using the LDQ

The LDQ is a 10-item, 0 – 3 self-report measure (scores range from 0 - 30) designed to measure the severity of psychological dependence upon a variety of substances, independently of the *type* or the *quantity* of substance used, and to be sensitive to *change over time* (Raistrick et al., 1994). These attributes are important as the questionnaire is quickly completed, it can cater for participants who use many different *types* of pain medication and it can be used at different time points as in study 3 (Chapter 6). Moreover, The LDQ quantifies the graded severity of psychological dependence, with each question based on ICD-10 and DSM-IV criteria for substance dependence: salience, primacy of effect, preoccupation, compulsion to start, planning, , narrowing of repertoire, compulsion to continue, constancy of state, cognitive set and maximizing effect (Elander et al., 2014).

The LDQ has been well validated for use in opiate consumers (Raistrick et al., 2005; Kelly et al., 2010) and opiate consumers with chronic pain conditions (Ferrari et al., 2006 & 2009; Corbelli et al., 2012). Test–retest reliability was found to be high (r = 0.95). The LDQ total score is expected to increase with the degree of psychological severity of substance dependence and no cut-off score which is indicative of dependence has been set (Raistrick et al., 1994). The LDQ has also been successfully used in UK Addiction centres (UKATT Research Team, 2001).

2.7. Self-compassion and Self-criticism

The Forms of Self-criticizing/Attacking & Self-reassuring Scale (FSCRS; Appendix F) was developed by Gilbert et al., (2004) to measure people's critical and reassuring self-evaluative responses to a setback or disappointment. The original scale contained 24 items, but two items were dropped due to low psychometric properties, making a 22-item scale. Participants respond to a probe statement ''when things go wrong for me. . . .'' on a 5-point Likert scale (ranging from (0) not at all like me, to (4) extremely like me), to a series of questions designed to reveal self-criticism and self-reassurance. Self-critical items include: ''I am easily disappointed with myself; there is a part of me that puts me down; I have become so angry with myself that I want to hurt myself.'' Factor analysis suggested that the self-critical factor could be separated into two subfactors; one that focuses on feeling inadequate, defeated, and called ‘‘self-inadequacy’’ (9 items; α=0.90), while the other focuses more on a sense of disgust and anger with the self and called ‘‘self-hate” (5 items; α=0.86). Gilbert et al., (2004) found that these scales were significantly correlated with the Levels of Self-Criticism Scale (Thompson & Zuroff, 2000).

Self-reassurance (α=0.86) was measured by response to the probe statement ‘‘when things go wrong for me. ’’ On a 5-point Likert scale (ranging from (0) to not at all like me, to (4) extremely like me), participants rate a series of questions designed to measure self-reassurance that include ‘‘I am able to remind myself of positive things about myself; I encourage myself for the future.’’ This is a one-factor, 8-item measure, and will be referred to in this study as self-reassurance.

Research findings in experimental psychology over the past 20 years have shown a rising interest in self-relating processes and the effect they have on psychological health. Possessing (or aiming to acquire) a self-reassuring, compassionate attitude towards ourselves in times of distress is correlated with heightened resilience and improved psychological health (Trompetter et al., 2017). Of particular significance is the ability to self-reassure oneself by reminding oneself of one’s abilities and positive attributes when things are going wrong in life or when failures occur. The inability to do this has been shown to correlate with depressive symptomatology seen in clinical and non-clinical populations. (Castilho et al., 2015; Gilbert et al., 2004; Kupeli et al., 2013). These studies applied factor analysis to show that self-criticism and self-reassurance are separate entities and are not considered to be opposite ends of the same spectrum whereby one pole is a representation of the opposite or absence of the other. Longe et al., (2010) also showed that self-critical and self-reassured responses to a hypothetical emotive situation involving a negative event activated distinct neural regions. Specifically, the left temporal lobe and the Insula were activated when self-reassurance was stimulated. This area is thought to be responsible for expressing compassion and empathy towards others (Lutz et al., 2008). For this reason, it becomes clear that expressing self-compassion or expressing self-reassurance are very similar concepts as the neural architecture responsible for both is the same.

When self-criticism became activated, the researchers noted the left dorsolateral pre-frontal cortex and the dorsal anterior cingulate gyrus became activated. These regions are responsible for self-critical thinking, error processing and behavioural inhibition (impulsive decision making). Thus, the neural regions responsible for self-criticism are distinct from the neural regions for self-reassurance and are the same regions responsible for impulsive decision making (Paulus et al., 2002; 2003; Goldstein et al., 2009), a known risk factor for developing a SUD. These observations are likely to be seen also in the autonomic nervous system, where self-criticism stimulates the sympathetic nervous system (stress arousal) and self-reassurance/self-compassion will stimulate parasympathetic nerve fibres (content, warmth and safeness (Kirby, et al., 2017; Rockliff et al., 2008).

Both self-compassion and self-reassurance are ways of relating to oneself with warmth, wisdom, care and concern in a setting of personal limitations, perceived flaws, failures, and daily struggles. Self-compassion, as quantified by the Self-Compassion Scale (Neff, 2003), is branded by the three facets: being kind to oneself, seeing one's troubles as part of a common humanity, and being mindful of one's distress (Neff, 2003). Correspondingly, self-reassurance is the capacity to be soothing, non-judgemental, inspiring, and supportive to oneself during episodes of distress (Gilbert et al., 2004; 2005). Rather, these two constructs have been found to be highly correlated and often the literature uses the terms self-compassion and self-reassurance interchangeably (Hermanto & Zuroff, 2016).

Throughout this thesis self-reassurance will be operationalised as the self-compassionate component of the FSCRS scale while self-hate and self-inadequacy will be regarded as two separate entities belonging to the component of self-criticism in line with Gilbert's theory of social mentality and compassion (Gilbert, 2017). Positive mental health factors (such as affiliative, compassion-oriented interactions with ourselves and others, soothing positive affect and self-reassurance; Noorbala et al., 2013) function as resilience resources and protect against negative mental health factors (both externally – traumatic events and negative interactions with others – and internally generated – self-criticism; Neff et al., 2007, Leary et al., 2007). Cultivating skills in self-reassurance/self-compassion and taking acceptance towards one's setbacks (e.g. living with chronic pain) may buffer against the resulting shame and guilt that may ensue when living with a chronic debilitating condition such as chronic pain (e.g. unemployment or financial difficulties; Gilbert et al., 2007).

While the FSCRS scale itself does not aim to directly quantify self-compassion in the traditional sense (Gilbert, 2005), the sub-scales are taken from the scientific literature on self-compassion according to Gilbert et al., (2004; 2005; 2006; 2009). The statistical probing of the subscales (IS, RS and HS) do however provide the ability to assess whether they act as risk factors/protective buffers for dependence to painkillers and whether they moderate the role of other known risk factors for painkiller dependence (See section 3.3.). The three subscales also provide a means to gauge the relationship participants have with their thoughts and what "tone" their thoughts have (critical or reassuring). CFT and CMT (as used throughout this study) both aim to foster self-compassion (Gilbert, 2004; 2005) and through self-compassion it is hoped that the relationship people have with their thoughts will change from being harsh and self-critical to become warm, compassionate, soothing and self-reassured. The way one responds to their thoughts when engaged in health-related behaviour change has been found to be an important factor for successful outcomes (Learey et al., 2007). Thus, by having participants engage with a CMT intervention, which endorses self-compassion, it is hoped that they become more self-reassured (positively associated with well-being, self-regulation and behaviour change related to health) and less self-critical (risk factors for dependence to painkillers and negatively associated with well-being, self-regulation and behaviour change related to health; Duarte et al 2017).

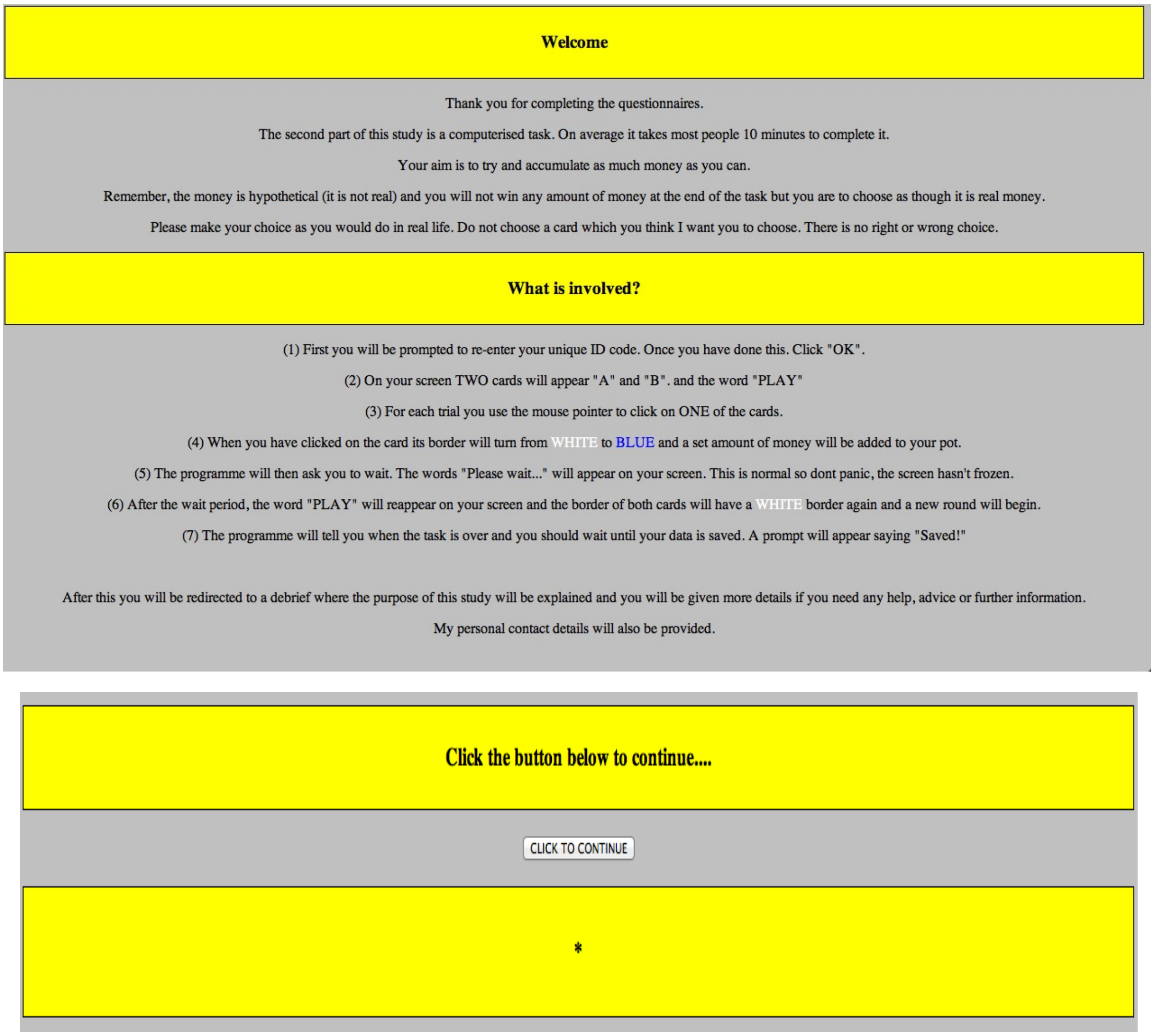
Relapse prevention models (Neff et al., 2007; Yarnell et al., 2013) have begun to incorporate third-wave psychotherapeutic models (Acceptance & Commitment Therapy (MacBeth et al., 2012), Mindfulness-Based Cognitive Therapy (Van Dam et al., 2011) and Compassion Focused Therapy/Compassionate Mind Training (Krieger et al., 2013). This could be because there is now substantial evidence to indicate that those who accept and manage emotional responses to external or internal stressors associated with relapse can generate prospects for behavioural self-regulation (Wong et al., 2013). This may include making less impulsive choices which may have negative consequences (Kroenke et al., 2001). Self-regulation of behaviour change related to health outcomes has been found to be supported by psychoeducation that promotes emotional management and emotional regulation through self-reassuring compassionate abilities (Noorbala et al., 2013). Behavioural approaches in their third wave aim to aid individuals alter the *relationship* with their troublesome thoughts, emotions and bodily feelings in lieu of trying to change or control them, while engaging in adaptive behaviours towards effective and continued behavioural change and well-being (Martin et al., 2006). Of note, CMT aims to aid individuals to better cope with negative self-evaluations, shame and self-criticism (self-hate and self-inadequacy) through the cultivation of compassion and self-reassuring skills. Engaging in CMT inspires one to develop compassion motivation and engagement with adaptive behaviours with the chief aim of improving well-being (Krieger et al., 2013).

2.8. Behavioural Impulsivity

A behavioural measure of behavioural impulsivity was employed as the final component of the study. The DD paradigm (Appendix G) used in this study aimed to measure impulsive choice. Participants read an instructional brief before commencing 20 trial runs (training period) to familiarise themselves with the task.

Upon completing the self-report measures, participants were then greeted by a welcome screen prior to engaging with the DD measure. The welcome screen contained brief instructions on the DD task (Fig. 6 below).

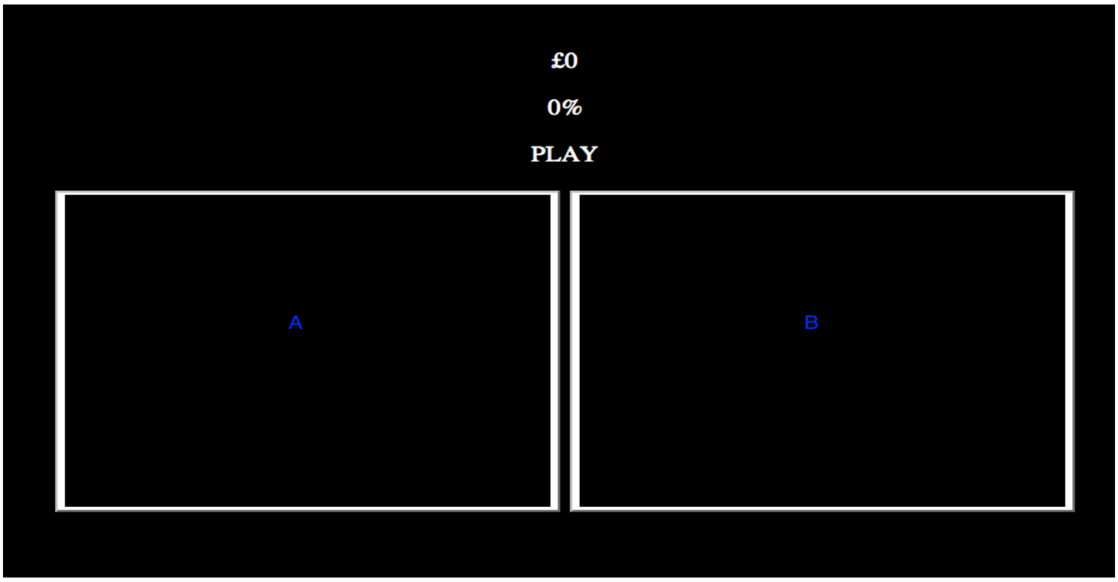
Figure 6 Instructions presented to participants for the DD Task



At the end of the 20 training trials, the screen displayed "Training Over." The purpose of the training session was to give subjects a brief exposure to the different monetary amounts and delays associated with the letters A and B.

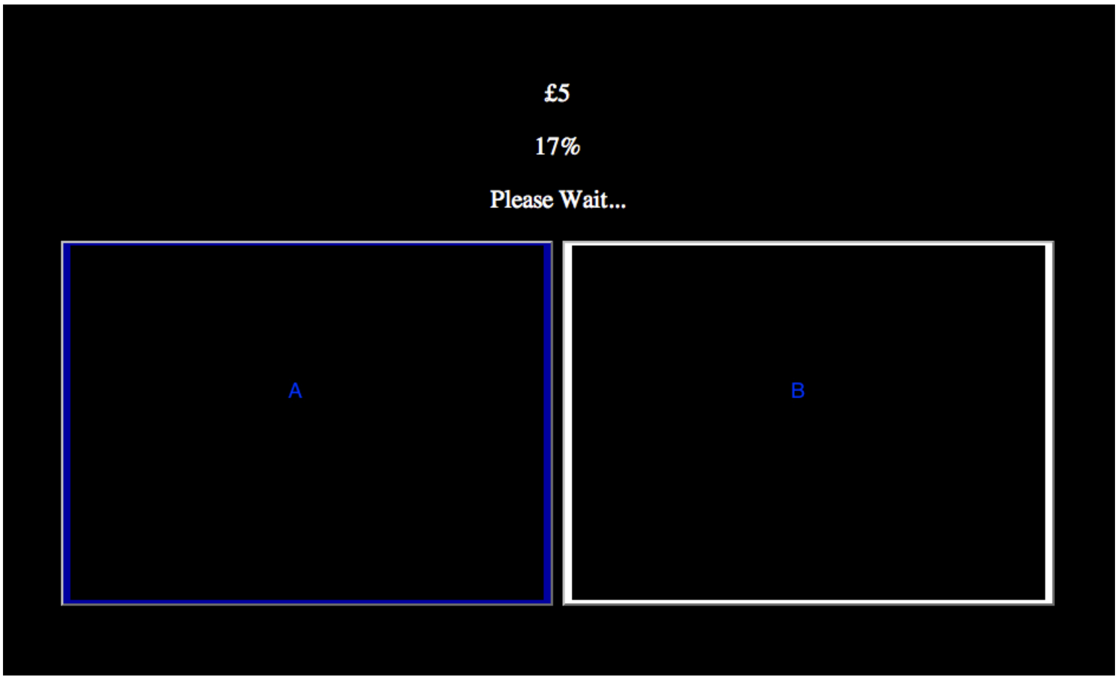
After the training period, participants complete 30 experimental trials. The online DD task itself showed a series of computer screens depicting two index cards, one for the S-S reward and one for the L-L reward. Card placement on the screen were counterbalanced (left-right) as shown in Figure 7.

Figure 7 Participants view of the layout of the online Delay Discounting task



Participants chose between the two cards either "A" or "B" which corresponds to an S-S reward card or a L-L reward respectively (Figure 8). Choosing card A results in the participant receiving a hypothetical reward of £5 and results in the participant waiting 5 seconds before the next trial begins. Choosing card B results in the participant receives a £15 hypothetical reward followed by an initial inter-trial interval of 15 seconds. The delay for card B varied during the session. Each time the subject selects card B, the next delay increases by 2 seconds. Conversely, each time the subject selects option A, the next delay for card B decreases by 2 seconds. The delay for card B was never less than 7 seconds and was thus always longer than the delay for card A, which was fixed at 5 seconds. At no stage were participants informed on how many trials to expect, rewards values or the times delays associated with card choice. Figure 8 below shows that that participant in this example has chosen Card A as the outer border has turned blue. The online DD task has also given the "Please Wait" signal indicating an inter-trial interval (5 seconds in this case as the participant has chosen Card A as denoted by the blue outline).

Figure 8 Participant view of the online Delay Discounting task



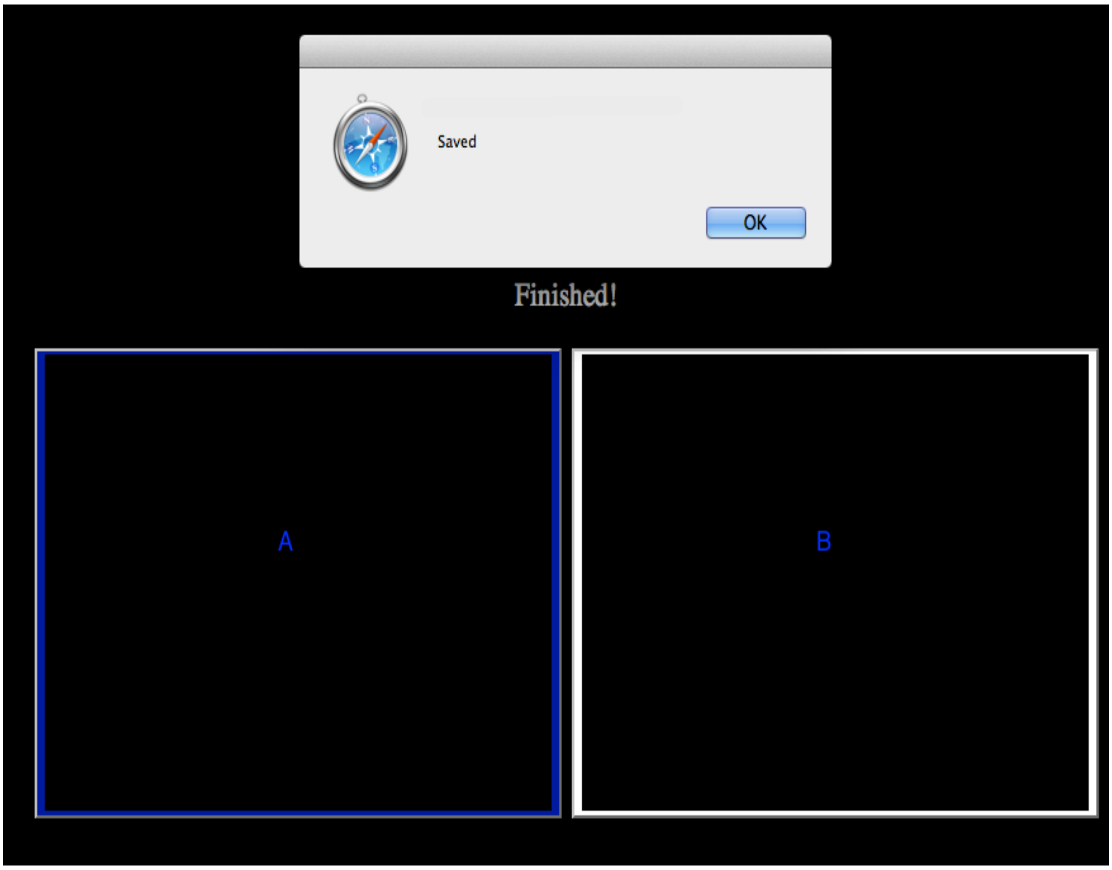
A total of 35 trials constituted the “live” task. Since the sessions were stopped after 35 trials the length of sessions varied depending upon participants choices.

At the end of the 35 experimental trials, participants would have accumulated a pot of hypothetical money. Those who scored nearest to the maximum amount achievable (£525; 35 x £15) were deemed to have made the most rational decisions, as the task was to accumulate as much money as possible. Those who scored nearer the lowest amount achievable (£175; 35 x £5) were deemed to have made more impulsive choices. A message would be displayed on the screen to signal the task is complete (Figure 9) followed by another message to indicate their score has been saved (Figure 10). While there was no inter-trial or end-of-trial monetary reward for any participant there was a single prize draw amongst the top 10 scorers of the DD task for studies 1 and 3. The prize was a £50 e-retailer voucher.

The behavioural measure was bespoke and coded in-house using HTML5, PHP, MySQL and JavaScript programming languages. Permission was sought for use of self-report measures where necessary. All self-report measures were delivered online using LimeSurvey after being uploaded to a secure private web server (Linux Apache).

Figure 9 Participants view of the online Delay Discounting task signalling the end of all trials and displaying the score obtained

Figure 10 Participants view of the online Delay Discounting task signalling their progress has been saved



To clarify, high scores on the DD task reflect more self-controlled/less impulsive decision making while low scores reflect a greater tendency towards impulsive decision making. This is because the aim was to obtain the highest amount possible which is only achieved by always choosing Card B and having to patiently wait longer to obtain a reward during each trial in comparison to choosing card A which always gives a smaller-but-sooner reward.

2.9. Rationale for using the DD task

Research findings and current theory indicates that impulsivity is composed of (1) behavioural impulsivity and (2) impulsive personality (Cyders & Coskunpinar, 2011). Both behavioural and personality models of impulsivity are related to substance use (Sharma et al., 2014) and so it is important to capture both elements in order to determine which, if any, have a greater influence on psychological dependence to painkillers.

Behavioural impulsivity can be further categorised as shown above (Figure 4, pg. 50). The DD task was used above other behavioural measures as the focus of this piece of research was to investigate impulsive decision making in those consuming opiate-based painkillers. Impulsive decision making is a separate entity from other facets of impulsivity (e.g. Impulsive disinhibition as captured by the go/no-go Task). There is also a plethora of research findings which have shown it is possible to differentiate opiate users from non-opiate users via the DD task (Kirby et al., 1999; Petry et al., 1999; Bickel et al., 2004, Madden et al., 2002). Furthermore, should DD prove to be a risk-factor for participants in these studies then there exists evidence that DD can be reduced by altering Temporal Attention (Radu et al., 2011; Scholten et al., 2019) and another study amongst smokers experienced a 16.7% reduction in DD scores (Yi et al., 2008). Guan et al., (2015) showed their participants positive, neutral, and negative pictures and then asked them to perform a DD task. They found that DD was attenuated in the neutral condition and even more decreased in the positive condition, compared with the negative condition. Ifcher & Zarghamee (2011) used short movie clips, and Pyone & Isen (2011) used words to induce positive or neutral affect, and both found that positive affect reduced DD. In the experiment by Raeva et al., (2010), both regret and rejoicing were induced. Results showed that when regret was experienced, participants preferred the immediate rewards, whereas when rejoicing was experienced, participants chose the delayed reward more often. Authors of the meta-analysis on reducing DD scores (Scholten et al., 2019) conclude by stating that most of the published studies (*n* = 119; 79%) were able to reduce DD scores and the that the most hopeful paths to engage in future research would be acceptance-based and mindfulness-based trainings.

Thus, applying an intervention which aims to produce positive affect (e.g. Self-reassurance), reduce impulsivity and reduce negative affect (e.g. feelings of shame, guild, self-criticism), such as CMT, and substituting negative thoughts/feelings with positive thoughts/feelings (such as with the online CMT intervention) may aid in the reduction of developing a SUD.

Chapter 3. Study 1: Exploring Cognitive and Behavioural Risk Factors associated with Psychological Dependence to Painkillers.

3.1. Introduction

Chronic pain sufferers are an under-served community who are vulnerable and susceptible to painkiller addiction. The issue of dependence to painkillers has grown to become a global problem and there is limited research in the area. This study aimed to fill some of the knowledge gap by aiming to elucidate the associations between psychological dependence to painkillers and self-criticism and self-reassurance and impulsivity (cognitive and behavioural). This study will also explore painkiller consumption, pain intensity and pain frequency to see if they also have a relationship with painkiller dependence.

A web-platform was built to host a series of self-report measures and a behavioural measure of impulsivity (Section 3.6) from which participants entered their responses. Data was analysed to see if there were any associations between study variables and if any identifiable risk factors emerge.

3.2. Rationale for study

Chapter 1 highlights the ever-increasing knowledge that both cognitive and behavioural impulsivity are risks factors for many addictive substances (Madden et al., 1997; Reynolds et al., 2006). However, very little is known about the prevalence of painkiller dependence in the chronic pain community and even less is known about the roles of cognitive and behavioural impulsivity on psychological dependence to painkillers and so warrants exploration.

In addition to impulsivity, the role of self-reassurance towards developing a SUD has yet to be investigated in those with chronic pain. It is entirely possible that those living with chronic pain are within the confines of an environment which provides opportunity for one's internal dialogue to become more self-critical and less self-reassured. This is based on the fact that many chronic pain sufferers spend a lot of time in isolation (e.g. loss of job, unable to attend social events, lack of support from friends/family, limited interpersonal relationships, loneliness) and this can foster development of internally generated self-critic (Dinger et al, 2014).

Whether one's internal dialogue is largely self-critical or self-reassured has significant impact on their quality of life. Theory suggests the tone of our internal dialogue plays an important role in guiding our decision-making strategy (Wong et al., 2013; Kroenke et al., 2001). A deficient decision-making strategy influenced by self-critical thinking could have detrimental effects on the individual (e.g. propensity to consume drugs when in distress). CMT principles propose that certain individuals who have not had the opportunity to develop their soothe system become less self-reassured in the context of setbacks and disappointments, and instead are highly threat focused (internally and externally generated threats). Therefore, they are more likely to develop a Self-critical internal voice. As there is affect attached to the tone of one's internal voice (Self-reassured voice = Positive affect; Self-critical voice = Negative affect) there may be a propensity to fuel a facet of impulsivity (e.g. Positive Urgency or Negative Urgency) which may promote drug-seeking behaviours (Kirby & Petry, 2004).

Thus, it is important at this stage to identify whether there are any relationships between psychological dependence to painkillers and (1) facets of impulsivity and (2) the dominant tone of our internal dialogue (Self-critical vs. Self-reassured).

3.3. Aims and Objectives

This study has four aims with accompanying objectives and are outlined below.

Aim 1: Quantify painkiller misuse and psychological dependence in a sample of chronic pain sufferers.

In order to address the first aim, there is an accompanying objective:

1. Ascertain the level of psychological dependence to painkillers within the study sample (Table 3).

This aim and objective were placed to see if any dependence occurs in the sample population. If so, then this would allow for further investigation. It is hypothesised that given the severity of the current situation and reports from other studies (Elander et al., 2014) that there will be some degree of dependence to painkillers within the sample.

Aim 2: Investigate the role of Impulsivity towards psychological dependence of painkillers. In order to address the second aim, there are two objectives:

2. Ascertain the association between specific facets of cognitive impulsivity and psychological dependence to painkillers.
3. Ascertain the association between behavioral impulsivity and psychological dependence to painkillers.

As impulsivity is a very well-documented risk factor for drug dependence, it is hypothesised that some facets of impulsivity will be revealed as contributory risk factors for dependence to painkillers. Specific facets cannot be hypothesised at this stage and so will warrant further statistical analysis.

Aim 3: Investigate the role of self-criticism and self-reassurance towards psychological dependence of painkillers. In order to address the third aim, there is one objective:

4. Ascertain the association between specific facets of self-criticism/self-reassurance and psychological dependence to painkillers.

The existing literature has revealed that meta-cognitive risk factors can change our affective states. Usually, negative affective states can affect behaviour. Therefore, it was hypothesised that some facets of self-criticism will have an effect on dependence to painkillers.

Aim 4: Investigate the relationships between impulsivity and self-reassurance/self-criticism.

In order to address the fourth aim, there are two objectives:

5. Ascertain the association between cognitive impulsivity and self-criticism. (Table 4).
6. Ascertain the association between behavioral impulsivity and self-criticism.

It is thought that some facets of our internal dialogue (critical or compassionate) can affect our behaviour. In conjunction with impulsive traits and our decision-making principles, it remains to be seen what correlations, if any, exists between these potential risk factors. This portion of the study will largely be exploratory as no evidence currently exists which has explored the relationship between these variables.

Fulfillment of aims and objectives will satisfy the knowledge gap, provide a springboard for the wider scientific community and create opportunity to design a psychological intervention for reducing painkiller dependence.

3.4. Methods

3.4.1 Study design

This was a web-based correlation study (cross-sectional). A single group of participants who suffered with chronic pain and consumed painkillers were recruited to ascertain the influence of impulsivity (cognitive and behavioural) and Self-compassion on psychological dependence to painkillers. All participants completed a battery of self-report measures (discussed in detail in Chapter 2) pertaining to their demographics, chronic pain condition (intensity and frequency), painkiller consumption, levels of impulsivity and Self-criticism. This was followed by an objective behavioral measure of impulsivity (DD Task).

A cross-sectional design was used in this study as several potential risk factors are explored and data is collected at a single time point for each participant. This design will offer descriptive statistics for the chronic pain population regarding the prevalence of painkiller dependence (Aim 1; Section 3.8.1.) and a set of potential risk factors (e.g. facets of impulsivity). This design will also allow for analysis to be applied that will define relationships between study variables (Aims 2 and 3).

3.5. Participants

3.5.1. Participants and Recruitment strategy

The participants in this study comprised of 259 members from the general population who completed a series of self-report measures and a behavioral measure. All participants who expressed interest were provided with general study information (Appendix H) and an invitation to participate (Appendix I). Next, they were screened for inclusion criteria (see 3.5.2. below) and those who met entry criteria were briefed (Appendix J), completed an informed consent form (Appendix K) and instructions were provided (Appendix L). At the end of the study, all participants were thanked and debriefed (Appendix M). Those who did not meet inclusion criteria were also thanked and debriefed (Appendix N). Participants were informed of the inclusion and exclusion criteria before they took part in the study (See section 3.5.2. and 3.5.3. below). Participants were not required to reside in specific geographical locations as the study was designed to be open to people from all over the world.

Participants were recruited via digital invitation. An outline of the study, inclusion/exclusion criteria and a web-link were provided. Adverts were placed in appropriate Facebook groups and on digital bulletin boards. Permission was sought and retained from web administrators. Geographical location of participants was not restricted.

The entire project was hosted on a private Linux web server (Ubuntu/Apache https). The behavioral measure was bespoke and coded in-house using JavaScript, CSS and HTML5. It operated successfully on all web browsers (PC and Mac) and on mobile and tablet devices (Android, Apple iOS and Microsoft Windows). Upon completion of self-report measures a behavioral measure was introduced to assess impulsive decision-making (DD). The top 10 scores were placed into a prize draw for a £50 Amazon voucher. When the study was complete, participants were debriefed, thanked and released from the study. The aim was to collate a nonclinical sample with common forms of chronic pain, which would be broadly representative of people with pain in the general population.

3.5.2. Inclusion criteria

1. Minimum age for participation = 18 years; No maximum age limit.
2. Have experienced some form of pain at least 15 days per month for the last 3 months.
3. Have consumed at least one over-the-counter (OTC) or prescription painkiller in the last 30 days.
4. Must be literate and able to provide informed consent.

3.5.3. Exclusion criteria

1. Have consumed an illegal substance in the last 30 days.
2. Currently consuming psychotropic medication; or have in the last 30 days.
3. Unable to provide informed consent.
4. Diagnosed with ADD/ADHD.
5. Currently undergoing any form of CBT/psychotherapy.
6. Have a friend or family member in the study.
7. Suffering from a terminal illness.

3.6. Materials and Measures

Measures used in this piece of research consisted of self-report measures and one behavioural measure. All measures were placed on a web-platform where participants entered their responses. Detailed descriptions of all measures used in the study are provided above in Chapter 2 while a brief overview is provided below.

3.6.1. Cognitive impulsivity

Cognitive impulsivity was measured using the UPPS-P self-report measure (Whiteside & Lynam, 2001; 2003). The 59-item self-report assesses five subscales (negative urgency, lack of premeditation, lack of perseverance, sensation seeking, and positive urgency) that are used to measure five distinct dimensions of impulse behaviour in adolescents and adults (ages 12-80).

3.6.2. Pain (Typology, Intensity, Duration, and Frequency)

For study 1:

Participants began this section by reported their most common type of pain e.g. Neuralgia, Lower Back Pain, Fibromyalgia, Chronic Migraine, Ankylosing Spondylitis.

Pain Intensity within the last 30 days was calculated as an average of 4 separate ratings ("1. Pain intensity at its worst", "2. Pain intensity on average", "Pain intensity at its least", and "Pain intensity right now"). Each of the four questions had a 11-point scale labelled "0 – No pain" to "10 – Worst pain possible".

Pain Frequency was confirmed by participants who provide a numerical value which they typed into a text box to indicate how many times they felt pain within the past 3 months i.e. "7 times per month".

In addition, participants stated the duration of their most common pain by choosing one option from the following: "Less than a month", "1-2 months", "2-3 months", "3-4 months", "4-5 months", "5-6 months", "More than 6 months", More than 1 year".

3.6.3. Painkiller consumption

Participants stated their most commonly consumed OTC and/or prescription painkiller(s) consumed in (a) the last 30 days, (b) the amount of active ingredient per tablet and (c) how many tablets they consumed per day. Answers were provided on a 14–point scale: "None", "1 per day", "2 per day", "3 per day", "4 per day", "5 per day", "6 per day", "7 per day", "8 per day", "9 per day", "10 per day", "10-15 per day", "16-20 per day", "More than 20 per day". See Appendix D for full self-report measure.

3.6.4. Painkiller misuse

Painkiller misuse was determined by asking how often participants consumed their painkillers for (a) longer than the prescribed time period and/or (b) more than the Recommended Daily Allowance (RDA). Responses were presented on a 4-point scale: "1. Never", "2. Sometimes", "3. Usually" and "4. Always". Misuse here is defined as using medication "for a legitimate medical reason but in higher doses or for a longer period than recommended".

3.6.5. Psychological dependence to painkillers

The Leeds Dependence Questionnaire (LDQ) measures the graded severity of psychological dependence. The 10 item self-report measure is based on ICD-10 and DSM-IV criteria for substance dependence. The items have a 4-point response scale labelled “Never” (0), “sometimes” (1), “often” (2), and “nearly always” (3). A single score is calculated as the total across the 10 items (Raistrick et al., 1994).

3.6.6. Self-criticism/Self-reassurance

The Forms of Self-criticizing/Attacking & Self-reassuring Scale (FSCRS) was used to measure self-criticism and the ability to self-reassure (Gilbert & Irons, 2004). This 22-item scale measures different ways people think and feel about himself or herself when things go wrong for them. The responses are given on a 5-point Likert scale (ranging from 0 = not at all like me, to 4 = extremely like me).

3.6.7. Behavioural impulsivity

A measure of behavioural impulsivity (DD Task) was used as the final measure in this study.

In order to quantify behavioural impulsivity, the study employed the Delay Discounting task. An explanation of this task and how to interpret the outcomes of this measure are outlined in detail in section 2.8.

3.7. Procedures

Participants were recruited as per section 3.5.1. All participants meeting inclusion criteria completed the demographics questionnaire (Appendix A) and then went on to complete self-report measures shown in sections 3.6.1. – 3.6.6. and a behavioural measure outlined in section 3.6.7. (Appendix G). Participants were then thanked and released from the study. Data was collected and analysed as per section 3.8. below.

3.8. Analytic strategy used to address study aims and objectives

This section will cover the aims and objectives for the study and provide some detail on the statistical analysis used to answer the aims.

3.8.1. Aim 1: Quantify painkiller misuse and Psychological Dependence in a sample of chronic pain sufferers

In order to address the first aim, there is an accompanying objective:

1. Ascertain the level of psychological dependence to painkillers within the study sample (Table 3).

For objective (1) the mean and standard deviation of the Leeds Dependence Questionnaire scores were calculated for all participants and compared with data from the scientific literature.

3.8.2. Aim 2: Investigate the role of Impulsivity towards psychological dependence of painkillers

In order to address the second aim, there were two objectives:

2. Ascertain the association between specific facets of cognitive impulsivity and psychological dependence to painkillers.

For objective (2) a Pearson's Correlation Coefficient between all five sub-scales of cognitive impulsivity derived from the UPP-S self-report measure will be used and the scores obtained from the Leeds Dependence Questionnaire for the entire study sample (Tables 4).

3. Ascertain the association between behavioral impulsivity and psychological dependence to painkillers.

For objective (3) a calculated Pearson's Correlation Coefficient between the Delay-Discounting score and the scores obtained from the Leeds Dependence Questionnaire for the entire study sample (Table 4).

3.8.3. Aim 3: Investigate the role of self-criticism and self-reassurance towards psychological dependence of painkillers.

In order to address the third aim, two objectives were developed:

4. Ascertain the association between specific facets of self-criticism/self-reassurance and psychological dependence to painkillers.

For objective (4) a Pearson's Correlation Coefficient will be calculated between all three sub-scales of Self-criticism and look at correlations with scores obtained from the Leeds Dependence Questionnaire (Table 4).

5. Ascertain the role of self-criticism/self-reassurance as moderating variables for psychological dependence to painkillers.

For objective (5) to conduct a hierarchical multiple linear regression analysis (See section 3.8.4.) followed by a moderation analysis (JN analysis) on significant interaction terms (See section 3.13.).

3.8.4. Regression analysis

To address aims 2 and 3 a hierarchical multiple linear regression will be performed (Table 5) to further confirm which independent variables are predictors for psychological dependence to painkillers and then to allow for moderation analysis. Hierarchical multiple linear regression is a way to show if variables of interest explain a statistically significant amount of variance in the dependent variable (LDQ scores) after accounting for all other variables. The scores from the LDQ will be used as the dependent variable for the regression analysis. Independent variables will be placed in five "blocks" according to which *theme* they fall into. Those IVs that fall into a given theme are shown next to the theme. Themes are shown below:

Theme 1: **Demographics/Pain statistics** [Age, Gender, Pain frequency, Pain intensity, Prescription painkillers consumed per day, OTC painkillers consumed in the past 30 days].

Theme 2: **Self-compassion** [Self-inadequacy, Self-Reassurance, Self-hate].

Theme 3: **Cognitive Impulsivity** [Negative urgency, Positive urgency, Lack of premeditation, Sensation seeking, Lack of perseverance].

Theme 4: **Behavioural impulsivity** [Delay-discounting score].

Theme 5: **Interaction Effects** [Self-hate & Pain frequency; Self-reassurance & Pain frequency; Self-inadequacy & Pain frequency].

Data sets organised into themed "blocks" will be placed in order of theoretical importance i.e. those which were deemed to be superior predictors for psychological dependence to painkillers will be placed earlier in terms of causal order. The ordering was also based on the regression analysis conducted by Elander et al., 2014.

3.8.5. Moderation analysis

Regarding moderation analysis, it was decided to investigate the interaction effects between a potential *psychological* risk factor (Self-compassion sub-scales as shown in Theme 2) and a *physical* risk factor (Pain Frequency) to ascertain what effect they may have on painkiller dependence. A moderation analysis will be performed on any of the three interaction terms in block 5 which are found to be significant in the regression analysis. Furthermore, there will be the application of the Johnson-Neyman Technique to produce appropriate graphs highlighting regions of significance and confidence intervals. Moderators used in the analysis will include variables from Data set 2: IS, RS and HS. While much has been explored regarding impulsivity and developing a SUD, little has been studied in regard to facets of self-compassion and developing a SUD hence IS, RS and HS will be included in the moderation analysis.

3.9. Ethical issues

All participants provided informed consent and were made aware of what the study involved and were then debriefed at the end of the study. The study was approved by the Ethics Committee at the University of Derby, UK. Issues raised by the Ethics committee included use of Google Docs and inclusion of a vulnerable population. To remedy this, the study did not include a group of heroin users as a control group, rather the study sought a single group of participants. LimeSurvey, a free piece of software was installed on a website to collect data. All data was saved to a privately-owned encrypted web server. The web server was tailor made using the Linux operating system and HTML5 to host the website. As the behavioural measure was not available. The programming languages JavaScript and CSS were used to produce a bespoke version of the DD paradigm to run on the Linux server (See Appendix G; and Appendix H for general study information).

3.10. Results

3.10.1. Descriptive data

The study comprised of 259 participants (*n*=259). Descriptive data was first analysed and is provided in Table 3 below. Normality of distribution was assessed using measures of skewness, kurtosis and histograms. Skewness ranged from -0.76 to 1.97, with the exception of "OTC consumption per day" (2.35). Kurtosis ranged from -0.95 to 4.9 with the exception of "prescription painkillers consumed in the last 30 days" (8.86) and "OTC consumption per day" (14.42). All variables which were within the acceptable range of –2.0 to + 2.0 for skewness and –5.0 to +5.0 for kurtosis (Kendall & Stuart, 1958) were entered into the multiple regression model. Mahalanobi's distance was used to screen for outliers. A single case was found to exceed the critical value (43.82) for the 19 variables entered into the regression model. This case was discarded from any further analysis.

The study had a high proportion of Females (67.68% [176/259]), compared with males (36.29% [84/259]). There were no differences in mean age between genders. Medical diagnosis was reported by 62.9% of the sample [163/259].

3.10.2. Pain (Typology, Intensity, Duration, and Frequency)

The most common forms of pain reported in the last 30 days were Fibromyalgia 36.3% [94/259], Arthritis 26.64% [69/259], Back pain 22.78% [56/259], Ankylosing Spondylosis 11.2% [29/259] and Migraine 4.63% [12/259].

Within the sample, the mean value for "Pain Intensity" in the last 30 days "at its worst" was 8.23 (SD=2.11); "on average" was 6.44 (SD=2.38); "at its least" was 5.76 (SD=2.09) and "right now" was 6.01 (SD=2.47).

When participants stated how long they had lived with the chronic pain condition, 96.91% [251/259] stated "More than 1 year."

The mean response for the "number of times they felt pain in the last 3 months" (i.e. frequency of chronic pain) was 89.8 (SD=14.09).

3.10.3. Psychological dependence to painkillers

Psychological dependence scores ranged from 0-21 and had a mean value of 4.52, which reflects similar results obtained in a study by Elander et al., 2014. Results of consuming behaviours also reflected scores from the study by Elander et al., 2014 whereby OCT painkiller consumption in the last 30 days ranged from 0-235 with a mean of 2.83 tablets. Similarly, prescription painkiller consumption within the last 30 days ranged from 0-330 with a mean value of 78.46.

3.10.4. Self-compassion

Regarding scores from the self-compassion subscales, self-inadequacy ranged from 0-30 with a mean score of 13.74, self-reassurance ranged from 8-33 with a mean score of 20.54 and self-hate ranged from 0-14 with a mean score of 2.41. These scores were very similar to those obtained in a Dutch study of 329 participants whereby the mean scores for self-inadequacy, self-reassurance and self-hate were 14.66, 21.5 and 2.83 respectively (Fritzsche, 2016).

3.10.5. Cognitive and behavioural impulsivity

The overall score for impulsivity obtained via the UPPS-P ranged from 74-154 with a mean score of 115.19. Scores from the subscales are found in Table 3 below.
Behavioural impulsivity was assessed using the online DD task and the mean score was 376.54 (£) with a range of 175-525.

Table 3 Descriptive statistics for study variables

	Mean (SD)	Range
Age	39.69 (12.21)	19-71
Gender	84 Male / 176 Female	
Psychological dependence to painkillers	4.52 (5.93)	0-21
Number of OTC tablets consumed per day	2.83 (1.6)	0-15
Number of OTC tablets consumed within the last 30 days	64.06 (41.93)	0-235
Number of prescription painkillers tablets consumed per day	2.97 (1.48)	0-11
Number of prescription painkillers tablets consumed within last 30 days	78.46 (46.76)	0-330
Pain Intensity within the last 30 days	6.32 (2.31)	1-10
Pain Frequency within the last 3 months	89.8 (11.61)	32-94
Self-inadequacy	13.74 (6.65)	0-30
Self-reassurance	20.54 (5.84)	8-33
Self-hate	2.41 (3)	0-14
Impulsivity (overall score)	115.19 (18)	74-154
Negative urgency	25.78 (6.32)	13-42
Lack of premeditation	20.51 (4.12)	10-30
Sensation seeking	28.16 (7.67)	13-46
Positive urgency	22.76 (6.95)	14-38
Lack of perseverance	18.47 (4.43)	10-29
Delay Discounting score	376.54 (80.95)	175-525

SD = standard deviation

Scores for LDQ were comparable to scores found by Elander et al., 2014 (M = 4.32; SD = 4.24; Range = 0-23). The mean Age was also similar (M = 44.5; SD = 13.5; Range = 19-76). The study sample investigated by Elander et al., stated their most common forms of pain being Fibromyalgia, Arthritis, Back pain and Migraine which were similar to this study. Scores for self-criticism, self-inadequacy and self-reassurance were also similar to findings in the scientific literature (Fritzsche, 2016).

3.10.6. Painkiller consumption

Data was also collected on the types of painkiller consumed. Ibuprofen was the most commonly consumed OTC painkiller (40% of study sample; Fig. 11). Oxycodone, a powerful opioid-analgesic linked to the painkiller addiction epidemic in the USA, was the most commonly consumed prescription painkiller (25% of study sample; Fig. 12). Analysis revealed the average total OTC pills consumed in the past 30 days were 52 pills. The total number of prescription painkillers consumed in the past 30 days was 70.24 pills on average. The amount of active ingredient reported to be in each tablet ranged from 5mg – 600mg.

Figure 11 The most commonly consumed OTC painkillers by study participants

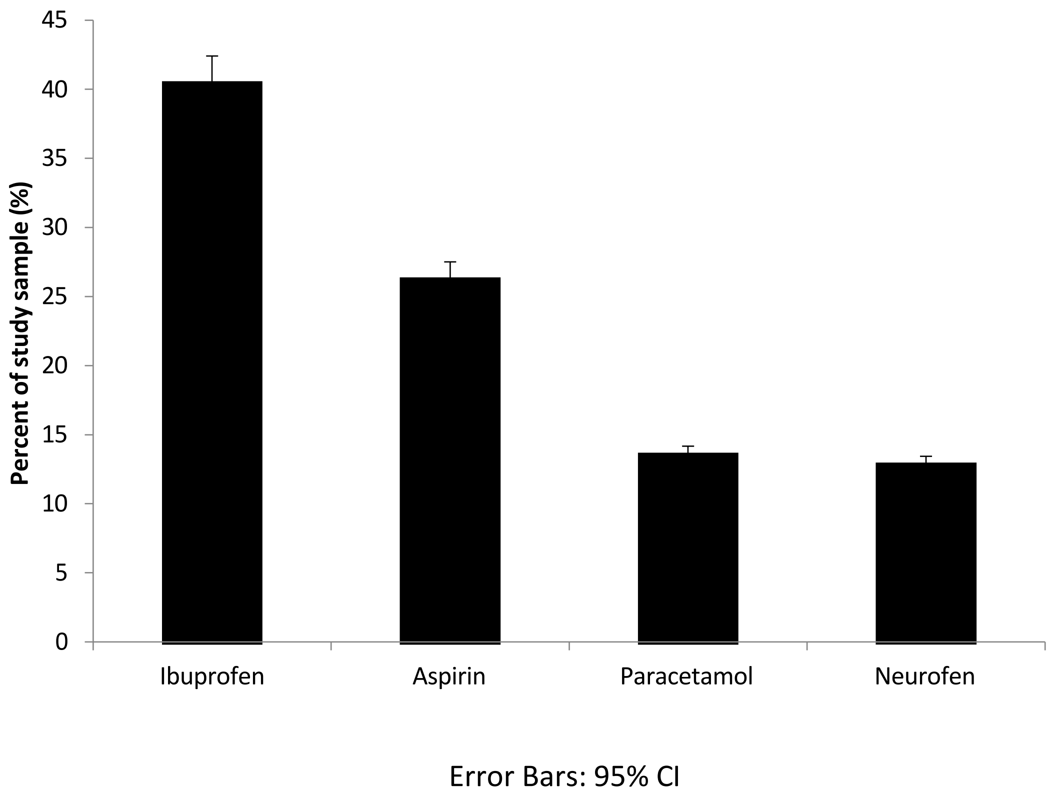
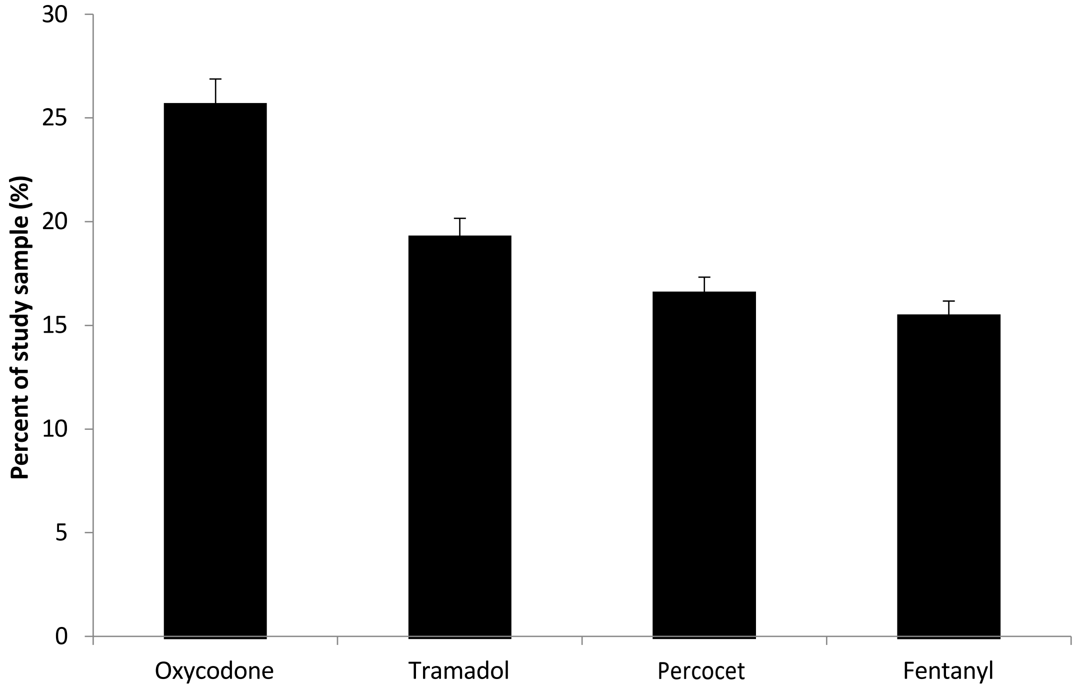
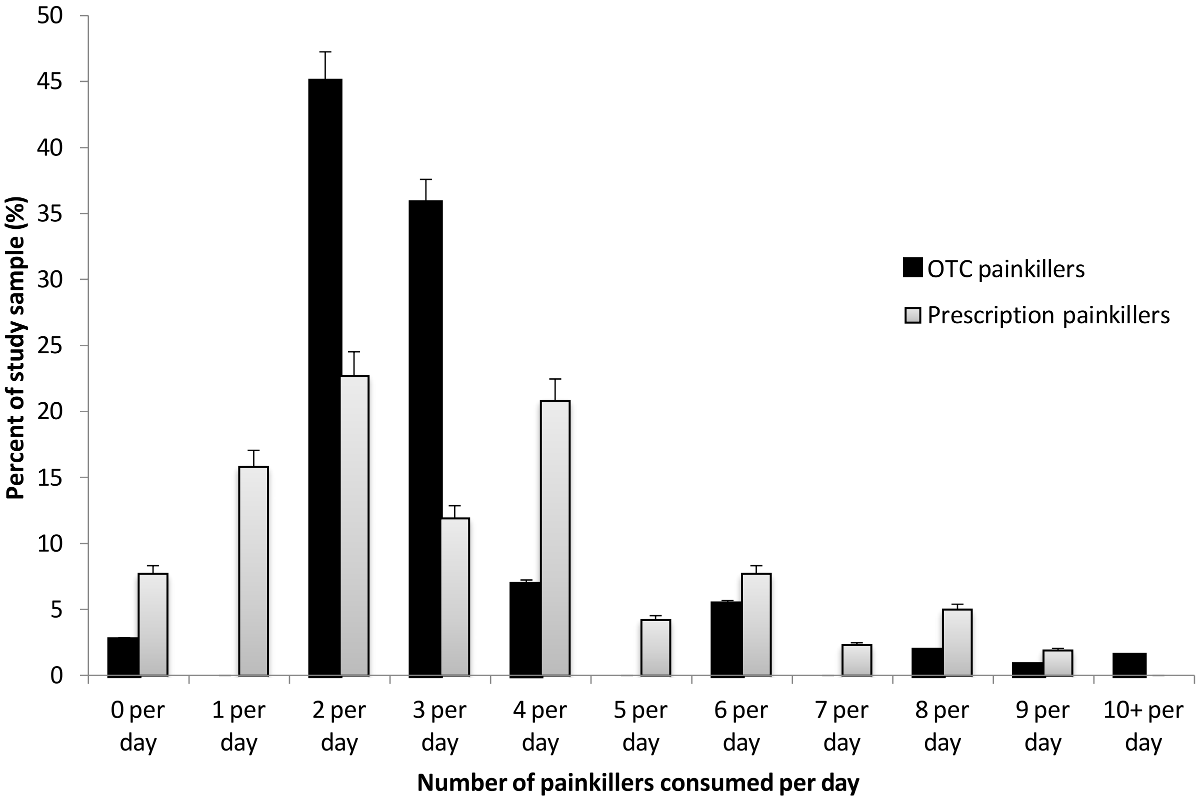


Figure 12 The most commonly consumed prescription painkillers by study participants



Error Bars: 95% CI

Figure 13 Daily painkiller consumption by study participants



Error Bars: 95% CI

Data on daily painkiller consumption revealed 15/259 [5.79%] participants to consume OTC painkillers only. Of this sample none reported to use more than the RDA. Seventeen participants [6.56%] solely consumed prescription painkillers and 3 participants consumed painkillers for more than the RDA. The remaining participants used both OTC painkillers and prescription painkillers. Mean daily consumption was 2.9 painkillers (OTC and/or prescription) per day. Presciption painkiller consumption ranged from 0 – 10 per day (Fig. 13). Of those who consumed presciption painkillers, almost a quarter (24%) reported to have misused their medication.

3.11. Correlation analysis

Pearson's correlations analysis was performed amongst all study variables and results provided in Table 4 below.

3.11.1. Significant positive correlations

Painkiller dependence showed significant positive correlations with Age, the number of prescription painkillers consumed per day, prescription painkillers consumed within the last 30 days, mean pain intensity within the last 30 days, mean pain frequency within the last 30 days, IS, HS, negative urgency, lack of premeditation and Lack of perseverance. Negative urgency was found to have significant correlations with HS and IS.

3.11.2. Significant negative correlations

Significant negative correlations were found between LDQ scores and sensation seeking, RS and DD. Negative urgency was found to have a significant negative correlation with RS.

No significant correlations were found between painkiller dependence and Impulsivity (overall score), positive urgency and OTC painkiller consumption. Thus, we can see a pattern emerging between painkiller dependence, self-compassion and some facets of impulsivity.

Further analysis to elucidate predictive variables was conducted using a regression analysis. Results are discussed below.

Table 4 Correlation analysis among study variables

Predictor variables	1	2	**3**	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. Age																		
2. Gender	-0.4																	
3. Painkiller dependence	0.45**	-0.05																
4. OTC painkillers consumed per day	-0.05	-0.02	**0.08**															
5. OTC painkillers consumed in last 30 days	0.02	0.01	**0.03**	0.7**														
6. Prescription painkillers consumed per day	-0.02	0.03	**0.25****	0.2**	0.3**													
7. Prescription painkillers consumed in last 30 days	-0.03	-0.07	**0.13***	0.2**	0.32**	0.74**												
8. Mean pain intensity in last 30 days	0.26**	-0.06	**0.46****	0.04	0.05	0.13*	0.87											
9. Mean pain frequency in last 30 days	0.3**	0.02	**0.5****	0.05	0.1	0.13*	0.08	0.8**										
10. Self-inadequacy	-0.2**	0	**0.14***	0.08	0.07	0.05	0.05	0.19**	0.05									
11. Self-reassurance	-0.18**	-0.06	**-0.27****	-0.15*	-0.2**	-0.06	-0.09	-0.2**	-0.19**	-0.45**								
12. Self-hate	0.05	0.02	**0.13***	0.05	0.06	0.08	0.05	0.22**	0.08	0.44**	-0.4**							
13. Impulsivity	-0.15*	-0.08	**0.09**	0.02	-0.1*	-0.04	-0.03	0.11	-0.006	0.44**	-0.25**	0.31**						
14. Negative urgency	-0.11	-0.02	**0.2****	-0.02	-0.1	0.02	-0.02	0.1	0.02	0.52**	-0.37**	0.30**	0.71**					
15. Lack of premeditation	0.26**	-0.05	**0.28****	0.06	-0.05	0.05	0.04	0.19**	0.19**	-0.03	-0.2**	0.18**	0.43**	0.13*				
16. Sensation seeking	-0.27**	-0.1	**-0.26****	-0.02	-0.1	-0.09	0	-0.03	-0.2**	0.1	0.25**	-0.11	0.43**	-0.09	-0.09			
17. Positive urgency	-0.11	0.1	**0.04**	-0.02	-0.1	-0.05	-0.06	0.09	-0.14*	0.41**	-0.2**	-0.35**	0.82**	0.66**	0.23**	0.22**		
18. Lack of perseverance	-0.04	0.1	**0.23****	0.06	-0.05	.003	-0.04	0.09	0.13*	0.2**	-0.36**	0.28**	0.5**	0.37**	0.47**	-0.21**	0.25**	
19. Delay Discounting	-0.06	0.03	**-0.13***	0.08	0.05	0.05	0.04	-0.09	-0.09	0.07	-0.09	0.09	0.1	0.19**	0.08	-0.1	0.13*	0.08

3.12. Regression analysis

Results of the hierarchical regression analysis (step-wise) are provided in Table 5 below. Variables were entered in 5 blocks containing the variables as shown in Table 5. The LDQ score (psychological dependence to painkillers) was the dependent variable. All other variables entered were independent variables (Table 3). Age, Pain frequency, the number of prescription painkillers consumed per day and DD score were the strongest predictors of painkiller dependence in the final model. Other significant predictor variables included Lack of Perseverance, Negative Urgency and Self-Inadequacy.

Low scores on the DD measure and high scores on Lack of Perseverance, Negative Urgency and Self-inadequacy predicted higher levels of Painkiller Dependence.

Lack of Premeditation and Sensation-Seeking were significant predictors upon entry but not in the final model.

Table 5 Proportions of variance accounted for (R2), adjusted R2, changes in R2 (Δ R2), and beta weights from hierarchical multiple linear regression with painkiller dependence as the dependent variable

Block and predictor variables†	Entry **β**‡	Final **β**‡	R^2	Adjusted R^2	**Δ** R^2
1.Demographics/Pain statistics			0.251	0.248	0.251
Age	0.34***	0.37***			
Gender	-0.05	-0.04			
Pain frequency	0.5***	0.39***			
Pain intensity	0.16	0.02			
Prescription painkillers consumed per day	0.21***	0.18***			
OTC painkillers consumed in last 30 days	-0.02	-0.09			
2. Self-compassion			0.422	0.413	0.171***
Inadequate Self (IS)	0.18***	0.12*			
Reassured Self (RS)	-0.18***	0.05			
Self-Hate (SH)	0.1	-0.05			
3. Cognitive impulsivity			0.448	0.438	0.03**
Negative urgency	0.14**	0.12*			
Lack of premeditation	0.11***	0.03			
Sensation seeking	-0.1***	-0.1			
Positive urgency	0.09	-0.14			
Lack of perseverance	0.17**	0.11*			
4. Behavioural impulsivity			0.474	0.459	0.03**
Delay Discounting score	-0.12**	-0.14**			
5. Interaction effects			0.497	0.481	0.02***
HS x Pain frequency	0.14**	0.07**			
RS x Pain frequency	-0.2***	-0.22***			
IS x Pain frequency	0.17***	0.06***			

*p < .05, **p <.01 and ***p < .001.

† Variables were added to the model using the stepwise method in each block. The criteria for entry and removal were p <.005 and p >.01 respectively.

‡Standardized regression coefficient. HS=Self-hate; RS=Self-reassured; IS=Inadequate-self.

It is also noted that the value for R^2 increased with each subsequent addition of a block. Initially, the Demographics/Pain statistic variables accounted for 25% of the variance and the addition of psychological measures meant that almost 50% of variance was accounted for. Thus, the addition of psychological variables doubled our understanding of dependence for painkillers.

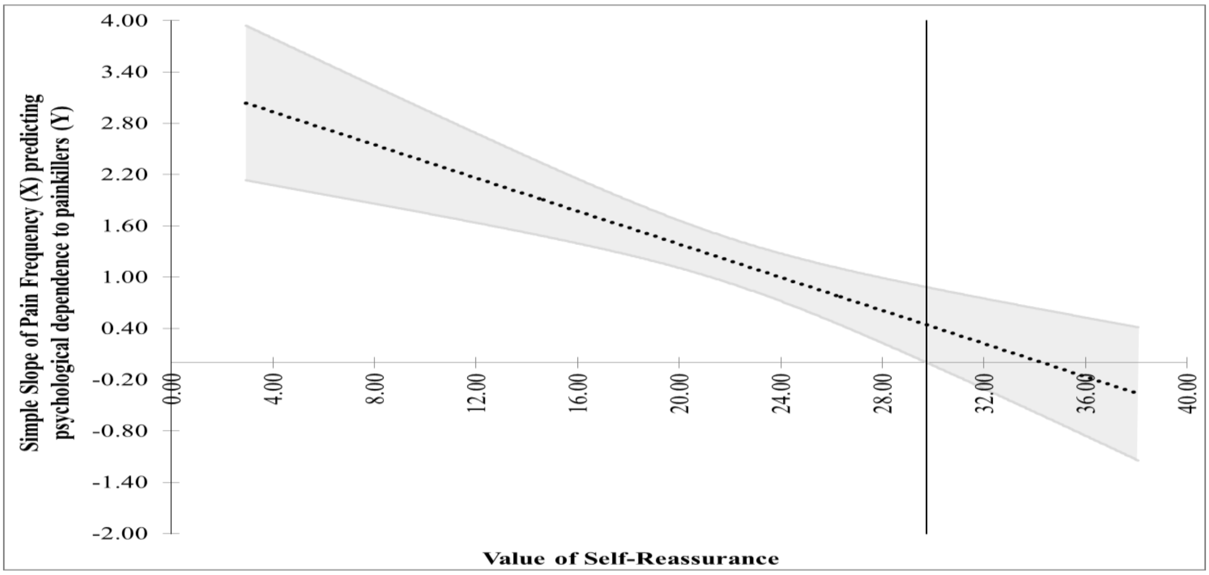
3.13. Moderation analysis

The output of the regression model (Table 5) provided three significant interactions (HS x Pain Frequency, $p < .01$; RS x Pain Frequency, $p < .001$ and IS x Pain Frequency, $p < .001$). These results suggest that metacognitive factors (HS, RS and IS) moderate Pain Frequency on Painkiller Dependence and so these results will be described below. Three separate analyses for moderation were conducted using the Johnson-Neyman Technique (J-N; Johnson & Neyman, 1936; Carden et al., 2017). Pain Frequency was entered as the explanator variable (X) and LDQ scores were entered as the response variable (Y). Either RS, HS or IS were used as the moderator variables (M) to produce the J-N graphs below (Figs 14-16). Confidence bands are show in figures 14-16 and shaded grey areas represent the confidence region (95%).

3.13.1. Moderating effects of Self-reassurance

Figure 14 shows that at a 95% confidence level, the effect of Pain Frequency on Painkiller dependence is significant when values of self-reassurance are greater than 2.89 and less than 29.91. This suggests that self-reassurance may act as a protective buffer for dependence to painkillers.

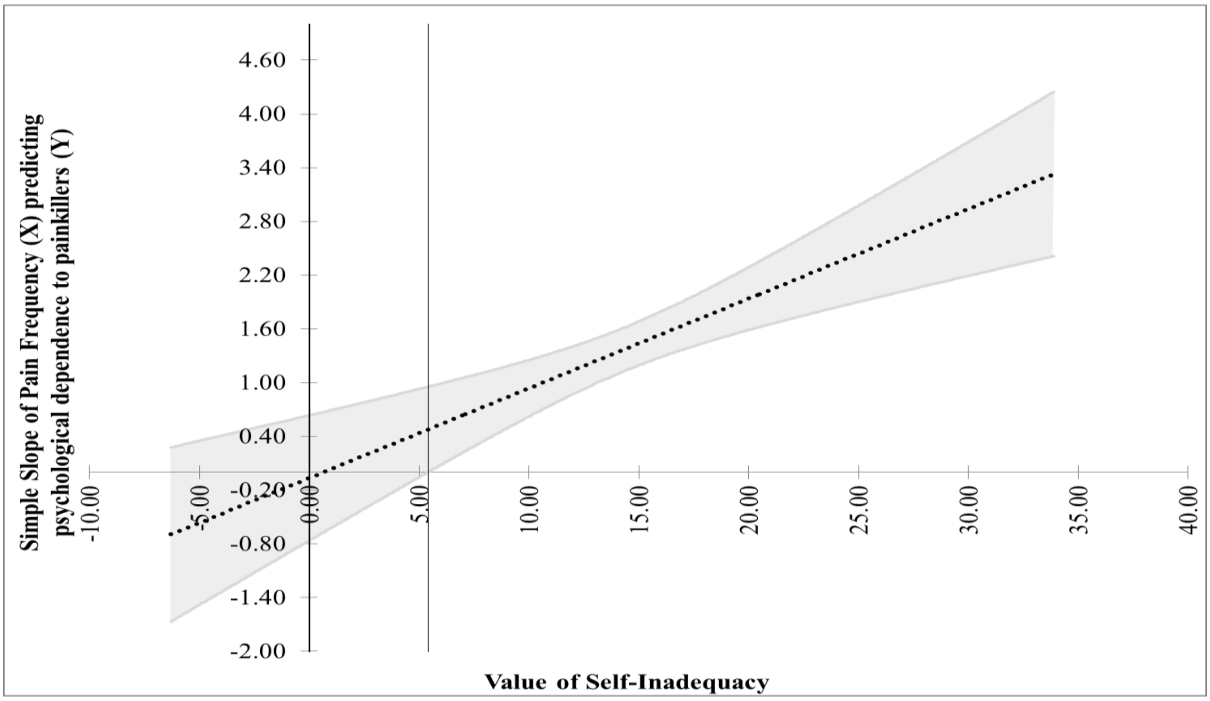
Figure 14 Effects of pain frequency and Self-reassurance on painkiller dependence



3.13.2. Moderating effects of Self-inadequacy

Figure 15 shows that at a 95% confidence level, the effect of Pain Frequency on Painkiller dependence is significant when values of self-inadequacy are above 5.56. This suggests that those participants who felt more self-inadequate were more likely to become dependent on their painkiller medication when the frequency of their pain was high.

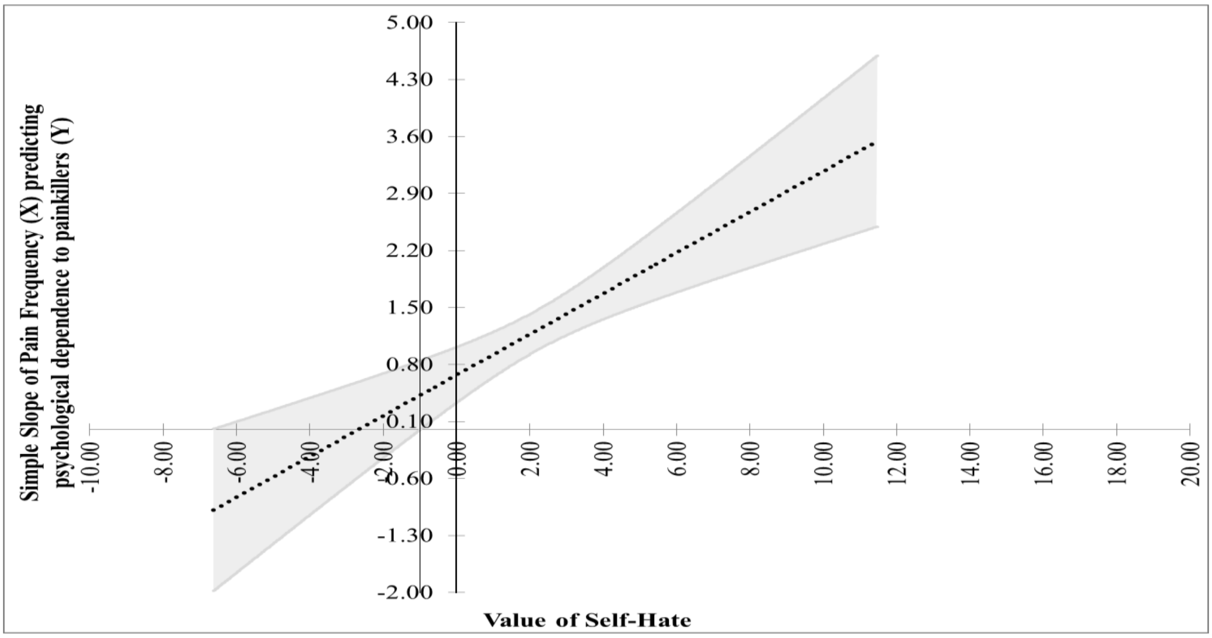
Figure 15 Effects of pain frequency and Self-inadequacy on painkiller dependence



3.13.3. Moderating effects of Self-hate

Figure 16 shows that at a 95% confidence level, the effect of Pain Frequency on Painkiller dependence is significant when values of self-hate are above -0.6. This suggests that those participants who felt more self-hate were more likely to become dependent on their painkiller medication when the frequency of their pain was high.

Figure 16 Effects of pain frequency and Self-hate on painkiller dependence



3.14. Discussion

3.14.1. Major outcomes of Study 1

The major outcomes for this study were that psychological dependence to painkillers, quantified by LDQ scores (M=4.52; SD=5.9), did occur in the study sample, albeit at the low end of the spectrum (Section 3.10.3.; Table 3; Aim 1). The study has revealed that there is a prevalence of psychological addiction to painkillers in the chronic pain community. This allowed for further examination of which metacognitive variables may contribute to this.

Significant correlations were found between psychological dependence to painkillers (LDQ scores) and variables linked to impulsivity (Negative urgency, Lack of Premeditation and Lack of Perseverance) and behavioural impulsivity as measured by the DD task (Section 3.10.5.; Table 4; Aim 2).

In addition, self-inadequacy and self-hate showed significant positive correlations with LDQ scores while a significant negative correlation was found with self-reassurance and LDQ scores. These results prompted for a hierarchical multiple linear regression analysis which showed significant predictors for painkiller dependence to be: Age, Pain frequency, Number of prescription painkillers consumed per day, Negative urgency, Lack of Perseverance, Self-inadequacy, and Delay Discounting. Significant interaction terms were found between HS and Pain Frequency, IS and Pain Frequency and RS and Pain Frequency.

Significant interaction terms from the regression analysis allowed for a moderation analysis (J-N technique) which revealed that HS, RS and IS moderate the effect of pain frequency on psychological dependence to painkillers but operate within a specific range of values as explained above (See section 3.13; Table 4; Figs. 14-16; Aim 3).

3.14.2. Overall discussion

This research project assessed for the first time, to our knowledge, the role of impulsivity (cognitive and behavioural) and self-compassion as risk factors for psychological dependence to painkillers. The primary objective was to elucidate which components of impulsivity and self-reassurance make significant contributions.

The findings of this study showed affect driven states such as negative urgency (the propensity to act impulsively when in a low mood) and self-inadequacy significantly contributes to painkiller addiction. It is conceivable that over time, and with increasing frequency of pain (Figs. 14 - 16), negative affective states would likely exacerbate and/or manifest in the form of an internal dialogue with tones of self-inadequacy. Such negative thoughts would likely nurture one's intrinsic propensity of engaging in impulsive behaviours. Combined with the low ability to make rational decisions, typical impulsive behaviours resulting from this habituation would result in greater consumption of painkillers or continuing to use painkillers for longer than the prescribed period i.e. substance misuse (Martel et al., 2014; Vest et al., 2016). Both aforementioned acts would heighten likelihood of psychological dependence to painkillers and both acts of impulsive decision-making are within the circumference of opting for the S-S reward with disregard for negative future consequences – a hallmark of impulsive choice; as captured by the DD paradigm (Yi et al., 2010).

A marked distinction between NU and other aspects of the impulsive spectrum lies in its contingency on negative emotions and/or low mood. Contemporary research provides empirical evidence of a prominent relationship between emotional oscillation and impulsivity amongst substance abusers. Simons et al., 2004 suggest emotional fluctuations and impulsivity operate in synergy to increase the risk for alcohol and methamphetamine abuse and related problems. Semple et al., (2005) demonstrate that depression scores best distinguished between methamphetamine abusers who scored high on impulsivity and abusers with low impulsivity. Additionally, those with elevated scores on impulsivity showed greater tendency to binge on methamphetamine, suggesting that impulsive users are more disposed to binge and abuse substances with the aim of appeasing a negative affective state.

In a similar framework, it could be hypothesised that those dependent on painkillers with elevated scores on negative urgency are more likely to engage in impulsive behaviours in order to relieve themselves from negative affective states associated with chronic pain (Whiteside & Lynam, 2001). This could be due to another important difference between NU and other aspects of impulsivity - its emphasis on negative reinforcement; the individual acts impulsively to avoid or escape a negative condition such as a prolonged experience of pain (emotional and/or physical). One likely explanation is that participants refer to negative affective states related to their chronic pain when answering the items on the negative urgency sub-scale. Furthermore, results explicate the role of impulsivity such that it is a highly pertinent variable for understanding the development of painkiller addiction. This is partly due to its stand-alone role as a distinct personality trait and partly due to a property that allows it to be influenced by our internal dialogue i.e. thoughts of self-inadequacy (Cyders & Smith, 2008).

Negative urgency is a trait that refers to individual differences in the disposition to engage in rash /impulsive action when experiencing negative affect. Self-critical thoughts are known to be highly prevalent in those who experience isolation, loss of job, lack of a support network, experience loneliness. These features are common amongst those with chronic pain and are also known to generate internal feelings of criticism (Dinger et al., 2014). When an individual has an internal dialogue that largely consists of self-inadequate or self-hate thoughts then these would likely place the individual in a state of negative affect (Gilbert, 2005, 2009), which would spur the action of negative urgency (Zorilla & Koob, 2019) in the form of drug-seeking behaviours. The sample in this study were seen to be psychologically dependent to painkillers and the consumption of drugs (e.g. painkillers) are well known to relieve the individual of negative affect, calm any unpleasant sensations associated with withdrawal from drug consumption and restore emotional homeostasis. Gilbert (2005) has shown that biases in self-critical thinking are influential in the development and maintenance of psychopathology. These results reflect this by highlighting the moderating roles of self-reassurance and self-inadequacy on painkiller dependence. This observation is encouraging when considering development of a psychological intervention for painkiller addiction as a future research endeavor.

3.14.3. Theoretical implications of the findings

Results from this study have contributed to the wider theory of impulsivity and its role towards addiction by showing positive correlations between psychological dependence to painkillers (LDQ scores) and facets of impulsivity (Table 4). This finding is consistent with the scientific literature, which shows impulsivity to be an influencing factor for substance dependence (Kirby et al., 1999; Nielsen et al., 2012; Robles et al., 2011). The literature states that individuals deemed to be high on the spectrum of impulsivity show a greater proclivity to try illicit substances in the first instance, as outlined in section 1.2.1. and in Figure 3 above, and then progress towards a state of dependence as consumption of the substance continues. In addition to cognitive impulsivity, behavioural impulsivity also made a contributing factor as demonstrated by a significant negative correlation between LDQ scores and DD scores. When interpreting the DD scores, a low score indicates impulsive decision making while a high score indicates rational decision making. Although the correlation was negative (i.e. low DD scores equate to lower dependence to painkillers) this could imply that those who were better at self-regulating behaviours were more cautious (and less impulsive) and so they stood a better chance at remaining free from painkiller dependence. A low DD scores equates to a higher level of behavioural impulsivity while high scores on DD equates to low level of behavioural impulsivity.

Lack of perseverance has been related to one's ability to inhibit previous information that is no longer relevant, a reduced diligence of ongoing tasks (Rochat et al., 2018) and may also interact with stress. A recent study showed that individuals with low levels of perseverance gambled more after experiencing a loss in a stressful situation (Canale et al., 2017). Other studies have linked lack of perseverance to food addiction (Murphy et al., 2014), Cocaine addiction (Albein-Urios et al., 2012) and Opiates (Sargeant et al., 2012). This cognitive process may help explain the reported associations between lack of perseverance and LDQ scores. People with a lack of perseverance might have a difficult time following through with attempts to change addictive behaviours, which could also allow for a SUD to remain. However, once an addictive behaviour is being engaged in regularly, other traits may play an important role in its maintenance. Individuals who engage in aberrant opiate consumption (e.g. consuming more than the RDA) often attempt to reduce or stop the behaviour. A study by Cicero et al., (2014) found that up to 85% of recent addicts report a desire to stop engaging in drug consumption. However, stopping this behaviour requires one to persevere through upsetting emotions and high levels of negative affect, which are thought to increase the urge to engage in the behaviour (Bresin et al., 2013). A lack of an ability to maintain focus on the goal of stopping the behaviour; that is, weak ability to persevere in pursuing that goal, may increase the likelihood of maintaining the behaviour. It is thus hypothesised that lack of perseverance to be a primary trait predictor for the maintenance of painkiller dependence in this study sample.

Results also showed self-criticism (self-hate and self-inadequacy) to have a statistically significant positive correlation with LDQ scores while self-reassurance to have a statistically significant negative correlation with LDQ scores (Table 4).

These findings bolster the wider literature of addiction studies in that the meta-cognitive risk factors identified in this study need to be considered when therapeutic interventions are devised and administered for those with psychological dependence to painkillers.

3.14.4. Translation of findings

This study has shown cognitive components of impulsivity and self-criticism to be risk factors for painkiller dependence with the phenomenon of painkillers themselves being a relatively new substance of abuse being researched. The results from this study pave way for a therapeutic intervention(s), which incorporate principles of CFT and CMT as a means of targeting psychological dependence to painkillers. In addition to painkiller dependence it would also be of great importance to test whether such an intervention would also be as effective for other types of substances such as alcohol, nicotine, heroin and "process addictions" such as gambling and problematic spending.

Results showing self-criticism to be a risk factor for psychological dependence to painkillers should inform theory and practice towards the importance of these meta-cognitive risk factors. Practitioners of CFT and professionals within the field of addiction treatment may find that application of CFT principles towards treatment of addiction may benefit their service users when other methods may become unsuitable.

3.15. Limitations of study

This section will explore some of the limitations observed in the study and will provide some strategies for reduction.

3.15.1 Limitations of self-report measures

Despite attempts to produce a robust study there did exist some limitations. This study used self-report measures in order to quantify consuming habits of opioid analgesics. It is possible that participants may have been inclined to answer less than actual amount of consumption and could possibly skew results or give inaccurate results. However, painkiller consumption from participants in this study are similar to those obtained by Elander et al., 2014. The general use of self-report measures in research hold problems as they are subject to subterfuge i.e. participants do not have to answer honestly in the questions. More so, participants may not have sufficient knowledge or insight to answer the questions.

3.15.2. Limitations of the behavioural measure

In order to quantify behavioral impulsivity, this study used the DD task and participants were given a hypothetical monetary reward for their choices. Previous studies have demonstrated that money is less steeply discounted that other reward outcomes. One study found that participants with opioid dependence discounted monetary rewards less that they did when heroin was used as a reward i.e. they behaved more impulsively when heroin was a reward than when money was a reward (Madden et el., 1997). This finding is not unique to heroin dependent individuals but has been replicated in those with dependence to cocaine, nicotine and marijuana (Bickel et al., 1999; Coffey et al., 2003; Johnson et al., 2010; Petry, 2001). While it has been suggested that differences in discounting in reward types (drugs vs. money) is related to addiction, studies have found that participants who do not have problematic drinking also discount alcohol more steely than monetary rewards (Odum & Rainaud, 2003). For these reasons monetary were chosen to be used rewards in lieu of hypothetical painkiller pills as a reward.

Investigation of various reward outcomes permits one to examine the other side of the personality trait i.e. the propensity to react in specific ways under specific situations. Those who display steep discounting of one reward type (e.g. drugs) should then also display steep discounting of another reward type (e.g. food) if they behave comparably in diverse outcomes. To quote Green & Myerson (2010, pg. 68), "*If impatience is a trait, [impatient] individuals would be expected to consistently discount delayed outcomes more than do other individuals, regardless of what the outcome is …*". However, a very limited number of studies have attempted to address this matter. Researchers have reported moderate to strong positive correlations of discounting rates between forms of entertainment (e.g. DVDs, CDs, Books), money and food (Charlton & Fantino, 2008). Other researchers have found similar outcomes. A strong positive correlation (r = .72) was found in current marijuana users between the rate of discounting hypothetical marijuana and money Johnson et al., (2010).

In order to investigate these concerns within the chronic pain community, a study that provided participants with hypothetical monetary reward for one group and a second group given a hypothetical reward of painkillers would aim to answer this question.

3.15.3. Limitations of a web-based study

In addition to the above, the fact that the study was placed on the internet and participants were unknown to the experimenter poses some problems. The anonymity provided by the study design means that it is possible for a participant to be not living with chronic pain and/or may not ben consuming painkillers. It is also possible that a participant may have multiple accounts set up with a view of increasing the probability that he/she may win the prize draw on offer. Furthermore, a participant may not have met the eligibility requirements and would have falsely been allowed to enter the study. Future studies would aim to recruit participants and have them thoroughly screened prior to being given login details.

3.15.4. Limitations of the participant sample

Finally, it could be said that the sample of participants used in this study may not be an accurate representation. However, the data form this study, particularly demographic data and LDQ scores are observed to be similar to those obtained in other published studies (i.e. Elander et al., 2014).

Priming is a nonconscious form of memory related to perceptual identification with words and/or objects. The effect of priming could have occurred in the CMT group as the consent form contained salient cues in the wording such as "self-critical thoughts." Future studies would aim to reduce the effect of priming. It should also be noted at this stage that participants were recruited from across the globe and the influence of culture may have had an impact on results. Below is a balanced critique on the role of language, culture and illness perception across cultures and offer potential solutions.

3.15.5. Limitations from Language, Culture and Perception of Illness

When conducting cross-cultural studies it is important to be mindful of participants' language and culture and the biases it may bring to experimental design and research outcomes. This section will explore the role of language, culture and how one's perception of illness may possibly contribute to limitations within this study.

3.15.5.1. Language and its implications on validity of measurements in cross-cultural studies

Researchers are conscious of the pitfalls of cross-cultural comparability and have developed a set of guidelines. As such, self-report measures should use accurately translated questions (Harkness & Schoua-Glusberg 1998, Harkness et al., 2010b); apply comparable probability sampling designs (Hader & Gabler 2003, Heeringa & O'Muircheartaigh 2010); achieve comparably high response rates (Billiet et al., 2007); continually apply the same mode of interviewing (Kalgraff-Skjak & Harkness 2003); and include highly reliable, valid, and comparable measurement instruments (although there is disagreement in the literature about the standards (Brown 2006). Unfortunately, not all research studies adhere to these standards, usually due to monetary and organisational constraints. The European Social Survey administrators have made continued advances to advise on the highest standards of data collection. However, even the most rigorous application of current standards cannot guarantee that measurements are comparable across nations (Jowell et al., 2007).

To circumvent construct bias, it is vital to acquire cross-cultural similarities and differences in a variety of experiences, thoughts, feelings and behaviours. Subject matter experts may be consulted to gauge whether self-report measure items are suitable in their culture specific contexts and ensure pertinent matters are considered (Johnson 1998). To circumvent method bias sampling methodologies should be analogous and interviews must also be performed by well-trained persons (Johnson 1998). To avoid item bias, merely translation from one language to the other is not deemed to be a satisfactory method, as it does not reveal the way specific items are recognised in the other culture/linguistic equivalent. A good quality translation can largely avoid item bias. For example, in translation and back-translation (Johnson 1998), a bilingual participant translates the item from one language to another, while another bilingual participant translates them back to the original language.

As this study had participants from across the globe, there could have been some bias introduced through the use of self-report measures written in the English language and English may not have been the first-choice language for some study participants.

3.15.5.2. Cultural differences in Compassion

Across different cultures, people have different conceptions of compassion and other related states such as sympathy, empathy and emotions (Shaver et al., 2001). Simultaneously, cultures diverge in what it means to “be compassionate”. Western concepts of compassion assume people ought to feel the most compassion for people who they can identify with (Batson et al., 1983), whose perspectives they can relate to (Toi & Batson, 1982) and who they feel they have most common ground with (Batson et al., 1987). Juxtaposed to this, Buddhist frameworks of compassion state that we are all connect with each other regardless of race of culture (Dalai Lama, 1997), and so anyone can feel compassion for another human being including enemies and wrongdoers. Additionally, differences in the operationalisation of compassion have been highlighted between independent and inter-dependent cultural settings (Kitayama & Markus, 2000)

In contrast, some research findings have shown that triggers for sympathy are not too distinct across cultures (Zhang et al., 2007). Amongst Israeli, German and Malaysian cultures, children have shown to express sympathy by raising their eyebrows and spoke in a gentle tone when shown images of others expressing sadness (Trommsdorff et al., 2007). This is seen in other cultures whereby the majority of a study sample of Brazilian children and American children showed altruism and compassion by stating they wanted to give money to a stranger in need (Eisenberg et al., 2001).

Relatively little research has examined the expression of compassion. A seminal study by (Hernstein et al., (2006) showed that sympathetic touch can be differentiated from other emotional touches. The research group asked U.S. and Spanish participants to touch another participants hand in a manner than expressed specific emotions. Participants were not allowed to see or speak with the recipient participant. Both U.S. and Spanish participants were able to differentiate sympathetic touches from angry, afraid, disgusted, surprised, loving, and grateful ones. Other research findings highlight cultural practices to heighten the propensity for expressing compassion. A notable example being the practise of meditation which has shown to heighten expressions of compassion (Condon et al., 2013; Kemeny et al., 2012; Weng et al., 2013). Condon et al., (2013) showed participants who were in an eight-week meditation course (versus a no intervention control group) were more likely to offer their chair to an individual who displayed signs of pain when standing.

Taken together, these findings indicate that subtle differences occur in various aspects of compassion (E.g. being more compassionate to those one identifies most with) although there are some universally common aspects of compassion (e.g. giving money to a stranger in need). As this study included participants from various cultures, individuals may have introduced bias as they formulate and apply their own views on what they deem to be compassion during the study.

3.15.5.3. Cultural influences on illness perception

With increasing ethnic diversity, clinicians, and researchers alike, are required to understand and meet the needs of people from varying cultures and offer culturally applicable healthcare. Thus, there is a need to comprehend the influence of race, culture and ethnicity in pain management and pain research. Culture influences illness behaviour in several way. These could include (1) defining what is regarded as ‘normal’ and ‘abnormal’, (2) determining the cause of illness, (3) influencing the decision-making control in healthcare settings and (4) impacting on health-seeking behaviour. While the subject matter of culture and its influence on illness perception is vast, it is beyond the scope of this thesis to cover all illnesses from all cultures and so the discussion and observations described below shall be limited to chronic pain.

Pain is a private and internal experience, however the behaviour surrounding this are influenced by cultural and psychological factors. These such factors govern whether private/internalised pain manifests as pain behaviour or not, the type of behaviour and the setting within which it occurs (Helman, 2007).

In some cultures, living with chronic pain may be viewed as a personal failing or weakness when unable to overcome the condition or fulfil culturally assigned roles in the family or society (Ludwig-Beymer, 2008). Certain individuals could perceive their outcomes as consequences of their own behaviours (Baker et al., 2008). Living with chronic pain may also be considered a subject matter to be hidden from spouses and children so as not to appear a burden (Katz et al., 2011). Additionally, this may prevent one from seeking help from a professional/clinical setting in the first instance.

To conclude, this section has explored how language, culture, conceptualisation of compassion and perception of illness may shape the outcomes of research validity. Language is a method by which ideas are expressed and meanings are interpreted. This presents a challenge particularly for bilingual individuals who may translate meanings (i.e. from self-report measures as used in this study) in different ways and interpret them in ways different to what the experimenter had intended; thus, skewing outcomes. While there are some preventative measures (Van de Vijver 1998; Johnson 1998; Jowell et al., 2007) which can reduce bias there remains mixed feelings about how, and if, language can skew results.

Conceptualisation of compassion appears to differ amongst cultures (i.e. Western cultures vs Buddhist cultures). While triggers to compassion seem to be similar across cultures, it is the experience of compassion which may differ. Despite differences in conceptualisation of compassion between cultures, there also appears to be differences within cultures themselves (Miller & Bersoff, 1994) which further complicates the impact of bias. Cultures also come with their own set of beliefs which may cause individuals to feel shame such that their illness has limited their capability to perform duties set out by their culture. Individuals may hide their illness (or addiction) from relatives and friends (Ludwig-Beymer, 2008; Katz et al., 2011). This may also transpose to seeking help from a clinical setting. Therefore, creating a safe and private environment where individuals can seek treatment in their own time with privacy whilst remaining anonymous, such as a web-platform, could be a potential remedy to this situation.

3.16. Future research aims

To nourish the poverty of research in this population, future studies will aim to produce and assess a bespoke psychological intervention focused on ameliorating impulsive decision-making by substituting self-critical thoughts with self-compassionate thoughts and to investigate whether psychological dependence to painkillers can be reduced.

3.16.1. Revealing other facets of impulsivity as risk factors for painkiller dependence

While the literature has remained universally undecided on the definition of impulsivity, different models have suggested that the crux of impulsivity includes lack of planning, difficulties in concentration/attention, failure to inhibit actions and the attraction to smaller-but sooner rewards. More recently, research has revealed that impulsivity is triggered in conditions of extreme affect (Positive and Negative; Johnson et al., 2020). While this study revealed facets of cognitive impulsivity to act as risk factors for painkiller dependence, there remains other quantifiable facets of impulsivity which could also be predictors for painkiller dependence which could also highlight a pathway to painkiller dependence. Discovering these other facets of impulsivity would provide a more complete understanding of which types of impulsivity contribute to painkiller dependence in the chronic pain community. This aim could be tested using other self-report measures (e.g. BIS-11, I7 Questionnaire and the BIS/BAS Scale).

3.16.2. Quantifying other facets of behavioural impulsivity as risk factors for painkiller dependence

As mentioned in section 3.16.1., other facets of impulsivity may contribute to painkiller dependence which were not captured using the applied measure. Similarly, there could exist other behavioural measures which better explain the path to painkiller dependence and so to provide a complete understanding one would aim to include other measures of behavioural impulsivity which could be used in future studies (e.g. Go/No-Go task to measure Action Restraint, Iowa Gambling Task or Probability Discounting to measure Risky Choice; See also Fig. 4 above).

3.16.3. Varying reward outcomes in the DD task

Section 3.15.2. highlights a limitation in the behavioural measure for impulsivity such that hypothetical monetary rewards are less steeply discounted than rewards such as physical drugs reward (Madden et el., 1997). Future studies in the chronic pain community would aim to provide participants with hypothetical monetary reward for one group and a second group given a hypothetical reward of painkillers would aim to reveal if this makes a significant difference in quantifying behavioural impulsivity in this study sample.

3.16.4. Further explore the role of affect towards painkiller dependence

As study 1 results highlighted the role of several affect driven variables (e.g. Negative urgency, self-inadequacy, self-hate and self-reassurance) to be predictors for painkiller dependence, the role of affect could be further quantified to assess its contribution for SUD development. This could be achieved by introducing a measure that captures affect, such as The Positive and Negative Affect Schedule (Watson et al., 1988). Scores from this measure could be incorporated into the analytic strategy that was used in this study and seek correlations between other study variables and explore moderating aspects of affect to fully understand its influence.

3.16.5. Widening the theoretical knowledge on impulsivity and self-reassurance

Impulsivity is a known risk factor for other drugs of abuse and for process addictions such as eating, gambling and spending money (Flight et al., 2012). This study has shown self-reassurance to act as a moderator for painkiller dependence but is context specific to this study population (i.e. RS moderates painkiller dependence in the presence of pain and its moderating role is significant within a specific range of scores). The potential benefits of RS could be applied to those who struggle with addiction to other substances and perhaps also to those who have an Impulse Control Disorder (e.g. Intermittent Explosive Disorder, Kleptomania, Pathological Gambling, Pyromania and Trichotilliomania).

As discussed in section 3.15.6. – 3.15.7.2., the role of culture has a significant impact in comprehending concepts such as compassion, addiction and illness. These aspects need to be carefully considered and so future studies could aim to replicate this study in a more tightly controlled sample which aims to capture one given culture and then compare with another culture. In addition to reducing linguistic discrepancies, statistical procedures can be applied to limit bias as suggested in section 3.15.5.3.

3.17. Concluding comments

To conclude, this study has successfully shown three facets of impulsivity to significantly promote psychological dependence to painkillers in those with chronic pain. The study has also shown, for the first time, a behavioural measure that captures the propensity for painkiller dependence using an objective measure of impulsive decision-making in those with chronic pain. Finally, the study has demonstrated that when our internal dialogue comprises chiefly of self-critical thoughts then this too will promote painkiller dependence when there is increasing levels of pain frequency (See section 3.13). The following chapter will explore the role of CMT as a potential mechanism for reducing risk factors for painkiller dependence.

Chapter 4: Compassionate Mind Training as a potential intervention for reducing painkiller dependence

4.1. Introduction

Compassion based therapies and interventions are a rapidly growing area of research and publication numbers have continually increased year upon a year. A search for "compassion" on Google Scholar (January 2019) yielded 1.1 million results for publications containing the term. Given the differing stances, viewpoints and definition in compassion it is of no surprise that there exists a plethora of therapies which apply compassion. There exists at least six forms of accepted therapies that have been empirically tested and incorporate compassion as a central focus. While all six have been subjected to randomised controlled trials, only Loving-Kindness Meditations and Compassion Focused Therapy have also been subject to systematic review (Hoffman et al., 2011; Leaviss & Uttley, 2015)

4.2. What is Compassionate Mind Training?

Both CFT and CMT were devised to increase compassion (Gilbert, 2005). The associated interventions are regarded as manualised programmes which permit CFT and CMT exercises to be delivered with more flexibility which can be tailored to suit the individual while other compassion-based interventions are delivered as a "one size fits all" formula (Gilbert & Irons, 2004). Theoretical underpinnings of CFT and CMT are also unlike other forms of interventions as it was constructed using empirical evidence and theory from attachment theory, Buddhist philosophy, evolutionary psychology and neuroscience (Bowlby, 1969; Gilbert, 2010). This background rooted in scientific rigour has influenced the Three Circles Model in that the aim is to balance the system and endorse affiliative emotions and processes by using skills in compassion; (Gilbert, 2009; 2010; see section 1.5.9.2.). The theory of CFT and CMT can also be delivered to the individual engaged with the therapy or intervention by way of psychoeducational material (Gilbert, 2005; 2009).

Sections 4.2.1. – 4.2.4. below will outline exercises borrowed from CMT practices which will be used in the web-based intervention of this research study.

4.2.1. Compassionate imagery

The application of using imagined images as possessing compassion is not a novel concept and has been explored and applied for much time with great success (Leighton, 2003; Lee, 2005). In CFT/CMT the client is requested to imagine a "ideal compassionate other". This image can take the form of a human, an animal or even an object such as a tree. The image created is used to provide compassion for the client and the image is usually personal to the individual often possessing properties which are akin to the individual (e.g. life experiences; Gilbert, 2005; 2010).

The client is asked to give the compassionate image an ideal voice tone, facial features and expressions and characteristics (e.g. wisdom, warmth, compassion, encouragement). All these properties are explored in therapeutic sessions with the therapist.

Exercises which manipulate posture of the body whilst imagining possessing genuine compassion are employed within CFT/CMT practice as is often used in method acting (Gilbert, 2010). Other features such as voice tones, facial expressions, stance, thinking styles, response styles and age are also delved into. Daily practise is encouraged by requesting the client to "step into the shoes" of the compassionate image and mimic the features of their image (voice tones, posture, thinking styles, facial expressions).

The practice of compassionate imagery exercises, as used in studies 2 and 3, with an emphasis on self-compassion have been shown to be beneficial for impulse control as shown in a seminal study by Adams & Leary (2007), which investigated the effects of self-compassion on self-regulation. The study first assessed the proclivity for guilty and restrictive eating patterns. Participants were randomly allocated into groups in which they would either consume an unhealthy preload or eat nothing followed by a self-compassion induction or receiving no induction after which they took part in a tasting session of sweets. It was expected that restrictive eaters would have displayed the disinhibition effect of overeating upon breaking dietary rules (Herman & Mack, 1975), which was required by the preload condition. However, the authors discovered that restrictive eaters consumed less food after a preload if they were imbued with a self-compassion protocol. Therefore, this study suggests that self-regulation can be increased with self-reassurance within those participants who were thought to have difficulties in controlling their impulsive behaviour.

4.2.2. Compassionate sensation

The skill of compassionate sensation denotes to the method in which a therapist aids the client to delve into the sensations experienced within their bodies whilst they concentrate their efforts on becoming more compassionate (from others and self-compassion). This skill aims to foster self-generating compassion comprised of friendliness, reassurance and kind-heartedness (Gilbert, 2010).

4.2.3. Compassionate feeling

The skill of compassionate feeling is living the experience of receiving compassion from others, giving compassion to others and giving compassion to oneself. These feelings can be generated in a number of ways and some are outlined above (compassionate attention, thinking and behavior; Gilbert, 2010).

In addition to the skills of compassion, CFT and CMT practitioners will usually employ Soothing Rhythm Breathing and this too will be incorporated into this piece of research.

4.2.4. Soothing Rhythm Breathing

Soothing Rhythm Breathing (SRB) exercises permit participants to get a sense of calmness and allowed for a fluid transition into CMT practise. Breathing exercises such as SRB are used in this research (studies 2 & 3) and have shown to help regulate anxiety and impulsive behaviour (Broderick, 2009). SRB is designed to deepen and slow down the breath to a frequency of five to six breaths per minute while focusing the attention on the body (slowing down and becoming heavier and grounded (Gilbert & Choden, 2013). Empirical evidence also states that such a pattern of breathing can lower arousal rated and activate the parasympathetic nervous system to give feelings of tranquillity and composure (Lin et al., 2014; Streeter et al., 2012). Additionally, the sympathetic nervous system can become active and significant improvements in heart rate variability have been observed. This is associated with a reduction in feeling stressed, an increase in affiliative behaviours (Kogan et al., 2014) and supporting development of neural regions associated with impulsivity (frontal cortices; Porges, 2007) which is a risk factor for developing a SUD.

4.3. Rationale for using CMT to reduce impulsivity and painkiller dependence

Below is an exploration of reasons and supporting empirical evidence as to why CMT may be beneficial for individuals who are currently consuming analgesic painkillers and may potentially face the risk of developing a SUD.

4.3.1. Meta-analysis and systematic reviews on compassion-based therapies

Thus far there has only been one meta-analytic study available which has explored compassion-based intervention (Kirby et al., 2015). This study found 23 Randomized Controlled Trials (RCTs) in the past decade. The authors of this study explored seven outcomes (compassion, mindfulness, anxiety, depression, psychological distress, self-compassion and life satisfaction and happiness). For studies to be included in the analysis interventions had to have a clear focus on building compassion within individuals, have more than a single session, adhere to RCT protocols and have a self-report measure which quantified compassion and/or psychological well-being. Results showed twelve RCT studies which had significant short-term moderate effect sizes for compassion (d =.559), self-compassion (d = .691), and mindfulness (d = .525). When exploring the reduction of depression and anxiety, the meta-analysis showed significant moderate effects (d =.656 and d = .547 respectively). Small-to-moderate effects were found for psychological distress (d = .374). Finally, Significant to moderate effects were found for life satisfaction and happiness (d = .540). Kirby (2017) states that "*Of all the interventions, CFT has been the most evaluated, and is the most appropriate for use in clinical populations*."

The next section will provide the neurophysiological evidence and theoretical underpinnings which relate compassion with impulsivity and substance dependence.

4.3.2. Neural & Physiological changes which may benefit individuals with susceptibility to developing SUD

As mentioned in Chapters 1 and 2, Compassion-based exercises have been shown to be beneficial for well-being and changes in our physiology. Such changes include Heart Rate Variability (HRV; Rockliff et al., 2008) and neural changes in the prefrontal cortex, the area of the brain responsible for decision making (including impulsive decision making; Klimecki et al., 2014; Weng et al., 2013). Results from study 1 showed that behavioural impulsivity, as quantified by the DD task, and impulsivity in general is a risk factor for psychological dependence to painkillers. Application of an intervention that targets the neural physiology responsible for impulsive behaviour may be of benefit to individuals within the chronic pain community as a reduction impulsive behaviour would reduce psychological dependence to painkillers.

Porges (2007) set out the Polyvagal Theory which states that activation of the parasympathetic nervous system (PNS) is responsible for initiating feelings of calmness and maintaining a soothed feeling in our bodies when faced with threat or distress. This threat or distress can be in the form of pain experienced in our bodies or it can be the onset of a craving (psychological distress and discomfort). Skills in compassion, as outlined above, aim to activate the PNS and so could prove to be beneficial.

Additionally, the sympathetic nervous system (SNS) becomes activated when individuals experience a threatening circumstance. The SNS then inhibits one's aptitude in higher order cognitive capabilities (i.e. rational decision making is hampered). These can include decisions surrounding (safe) medication consumption, particularly in times of sufficient distress. Activation of the PNS alters the neural circuitry in the frontal lobes which permits feelings of content and safeness by activating the prefrontal cortices, the neural architecture responsible for decision making (Klimecki et al., 2014; Liotti & Gilbert, 2011; Thayer & Lane, 2000). Thus, we can see that by using an evidence-based therapy (Skills in Compassion/CMT exercises) we can temporarily activate neural circuitry (PNS) associated with decision making capabilities (Rockliff et al., 2008; Gilbert, 2014). This could provide potential benefit by allowing for optimal decision-making (i.e. not consuming painkillers over the RDA). This may be particularly useful for those who are prone to largely making impulsive decisions and as we know, impulsive decision-making (e.g. Negative Urgency) is a risk major factor for addiction (Madden et al., 1997). Therefore, reducing impulsive decision-making and impulsive behaviour by stimulating the PNS, by way of CMT, one may reduce the propensity for substance dependence.

Gilbert (2005; 2009) included a neuroscientific rationale during the inception of CFT and CMT with the prospect that clients would receive knowledge on self-regulation by incorporating self-compassion into their schemas. Gilbert proposed that individuals able to conjure thoughts of kindness, gratitude, compassion and warmth and engage with internally generated stimuli (e.g. compassionate imagery, compassionate voice tones) were in fact stimulating neural pathways associated with neuro-affective processes in similar ways that externally derived stimuli elicit similar responses (e.g. imagining food when hungry may stimulate the salivatory response). Thus, there is strong evidence that engaging in CFT and CMT has an effect on the neural architecture. This includes neural areas responsible for impulsivity and regulating behaviour. A seminal study (Adams & Leary, 2007) sought to deduce the effects of self-compassion on regulating behaviour (eating behaviours). The researchers gauged the level of participant's propensity for restrictive and guilty eating behaviours. Participants were randomised into one of two groups where one group ate an unhealthy preload and the other group who did not, and then to partake in a short self-compassion intervention or not. They were then requested to taste sweets and informed there was no limit on the quantity of sweets they could consume. Those deemed as restrictive eaters were expected to display disinhibition of overconsumption after breaking dietary rules (Herman & Mack, 1975) as was required by the preload condition. The results showed that participants who were restrictive eaters and had engaged with the self-compassion intervention consumed less after the preload compared to the other group. These results suggest that the mechanisms responsible for self-control and self-regulation of behaviour can be moderated by stimulating compassion in those who were expected to struggle with self-control. If the same principles can be applied to consumption of painkillers in lieu of sweets, then fostering feelings of self-compassion would be highly beneficial for those who regularly consume painkillers.

4.3.3. Buffering against emotional distress and building resilience

Anxiety and Depression give rise to emotional distress in an individual and fluctuations in emotion are known risk factors for SUD (Weiss et al., 2015). They also show a negative correlation with self-compassion (Smith & Book, 2008; Green et al., 2012; Neff & Dahm, 2014) and so the view of self-compassion being an emotional buffer has been accepted. This would be useful for those whose negative behaviours are governed by strong emotions (e.g. negative urgency). Neff et al., (2007) has shown that those who engaged with a CMT intervention gave a less anxious self-evaluation when they thought back to an incident where they felt emotionally low. These individuals also engaged in an ambiguous task and when they were given negative feedback on the task they responded with more positive emotions, more so when self-esteem was low (Leary et al., 2007). Such findings suggest that engaging in CMT can buffer an individual from distress and negative affect by providing them with tools which help them regulate emotionally driven behaviours better. In 2006, Gilbert & Proctor conducted a 12 session CMT intervention for those with chronic mental health issues. At post-intervention, participants' level of depression, self-criticism, anxiety and shame had reduced significantly and their ability to self-soothe had significantly improved. Kelly et al., (2009) applied a 2-week CMT intervention of daily exercises and at the end of treatment participants reported less shame and a reduction in skin complaints when compared to controls. This showed that engaging in CMT not only affects the cognitive elements of an individual but also the physiological makeup of those engaging with CMT.

The principles of CMT could be extended to those with at risk of developing SUD to help them self-soothe and reduce emotionally driven behaviours which are detrimental (e.g. negative urgency). Results from study 1 (above) showed that negative urgency is a risk factor for psychological dependence to painkillers. This facet of impulsivity is affect driven (negative affect) and so reducing the individuals response to negative affect should reduce the probability of negative urgency manifesting as a behaviour (i.e. consumption of painkillers). Therefore, it is important the intervention used will aim to dampen the effects of negative urgency by acting on the appropriate neural physiology. The effects of compassion-based interventions have been tested in those with chronic pain with promising effects. In the U.S. over 400, 000 individuals live with the debilitating condition of Multiple Sclerosis. These individuals, like most with chronic pain, live a life of unpredictable relapses of disabling conditions and a poorer quality of life than the general population. Nery-Hurwit et al., (2018) examined the role of self-compassion and resilience on perceived health-related quality of life for those living with Multiple Sclerosis. A sample of 259 adults had baseline measures taken for self-compassion, quality of life and resilience prior to engaging with then compassion based intervention. A moderation analysis revealed a significant direct effect between self-compassion and quality of life. Results from this study strongly suggest that individuals with chronic pain conditions who engage in compassion-based interventions may accrue strategies to better manage their debilitating conditions and reframe perceptions of their health. Additionally, increasing resilience may aid individuals overcome distressing events. Self-compassion and resilience are both modifiable constructs that can be targeted by programs seeking to improve overall wellness.

Gilbert (2005) suggests that individuals who are usually forceful and harsh with themselves (e.g. restrictive eaters; those coping with life while living with chronic pain) would benefit from CMT. These individuals are thought to have a hypoactive soothe system and a hyperactive threat-focused system (LeDoux, 1998). The threat system has evolved over millennia to protect the organism in times of threat and danger by integrating external signals which trigger internal feelings of anger and shame. In turn, this will activate the autonomic nervous system which generates a fight or flight response. It is perceivable that attempts to self-regulate or self-soothe in the presence of self-critical thoughts will stimulate this threat system making it much more difficult, if not impossible, to attain a state of calm which would otherwise provide tolerance to the distress associated with the challenge of self-regulatory actions. Moreover, possessing a self-critical dialogue would challenge the pursuit of self-compassion needed to motivate a change in behaviour. Those who are inclined to be self-critical and harsh towards themselves would find much benefit in applying the principles of CMT to the lives.

Following this, we will now provide an overview of web-based psychological interventions which have been used to increase well-being and improve health related outcomes.

4.4. Web Based interventions

The internet has become a part of modern society by changing the way we live our lives, communicate with others and conduct business. It can be said with some degree of certainty that it is here to stay. There is an overabundance in ways in which we interact with the internet and modern information technology has had a great impact on healthcare and increasingly the use of psychological assessments and interventions (Andersson, 2016). It has also had an impact on hard-to-reach populations and those with mobility issues whilst circumventing barriers to face-to-face contact where those with anxiety or those with taboo related issues would be reluctant to seek help. From a research perspective it allows for the gathering of large data sets from across the globe and often keeping costs low. Together, this permits for closer monitoring and improved delivery of health care. Sections 4.4.1. – 4.4.3. below intend to provide a perspective on internet-based interventions by covering the history of web-based interventions and commenting on the long- and short-term effects. The sections below will present findings between mainstream psychological treatment and web-based interventions, discuss the effectiveness of studies, mechanisms of change and predictors, attitude surveys and changing formats. The section will conclude with future developments while acknowledging that the future in this field of information technology is hard to predict and advancements in this field are rapid and depend on cultural aspects and economic influences.

The historical phylogenies of web-based interventions are mainly composed of three parts. The first is the appearance of evidence based psychological interventions and treatments which have come to be adopted as a core part of sustained healthcare. A recent example being the integration of web-based interventions within the Increasing Access to Psychological Interventions (IAPT) initiative (Clark, 2011). The second piece of the historical context is the ever-widening literature available on guide self-help, numerous controlled trials, usually used in conjunction with books and DVDs composed by clinicians (Watkins & Clum, 2008). Many of these were text-based and was mainly due to slow internet speeds which did not allow for the wide array of multimedia we in 2018 are well accustomed to (Andersson et al., 2008a). At around the same time as the wide reach of broadband internet came the advent of the smartphone which allowed for the reach to become much larger and allowed the internet to be accessible from more than one platform (Mohr et al., 2013). The third and final component is the rise of digital testing and interventions (Marks et al., 1998), with the early trailblazer programmes such as ELIZA (Epstein & Klinkenberg, 2001). While the focus of web-based interventions and clinical practise is often geared towards treatment, a corresponding area of equal importance is web-based testing using the internet, not just via online self-report measures (van Ballegooijen et al., 2016) but also cognitive and behavioural testing (Lindner et al., 2016) and the collection of data (Luxton et al., 2011).

Short-term effects: it is not uncommon for the results of randomized controlled trials to take years to complete and publish. Such trials are also very expensive to conduct. However, despite these potential hindrances there exist a very large number of controlled trials on web-based interventions for a wide array of disorders and conditions. This makes the process of reviewing the field a difficult task as there are now separate reviews for conditions such as chronic pain (Buhrman et al., 2016) and addictions (Riper et al., 2014). It has been shown that web-based interventions exist for a variety of conditions (somatic and psychiatric). In regard to health problems and somatic problems in general, research findings have been promising for chronic pain (Buhrman et al., 2004; 2013) where online interventions have shown to produce a reduction in self-reported levels of pain after participants have completed a web-based intervention. Of particular interest is how web-based interventions have been able to modify behaviour. Several published studies have concluded effectiveness of such interventions which also report moderate to large effect sizes for behaviours such as procrastination (Rozental et al., 2015b), perfectionism (Rozental et al., 2015) and interpersonal violence (Hesser et al., 2017).

4.4.1. Strengths of Web-based interventions

Web-based interventions offer various ways in which to deliver their treatments and this is one of the major strengths (Vlaescu et al., 2016). Once in place the web-platform can be used to monitor several variables. Studies which have taken advantage of this have monitored physical activity for depression (Ström et al., 2013), and exercises for stress urinary incontinence (Sjöstrom et al., 2013), to provide some examples. With regard to format, many research groups have completed trials via smartphone-administration (Ly et al., 2014) and blended treatments (Ly et al., 2015b). For some time now, web-platforms platform have been "responsive" in the sense that it is possible to access them using different devices (Vlaescu et al., 2016).

Another strength is that observations can be made when conducting a study that needs recruitment to be done swiftly. Studies often report that it takes only a few months to have a sample size with sufficient statistical power and participants are often recruited easily from social media outlets such as Facebook (Thornton et al., 2016). Some studies have reported sample sizes of 1000+ where all participants were recruited from social media sites (Klein et al., 2006) Additionally, we know from previous research that that online administration of questionnaires work efficiently (Hedman et al., 2010) which also saves time. In some circumstances it may be that researchers need to recruit participants from hard to reach populations such as the elderly or the disabled (Silfvernagel et al., 2018). Web-based platforms provide a route of access to these participants as they can take part in the study from the comfort of their homes. Additionally, addiction comes with the taboo in most cultures and such members of our society may not want to face the stigma when taking part in a face-to-face study. Should they wish to take part in a study where they can be involved without direct face-to-face contact then this may certainly be an appealing prospect.

4.4.2. Long-term effects of Web-based interventions

Most interventions housed on web-based platforms have included follow-ups to the original trial while some have been presented as separate publications. It has been common, particularly with Internet Cognitive Behaviour Therapy (ICBT) studies to include a 12-month follow up (Rozental et al., 2017a). Interestingly, some studies have incorporated 24-month follow up studies. Andersson et al., (2018) conducted a meta-analytic study on 14 studies involving 900+ participants and had an average follow up period of 3 years. Studies in this meta-analysis included a range of psychiatric disorders (panic disorder, social anxiety disorder, generalized anxiety disorder, depression, mixed anxiety and depression, obsessive-compulsive disorder, pathological gambling, stress and chronic fatigue). The duration of the interventions were often quite brief (8–15 weeks) as is typical of ICBT studies. Authors reported the pre-to follow-up effect size was Hedge's g=1.52 and the average symptom reduction across studies was 50% which makes these findings very promising. However, no studies have reported an optimal time period for when to conduct the follow-up study.

4.4.3. Effectiveness of Web-based interventions

It is often questioned as to whether a web-based intervention is as effective as face-to-face therapy (individually or in groups). While building a therapeutic alliance between client and practitioner is highly valued and of great importance, it does not retract any influence that web-based interventions yield. These studies can be difficult to run (participants have to travel to the location and be willing to be randomised into specific groups) however, Carlbing et al., (2005) conducted such trials where a web-based intervention was tested against a face-to-face intervention whereby the content of both forms were as identical as possible. Andersson et al., (2014) and subsequently Carlbring et al., (2018) conducted a meta-analytic to try and answer this question. The analysis included 20 studies with a total of 1418 participants. Studies included guided formats (Cognitive Behavioural Therapy and Acceptance and Commitment Therapy) for psychiatric and somatic conditions in which face-to-face delivery was compared to a web-based delivery method within the same trial. Results showed a pooled effect size of pot-treatment of Hedges g=.05 which clearly suggests equivalent overall effects. This provides increasing evidence that web-based interventions can be as effective as face-to-face treatments while still being cost effective whilst facilitating accessibility to appropriate treatment (Donker et al., 2015). Thus web-based interventions can be implemented to both complement and serve an alternative to face-to-face services. While there will always be clients in need of face-to-face treatment there are also those who prefer a web-based service over face-to-face meetings.

4.5. The potential role of CMT in reducing painkiller dependence (The Three Circles Model)

Empirical evidence has shown that when one experiences distress and resulting emotional fluctuations they may resort to the consumption of addictive substances in order to alleviate the distress (Khantzian, 1997; Weiss et al., 2015). This is commonly seen in those who consume drugs; alcohol and cigarettes being typical examples. As an example, a self-critical individual who has been abstaining from smoking may receive harsh criticism from a colleague and resort to smoking in order to calm themselves. Additionally, CFT and CMT have been shown to reduce SUD promoting behaviours such as cigarette smoking (Kelly et al., 2010). In those living with chronic pain then the consumption of painkillers would be a relevant example. In times of distress, the threat protection system would become active and generate feelings of wanting to protect the individual from pain and keep it safe and pain free. In turn this would feed into the drive system and generate feelings of "wanting, pursuing and consumption" being targeted towards painkiller consumption in order to alleviate the pain and distress. When the painkillers have been consumed and their effects begin to take place and the individual is pain free then the soothe system may become active and generate feelings of the desired outcome i.e. safe and pain free. This loop of positive reinforcement is clearly detrimental in some individuals as their strategy to become pain free is to continually consume painkillers. Painkillers by their very nature possess addictive compounds and so if one were to continually engage in such behavior then substance dependence will quickly ensue.

Gilbert (2005; 2009) states that a chief aim of CMT is to help balance the three entities within the three circles model. Taking the above into consideration, if it were possible to create an alternative way (opiate free) to stimulate the soothe system (e.g. by imagining receiving compassion from a compassionate other; compassionate imagery) then the need for excessive painkiller consumption would not be necessary and dependence would be reduced or eliminated. This statement is formulated from empirical evidence in that stimulating the soothe system will result in release of OXT which in turn can decrease analgesic tolerance and withdrawal (Kovacs et al., 1985; Sarnyai & Kovacs, 1994) and reduce drug seeking behaviors (Carson et al., 2010; Cox et al., 2013; Zhou et al., 2014). Additionally, reducing the drive system, a decision-making system, could also be a potential target particularly if the majority of decisions made are impulsive and not optimally constructed. Results from study 1 showed strong correlations between impulsivity and severity of dependence to painkillers and consumption of painkillers. If those with high levels of impulsivity also had a hyperactive/highly responsive drive system, then they may be more prone to impulsive behaviors and impulsive decision making. Therefore, if the soothe system was to become more engaged then this could dampen the drive system should the drive system be deemed responsible for impulsivity and subsequent psychological dependence to painkillers. Furthermore, should the threat and protection system be constantly on high alert then a great majority of signals entering the mind would be perceived as threatening. However, if one were to better filter these incoming signals (by mindfulness; SRB) and see them as they are rather than reflexively responding to them then this system would feed less signals into the drive system.

One such strategy to manipulate the entities in the three circles model is via CMT exercises (which include SRB and Compassionate imagery exercises). These will be employed in a pilot study delivering an online CMT intervention (Chapter 5) and are described in detail in section 1.5. At this stage these hypotheses remain as hypotheses and further empirical research will be needed to address the importance of these questions (See also section 1.5.10 on theoretical underpinnings of how CMT may reduce painkiller dependence).

Chapter 5: A pilot randomised control study to assess efficacy of an online CMT intervention in reducing dependence to opioid analgesics (Study 2).

5.1. Introduction

As outlined above in Chapter 4 we begin to see the benefits of web-platforms delivering evidence-based therapies and the potential of CMT as a therapeutic intervention for painkiller dependence. This pilot study of the full-intervention will combine these two observations and produce a web-platform to deliver CMT with the aim of assessing acceptability and feasibility within participants who suffer from chronic pain. Objectives to accompany the aims were to (a) build the web-platform and (b) obtain participant feedback so a more refined version of the web-platform can be created (Study 3; Chapter 6).

5.2. Methods

5.3. Design

This pilot study was a two-arm prospective randomised controlled trial (RCT) which aimed to assess the acceptability and feasibility of a web-platform. Feedback received from participants would permit *post-hoc* production of a refined web-platform to suit those with chronic pain. These changes will be implemented in the final version of the web-platform used in Study 3.

This study incorporated a between-groups and within-subjects design. *Groups* had two levels (CMT and RM). The CMT group was the experimental group while the RM group was the control group. One within-subjects factor, *Time*, had three levels (Baseline, Post-intervention and Follow-up).

5.4. Ethical issues

All participants provided informed consent and were made aware of what the study involved and were then debriefed at the end of the study. The study was approved by the Ethics Committee at the University of Derby, UK. Issues raised by the Ethics committee included use of Google Docs and inclusion of a vulnerable population. To remedy this, we did not include a group of heroin users as a control group, rather we sought a single group of participants.

LimeSurvey, a free piece of software was installed on a website to collect data. All data was saved to a privately-owned encrypted web server. The server was tailor made which relied on the Linux operating system and HTML5 to host the website. As the behavioural measure was not available, the programming languages JavaScript and CSS were used to produce a bespoke version of the DD paradigm to run on the Linux server (See Appendix G; and Appendix H for general study information).

5.5. Participants and recruitment strategy

Participants were recruited from social media outlets and pain-related internet forums. All participants who expressed interest were provided with general study information (Appendix H) and an invitation to participate (Appendix O). Next, they were screened for inclusion and exclusion criteria (See 5.3.1. - 5.3.2. below) and those who met entry criteria were briefed (Appendix P), completed an informed consent form (Appendix K) and instructions were provided (Appendix Q). At the end of the study, all participants were thanked and debriefed (Appendix R). Those who did not meet inclusion criteria were also thanked and debriefed (Appendix S).

The final cohort consisted of six adults (Female=4; Mean age=43.2; Age-range=34-56) diagnosed with chronic pain; were all painkiller consumers who were recruited from various internet forums and randomised into one of two groups.

5.5.1. Inclusion criteria

1. Minimum age for participation = 18 years; No maximum age limit.
2. Have experienced some form of pain at least 15 days per month for the last 3 months.
3. Have consumed at least one over-the-counter (OTC) or prescription painkiller in the last 30 days.
4. Must be literate and able to provide informed consent.

5.5.2. Exclusion criteria

1. Have consumed an illegal substance in the last 30 days.

2. Currently consuming psychotropic medication; or have in the last 30 days.
3. Unable to provide informed consent.
4. Diagnosed with ADD/ADHD.
5. Currently undergoing any form of CBT/psychotherapy.
6. Have a friend or family member in the study.
7. Suffering from a terminal illness.

5.6. Materials and Measures

Measures used in this study consisted of self-report measures and one behavioural measure. All measures were placed on a web-platform where participants entered their responses. Detailed descriptions of all measures used in the study are provided above in Chapter 2 while a brief overview is provided below. All measures outlined below were presented in a digital format housed on the web-platform.

5.6.1. Cognitive impulsivity

Cognitive impulsivity was measured using the UPPS-P self-report measure (Whiteside & Lynam, 2001; 2003). The 59-item self-report assesses five subscales (negative urgency, lack of premeditation, lack of perseverance, sensation seeking, and positive urgency) that are used to measure five distinct dimensions of impulse behaviour in adolescents and adults (ages 12-80).

5.6.2. Pain (Typology, Intensity, Duration, and Frequency)

Participants began this measure by reported their most common type of pain e.g. Neuralgia, Lower Back Pain, Fibromyalgia, Chronic Migraine, Ankylosing Spondylitis.

Pain Intensity within the last 30 days was calculated as an average of 4 separate ratings (”1. Pain intensity at its worst”, “2. Pain intensity on average”, “Pain intensity at its least”, and “Pain intensity right now”). Each of the four questions had a 11-point scale labelled “0 – No pain” to “10 – Worst pain possible”.

Pain Frequency was confirmed by participants who provided a numerical value which they typed into a text box to indicate how many times they felt pain within the past 3 months i.e. “7 times per month”.

In addition, participants stated the duration of their most common pain by choosing one option from the following: “Less than a month”, “1-2 months”, “2-3 months”, “3-4 months”, “4-5 months”, “5-6 months”, “More than 6 months”, More than 1 year”.

5.6.3. Painkiller consumption

Participants stated their most commonly consumed OTC and/or prescription painkiller(s) consumed in (a) the last 30 days, (b) the amount of active ingredient per tablet and (c) how many tablets they consumed per day. Answers were provided on a 14–point scale: “None”, “1 per day”, “2 per day”, “3 per day”, “4 per day”, “5 per day”, “6 per day”, “7 per day”, “8 per day”, “9 per day”, “10 per day”, “10-15 per day”, “16-20 per day”, “More than 20 per day”. See Appendix D for full self-report measure.

5.6.4. Painkiller misuse

Painkiller misuse was determined by asking how often participants consumed their painkillers for (a) longer than the prescribed time period and/or (b) more than the Recommended Daily Allowance (RDA).

Responses were chosen from a 4-point scale: “1. Never”, “2. Sometimes”, “3. Usually” and “4. Always”. Misuse here was defined as using medication “for a legitimate medical reason but in higher doses or for a longer period than recommended”.

5.6.5. Psychological dependence to painkillers

The Leeds Dependence Questionnaire (LDQ) measures the graded severity of psychological dependence. The 10 item self-report measure is based on ICD-10 and DSM-IV criteria for substance dependence. The items have a 4-point response scale labelled “Never” (0), “sometimes” (1), “often” (2), and “nearly always” (3). A single score is calculated as the total across the 10 items (Raistrick et al., 1994).

5.6.6. Self-criticism/Self-reassurance

The Forms of Self-criticizing/Attacking & Self-reassuring Scale (FSCRS) was used to measure self-criticism and the ability to self-reassure (Gilbert & Irons, 2004). This 22-item scale measures different ways people think and feel about himself or herself when things go wrong for them. The responses were given on a 5-point Likert scale (ranging from 0 = not at all like me, to 4 = extremely like me).

5.6.7. Behavioural impulsivity

A measure of behavioural impulsivity (DD Task) was used as the final measure in this study. In order to quantify behavioural impulsivity, the study employed the Delay Discounting task. An explanation of this task and how to interpret the outcomes of this measure are outlined in detail in section 2.8.

5.6.8. Feedback Questionnaire.

This measure (Appendix W) was developed to help assess acceptability and feasibility with the overall aim of refining future versions of the web-platform. Questions 1-10 were measured on an 11-point Likert Scale (0=Not at all; 11=To a high extent) and Question 11 was a text box where participants could provide qualitative feedback. This measure was only given to all participants at follow-up. This measure consisted of the following questions:

1) Did you find registration an easy process?
2) Were you able to log in easily on days you needed to?
3) Were you able to understand the questionnaires and what was required?
4) Were you able to complete the digital questionnaires easily?
5) Did you find your chronic pain hindered you from taking part in the study on days you were required?
6) How easy was it for you to navigate the web-platform?
7) Were you able to get in touch with us if/when you needed to?
8) How well did you understand what was required of you to do each day?
9) How well did you understand the principles and application of CMT?
10) How well did you understand what was required of you in the Computerised Task?
11) Please enter your thoughts on how we might improve future versions of the web-platform. Think about things you would want to keep and what things you would want to add or change to make the web-platform a better experience for you.

5.7. Procedures

A web-platform was built to allow participants to engage with the CMT intervention or the RM control option. The software code for the website, behavioural measure and the CMT intervention software was written by myself using JavaScript, MySQL, PHP and HTML. Participants who met the eligibility criteria were asked to click a button on the web-platform to continue. A new page would appear containing Participant Information, Confidentiality Statements and ways to contact the research team.

Participants deemed eligible for the study were randomised (See Section 6.5.3.3. below) into one of two groups. Once allocated, participants were given a unique URL which they were asked to Bookmark. This unique URL gave them access to a login page. When participants registered with their login details they were enrolled in the study. Each group of participants were presented with the procedures relevant to that particular group. They were then asked to tick a box on the web-page to confirm their participation and their consent. When a participant was designated into a study group (CMT or RM) they were provided with a short introductory video that explained the procedure of the study for that particular group. A text-based version of the introductory video was available for both groups.

To reduce placebo effects, participants were not informed at the time of testing that the study concerned the effect of CMT on painkiller addiction, but rather were told that the aim was to investigate the effect of a web-based intervention on psychological processes. All participants were shown how to register by first creating a username and password which they used each time they accessed the website.

As the procedures for the two groups differed, they will be outlined separately below.

5.7.1. Procedures for CMT group participants: Day 1 (Baseline) to Day 21 (Post-intervention).

Participants in this experimental group followed steps 1 through 4 as described below (see also Fig. 19; Appendices E and S).

5.7.1.1. Step 1: Registration, schedule of activities and obtaining baseline measures

Participants in the CMT group (Experimental Group) began by registering for the study with a username and password. They were provided with information on how to choose a secure password (i.e. a minimum length of 8 characters, must include a special character and a numerical value). Each participant was then given access to a schedule of activities which consisted of text-based instructions on what to do for each day. Next, participants began by watching a series of five psycho-educational videos on CMT as outlined in section 5.7.1.2.1. below. In addition, a separate video (web-link in Appendix T) was produced to teach participants how to navigate the web-platform. In order to obtain baseline measures, all participants completed a behavioural measure of impulsivity (DD Task) and completed self-report measures (See section 5.6.) after watching the CMT videos.

5.7.1.2. Step 2: Engaging with the CMT Psychoeducation video library

Upon completing the behavioural measure and self-report measures, participants in this group were required to click a button titled “Online Intervention”. The web-platform automatically redirected the participant to their group-specific task. Those in the CMT group were asked to watch a series of CMT videos and then engage with the online software. An outline of the CMT videos is described below.

5.7.1.2.1. CMT Video Library

Participants in the CMT group watched a series of psycho-educational videos on CMT. The titles of the videos are below:

- Chapter 1: Introduction to Self-Compassion (8 minutes)
- Chapter 2: Soothing Rhythm Breathing (6 minutes)
- Chapter 3: Voice Tones, Imagery & Facial Expressions (7 minutes)
- Chapter 4: Compassionate-Self (8 minutes)
- Chapter 5: Compassionate Coping (9 minutes)
- Chapter 6: CMT Exercises (15 minutes)

In Chapter 1, participants were introduced to the theoretical components of the compassionate mind model, the three circles model provided them with a critical exploration of how a "sense of self' is created, through:

- An interaction between one's genes and social experiences.
- Emotion regulation systems (threat, drive, soothing).
- The nature, origins, and functions of shame and self-critical judgement.
- Considering the "tricky brain" and how much of what goes on in the mind is "not our fault" (Gilbert, 2014) because we are genetically programmed for survival. Gilbert (2014) proposed that the brain has the capacity to be intelligent yet is essentially flawed and vulnerable to a variety of problems that may have an impact on wellbeing (e.g. fear, arousal, rumination, self-criticism and shame).

Chapter 2 introduced the concept of SRB as described in section 1.6.1. and formed one of the main exercises for this video as it was used in all following chapter exercises. Participants were taught how breathing helps us to become more attuned to our bodily sensations and being present in the moment.

Chapter 3 explained that the voices we hear in our own heads everyday can be harsh and critical or they can be soft, gently, warm and soothing. The focus of this video was to teach individuals to use a more self-compassionate voice tone with oneself and with others where possible as this may lead to changes in the way our nervous system operates and activate the soothe system. The use of compassionate imagery was also introduced where participants were asked to create a compassionate image from which they can send/receive compassion. It can be a living object, or not. However, they were asked to give it qualities such as wisdom, strength, warmth and non-judgement. Participants were asked the following in regard to their newly formed compassionate image: "How would you like your ideal caring-compassionate image to look – visual qualities?", "How would you like your ideal caring-compassionate image to sound (e.g., voice tone)?", "What other sensory qualities can you give to it?", "How would you like your ideal caring-compassionate image to relate to you?" "How would you like to relate to your ideal caring compassionate image?". Facial expressions were also briefly explained, and participants were asked to make a "half smile" (Gilbert, 2014) when engaging with all future exercises.

Chapter 4 (The compassionate self) taught participants about "recognising the different parts of yourself". Examples include an angry part, an anxious part, a "being in love" part and a "falling out of love" part and emphasised that we have many different potential patterns of personality within ourselves which can be expressed. Self-reassurance was introduced here such that having this quality can have a soothing quality on our fears, anxieties and when we are angry (states of negative affect). Equally, it can help develop courage to deal with such situations. Following this, we consider an example by Gilbert who talks of an actor who is able to express many emotions and have different qualities which he/she can call upon. Thus, if we are trying to become more self-reassuring and compassionate then we should try to bring about such qualities within ourselves. These qualities include wisdom, strength, warmth and responsibility. An exercise called "You at your best" was also used here where participants think of a time when they felt compassion and were asked to think about an inner sense of calmness and the tone of their supportive voice and then think about feelings of wanting to help and kindness.

Chapter 5 in the video series explored the skills of compassion and how best to utilise them. Participants delved into the following topics: Compassionate Attention, Compassionate Thinking and Behaviour and Feelings. The major aims of this video series were to explain the Key Targets of Compassion as well as the Threats and Blocks to Compassion. Gilbert (2014) states that our emotions can direct our thinking, and this too affects our behaviour (e.g. negative moods can lead to negative behaviours such as drug consumption which then have serious/detrimental consequences). Thought exercises in this video taught participants how to think in a more self-reassured way and probed the participants style of thinking by asking the following questions:

"Is this thinking helpful to me?"

"Would I think like this if I weren't upset?"

"Would I teach a child or friend to think like this?"

"If not, how would I like to teach them to think about these things?"

"How might I think about this when I am at my compassionate best?"

These questions help to shift the balance from being self-critical to being self-reassuring by moving away from a threat-based mentality to a self-reassured mentality as participants thinking is being guided by emotions which are very different to those of the threat system.

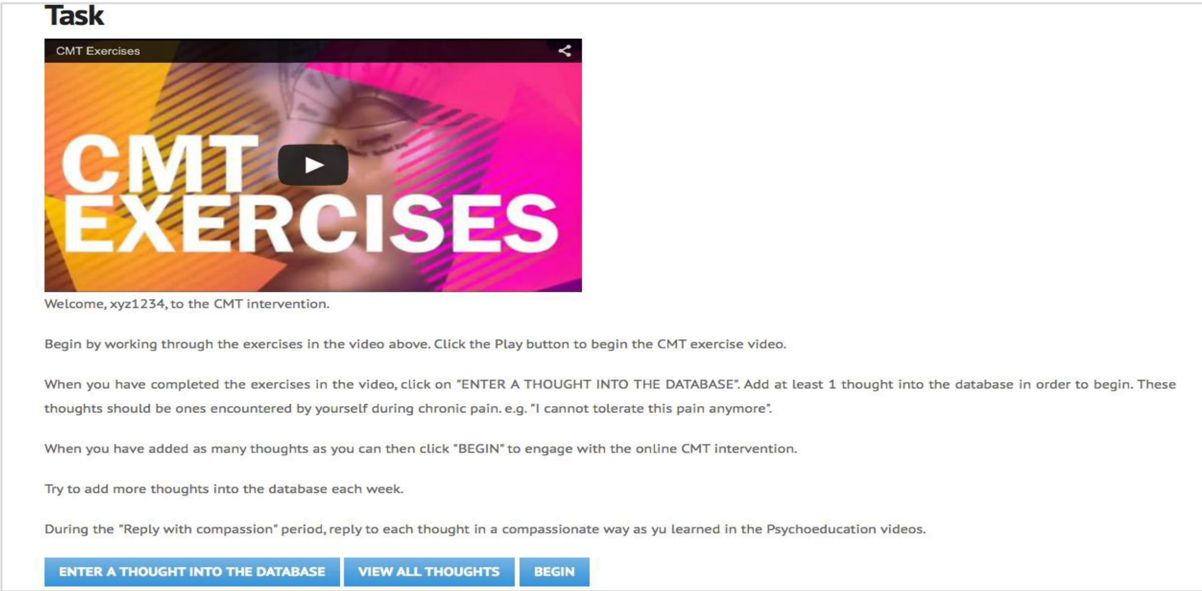
Chapter 6 is the final video and includes only the exercise portions from videos 1 to 5.

The aim of these videos was to develop knowledge of CMT and skills in self-compassion and self-soothing. Each video included practise exercises throughout and CMT group participants could access these videos at any time (Appendix T).

After watching the first 5 psycho-educational videos participants engaged with a final video titled "Chapter 6: CMT Exercises" (Fig. 17). This was a stand-alone video incorporating the full range of CMT exercises that participants practised in the first five psycho-educational videos. It included exercises such as Soothing Rhythm Breathing, Compassionate Imagery, Friendly Faces and Voice Tones, Developing the Compassionate Self and Mindfulness. An additional document (Building a Compassionate Image; Appendix U) was provided for all participants. This provided thoughtful questions on constructing a compassionate image.

The CMT videos were constructed in consultation with Prof. Paul Gilbert and produced/delivered by myself. Participants were not requested to watch the psycho-educational videos prior to engaging with the CMT software each day but could refer to them if needed, however it was made mandatory to watch the stand-alone CMT exercises video (Chapter 6: CMT Exercises; Fig 17) prior to engaging with the CMT software.

Figure 17 Preview of the stand-alone CMT exercise video (Chapter 6) homepage



5.7.1.3. Step 3: Engage with CMT Intervention Software

Immediately after watching the "Chapter 6: CMT Exercises" video, participants were redirected to a web page that allowed them to engage with the bespoke CMT intervention software. The CMT intervention software was designed to be interactive and aimed to (a) increase awareness of self-critical thoughts and (b) to develop the skills needed to respond to these thoughts using self-compassion learned from the psycho-educational videos. Participants began interacting with the CMT software by clicking on a button titled "*Enter a thought into the database*" (Fig. 17; bottom left button). This thought was placed into their personal database. The thought entered was advised to be one that was self-critical in nature and one that would occur often and/or when enduring an episode of chronic pain. Participants had to enter a minimum of one thought into their database. There was no upper limit on the amount of thoughts that could be entered. Participants could also view which thoughts they had entered into the database and had the option to edit their personal database by adding or removing thoughts (Appendix V). Thoughts entered into a personal database were not visible to any other persons other than the participant.

When at least one thought was entered into the database, the participant could begin interacting with the CMT intervention software by clicking the "*Begin*" button (Fig. 17). The website screen would fade to a black background and participants would be instructed to

"*Press a key to begin*". This would initiate the first trial. A star symbol (*) would appear on the screen for 3 seconds and then the screen would clear. Next, a thought that was entered into the participants' personal database would appear on the screen for 8 seconds. Then the screen would clear and present a star symbol for 5 seconds. The screen would then clear and the words "*Reply with Self-Compassion*" would appear on the screen for 120 seconds. It is during this period the participant would be using CMT techniques learned from the psycho-education videos to reply back to the thought they had previously read. After 120 seconds a bell sound was played to signal the end of the trial. A sound was used to allow participants to close their eyes during the self-talk process. If there was more than one thought entered into the database, then they were displayed in each successive trial until all thoughts from the database had been displayed. If only one thought was entered, the software would display that one thought for 7 trials. Each trial lasted 136 seconds. When all thoughts in the database had been displayed, the CMT software prompted the participant to whether they would like to enter any further thoughts into the database. The flow of a single CMT intervention trial is shown below (Fig. 18) and a flow of activities for participants in this group is shown in Figure 19 below.

Figure 18 Schematic of a single CMT intervention trial

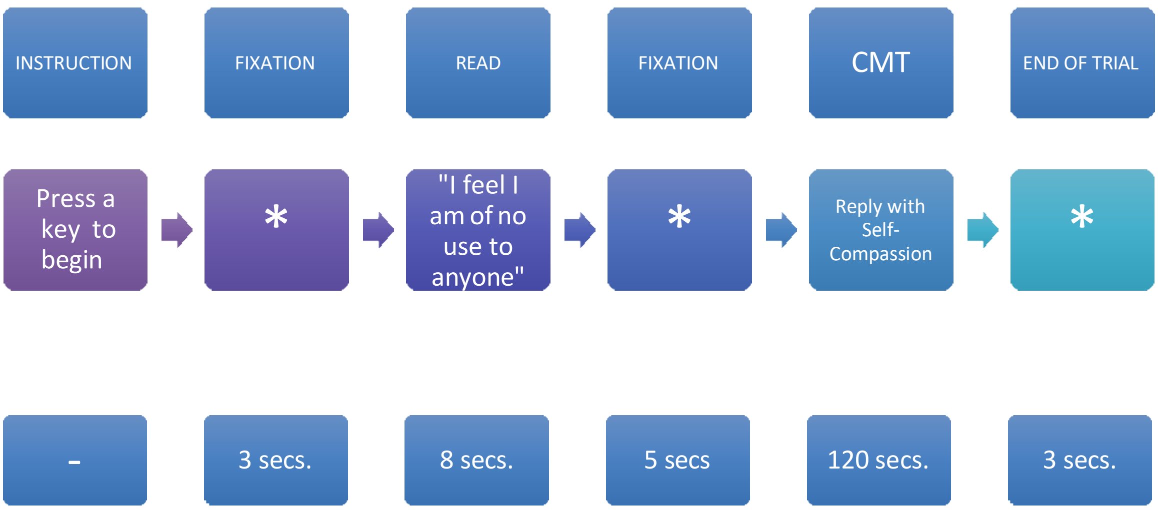
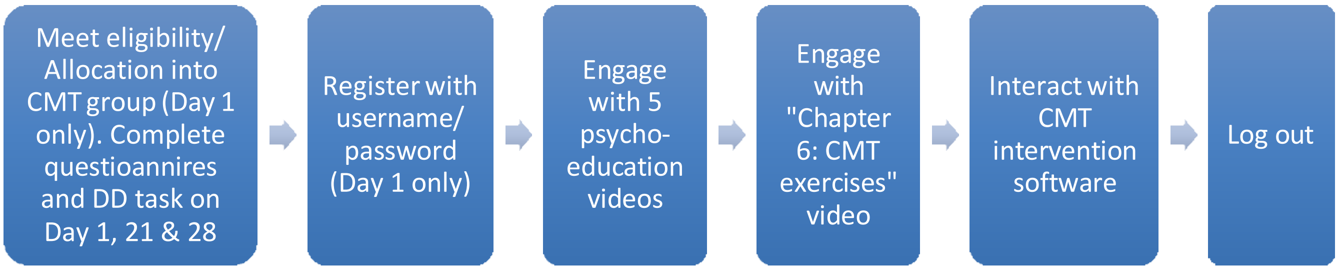


Figure 19 Flow of activities for CMT group participants



5.7.2. Procedures for Relaxation Music group participants

Participants in this control group followed Steps 1 to 2 as described below (See also Fig 20).

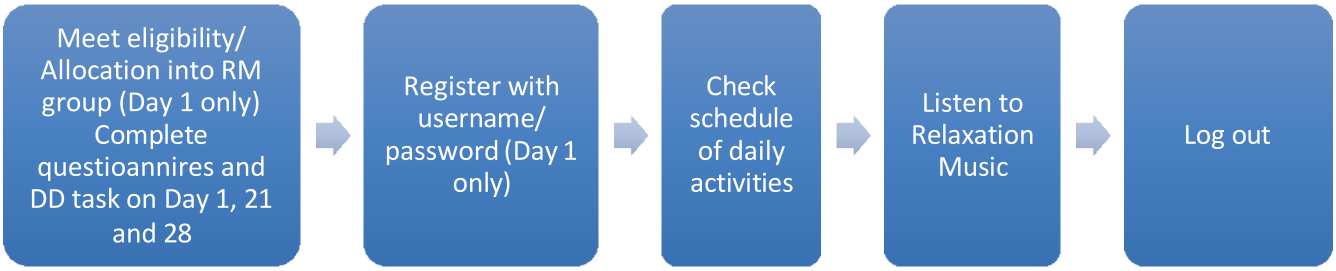
5.7.2.1. Step 1: Registration, schedule of activities and obtaining baseline measures

Participants designated to the RM Group (Control Group) began by first registering a unique username and password (i.e. a minimum length of 8 characters, must include a special character and a numerical value). They then watched a brief introductory video on what was expected of them during the study and how to navigate the website. Participants in this group had to complete the "Computer Task" and the "Online Questionnaire" which comprised of self-report measures. These two tasks were identical to those completed by CMT group participants on Day 1. Each participant was then given access to a schedule of activities which consisted of text-based instructions on what to do for each day.

5.7.2.2. Step 2: Engaging with Relaxation Music

When participants clicked on the button labelled "*Online Intervention*" they would listen to a randomly selected track from a relaxation music (copyright free) library. Track lengths varied between 6 and 9 minutes. This was done on the same days of the week and for the same number of days as when the CMT group participants engaged with the CMT videos and interacted with the CMT intervention software i.e. group timetables were identical aside from the task required. Figure 20 below shows the flow of activities for participants in the RM (Control) group on Day 1.

Figure 20 Flow of activities for RM group participants



The following procedures will describe the flow of activities for participants in *both* groups from day 21 onwards.

5.8. Post-Intervention (Day 21)

On Day 21 (Post-intervention) all participants from both study groups completed the behavioural measure (DD Task) and the same self-report measures as were done on Day 1 (Baseline), in addition to their group-specific task (i.e. engaging with the CMT Software or listening to relaxation music). This was conducted to assess any deviations from baseline measures taken on Day 1.

Participants then took a break for 6 days during which they could not engage with the web-platform. The break was to assess whether the effects of the intervention would endure until follow-up (Day 28).

5.9. Follow-up (Day 28)

On Day 28, all participants from both study groups were invited back for a Follow-up session. An automated email reminder was sent to them 3 days and 1 day prior to Follow-up. Participants did not engage with any group-specific tasks on this day. Instead, they only completed the same measures as those completed on Day 1 (Baseline) and Day 28 (Follow-up). This allowed for comparisons to be made with baseline and post-intervention scores. In addition, they were asked to complete a questionnaire on the web-platform so adjustments could be made for future versions of the web-platform (Appendix W). Participants were then thanked, debriefed (Appendix R) and released from the study.

5.10. Summary of procedures

Below is a brief summary of the procedures used in the study.

1. Depending on participant study group placing, participants engaged in a once-daily web-based CMT intervention, or listened to relaxation music, for 21 days to assess deviations in self-report-measure and behavioural measures scores at three time points (Baseline, Post-intervention and Follow-up).

2. A follow-up session on Day 28 was performed to assess maintenance.

3. Quantitative analysis was performed within and between two groups to assess efficacy of each experimental condition.

4. Participants were asked to provide detailed feedback on the aesthetics and usability of the web-based intervention with intent of producing a more optimal version.

5.11. Data Analysis

Data analysis was performed on SPSS Version 21. Due to the low sample size (N=6), only descriptive data will be provided in the section below. Qualitative feedback from all participants on Day 28 will also be taken into consideration for future versions of the web-platform.

5.12. Results

The final sample consisted of 6 participants (M=2; F=4). Participants were randomly assigned into one of two groups, CMT (n=3) and RM (n=3). Mean age was 48.67 (+/- 11.96) and ranged from 36-68. Participants were located in English speaking countries (UK, USA and Australia). Participants were also asked about their most commonly consumed painkiller. Responses consisted of Fentanyl (n=1), Oxycodone (n=3), Percocet (n=1) and Gabapentin (n=1). Data from self-report measures and the behavioural measure of Delay Discounting is shown in Table 6 below.

Table 6 Mean values of self-report measures from both study groups

Variable	CMT Group				RM Group			
	Mean at T1	Mean at T2	Mean at T3	Range across T1-T3	Mean at T1	Mean at T2	Mean at T3	Range across T1-T3
LDQ	8.67	7.67	7.33	8-12	10.67	8.67	10.67	8-12
DPPC	4	4.33	3.67	1-5	5.67	5.67	5.67	4-7
OTCPD	0.67	0.67	0.33	0-2	3.67	1.33	3.33	1-6
LTP	2.33	2.33	3	2-4	2	1.67	0.67	1-3
RDA	2.33	2.67	2.67	1-3	2.67	2	1.33	1-3
NU	24.67	25	25.67	21-28	23.33	24	21	15-28
LOPERSEV	12	13.33	12.67	10-16	20.67	21	21	15-28
SS	24.67	23.67	22.67	18-28	18.67	23	18	19-29
LOPREMED	23.33	22.33	24	18-28	17.67	20.67	20	10-24
PU	23.67	22.67	19.67	18-26	18.67	18	14.67	12-20
DD	343.33	430	443.33	150-450	403.33	430	440	350-440
IS	17.67	17.33	14	12-22	14.67	14.33	11.67	8-18
RS	18.33	16	15	12-24	19.33	15.33	15.33	8-28
HS	9.33	7.67	4.67	2-14	6	3.33	4	2-8
PI	8.33	6	6	4-10	6	5.33	6	3-9
PF	55	53.33	52.67	25-90	55	45	36.67	15-90

Key: ***LDQ***=Leeds Dependence Questionnaire; ***DPPC***=Daily Prescription Painkiller Consumption; ***OTCPD***=Over-the-counter painkiller consumption; ***LTP***=Consuming painkillers for longer than the prescribing period; ***RDA***=Consuming painkillers over the Recommended Daily Allowance; ***NU***=Negative Urgency; ***LOPERSEV***=Lack of Perseverance; ***SS***=Sensation Seeking; ***LOPREMED***=Lack of premeditation; ***PU***=Positive Urgency; ***DD***=Delay Discounting; ***IS***=Self-inadequacy; ***RS***=Self-Reassurance; ***HS***=Self-Hate; ***PI***=Pain intensity; ***PF***=Pain frequency

Within Table 6, the most notable observations were that LDQ scores (psychological dependence to painkillers) decreased over time with notable reduction in scores from Baseline to Follow-up for participants within the CMT group only. There was no obvious change in LDQ scores for participants in the RM group although the range of scores were similar for both groups.

Similarly, the scores for Daily Prescription Painkiller Consumption (DPPC) also decreased over the three time points for those in the CMT group only. Scores for DD also decreased over time for participants in the CMT group and not so much for the RM group participants. IS scores showed a reduction in scores between Post-intervention and Follow-up for participants in both groups. Scores for RS and HS reduced over time for CMT group participants and RM group participants over time. Scores for impulsivity (NU, LOPERSEV, SS, LOPREMED and PU) remained stable over time for participants in both groups. Scores for pain intensity (PI) showed a small decrease from baseline to post-intervention and from Baseline to Follow-up in the CMT group while there was relatively little change over time for those in the RM group. Scores for pain frequency (PF) remained stable over time for CMT group participants while the RM group participants showed a decrease in scores from Baseline to Post-intervention and from Baseline to Follow-up. Statistical analysis on the efficacy of the CMT intervention was not conducted as (1) this was not the aim of this study and (2) there was a small number of participants in the study (N=6).

In order to assess acceptability and feasibility, a feedback questionnaire (See section 5.4.8. and Appendix W) was developed. This measure also allowed for future versions of the web-platformed to be improved upon by applying a user-led design. Results from this measure are shown in Table 7 below. Measured on an 11-point Likert scale where 0 means "Not at all" and 10 means "To a high extent," the feedback questionnaire contained items regarding how well the web-platform was perceived in terms of user-friendliness/navigation, ease of task comprehension and theoretical understanding. The web-platform was to be regarded as acceptable if the mean score for the questions were 5 or higher. Questions which scored 5 or higher were Questions 1-4, 7, 9, 10. This meant that participants were easily able to register, log in each day, able to understand the self-report measures, complete questionnaires easily, get in touch with the study team when they needed, understood principles of CMT and understood what was required of them during the delay-discounting task. Question 5 asked if they felt their chronic pain hindered them from taking part in the study. Most felt that it did not (CMT group: M=3.33; SD = 1.37 and RM Group: M=2.66; SD=2.16). Participants in both groups scored below 5 for questions 6 and 8. Thus, they felt they could not navigate the web-platform easily and did not understand what they had to do each day.

Table 7 Mean scores (+SD) from feedback questionnaire

Question Number	CMT Group MEAN	SD	RM Group MEAN	SD
1	7.67	1.63	7.83	2.14
2	7.5	1.87	7.33	1.75
3	7.83	2.04	7.33	2.16
4	8.83	1.17	9	0.89
5	3.33	1.37	2.66	2.16
6	3.17	2.56	2.5	2.07
7	7.5	1.05	6.83	2.4
8	2.33	1.03	3.17	2.14
9	6.67	2.54	7.13	2.09
10	7.68	2.76	8.81	1.34

Questions 1-10: Q1. Did you find registration an easy process?; Q2. Were you able to log in easily on days you needed to?; Q3. Were you able to understand the questionnaires and what was required?; Q4. Were you able to complete the digital questionnaires easily?; Q5. Did you find your chronic pain hindered you from taking part in the study on days you were required?; Q6. How easy was it for you to navigate the web-platform?; Q7. Were you able to get in touch with us if/when you needed to?; Q8. How well did you understand what was required of you to do each day?; Q9. How well did you understand the principles and application of CMT?; Q10. How well did you understand what was required of you in the Computerised Task?

In response to the feedback to Question 6 the web-platform was redesigned by separating out each webpage so that each video had its own page with standalone videos and complementary information in text format. Each page had the font increased to improve legibility and key words were typed in bold. A menu system was applied to each web-page to allow ease of navigation to any section of the web-platform. A major change was the application of a vibrant colour scheme with nature-based pictures on each page as suggested by Paul Gilbert.

Question 8 asked "*How well did you understand what was required of you to do on each day?*" and answers provided were also below the threshold for acceptance. This prompted for a strategy to restructure instructions. Complimenting this line of thought, Question 11 asked participants for what improvements they would like to see in future versions, the following feedback was obtained: "*add a diary so I know what to do each day*" and "*if there was a calendar with daily tasks then it would be one less thing to worry about*" prompted the addition of a dynamic personalised schedule (See section 5.13.1. and Figs. 21 and 21 below) which showed each participant what they needed to do on each day and was colour coded so they knew if a task was "Complete" (Green box), "Must Complete Today" (Yellow Box) or

“Incomplete” (Red Box) for that particular day. In addition to this, an automated email reminder of when to log in will be sent to all participants in future studies.

Positive feedback from Question 11 included:

“I can do it all on my laptop and I don’t need to see my doctor”

“I can learn things online and practise in my own time…I don’t have to do it in a 40-minute session with a doctor.”

“Amazing! Now I don’t need to leave my home – I can do it in my own time.”

“…Thank you for letting me be a part of this study. I found I was using breathing techniques even when I wasn’t logged into the website”

Respondents also requested “*a space for me to write down my own thoughts*” and mentioned “*My head is constantly whizzing so somewhere for me to store my thoughts would be great.*” To this end a “Personal Pain Diary” was developed (Appendix AA). This feature was made to be optional to complete but gave participants a private area in which to record their thoughts and experiences and could serve as a reminder of self-critical thoughts they might have had/been having and so could later be entered into their personal database in the CMT intervention. Access/visibility to the Personal Pain Diary is not available to the experimenters or any other participants but was only available for viewing/editing to the user who entered their thoughts in their Personal Pain Diary (See also section 5.13.2 below).

Finally, as two participants (33.33% of study sample) stated “*I don’t always count how often I have pain…*” and “*…tricky to know how many times I have had pain in the last 30 days*” the Pain Intensity and Pain Frequency measure was restructured to include only two items to allow for ease of data entry and accuracy of information provided: “On average, how intense is your daily pain?” measured on an 11-point Likert scale (0 = “Not intense at all”; 10 = “As intense as I could possible imagine”) and “On average, how frequent is your daily pain?” measured on an 11-point Likert scale (0 = “Not frequent at all”; 10 = “Very frequent”).

Retaining the measure of Pain Frequency was also to retain the integrity of findings from the moderation analysis in study 1 (Figs 14 – 16).

5.13. Discussion

This pilot study provided the opportunity to gain valuable feedback from a sample of participants who had chronic pain and were interested in a web-platform housing an evidence-based intervention for helping their condition. The chief aims of the study were to assess for feasibility and accessibility. New additions to the web platform are outlined below and were based on participant feedback.

5.13.1. New addition(1): Personal/Dynamic Timetable for participants in both groups

This will be a new addition to the web-platform based on participant feedback to enhance acceptability and feasibility. Participants in study 3 will be provided with a unique and dynamic timetable (Figs. 21 & 22) which will highlight exactly which tasks they need to do on that day. The dynamic timetable feature will make site navigation simple whilst preventing participants from accessing or completing tasks specified for a day in the past or the future. Participants could also use the timetable to check their progress (Fig. 21 and 22). The progress feature of the timetable is colour coded and will show which tasks have been completed and which tasks need completing for that day. A red square would equate to "did not complete", a green square would be seen when a task has been completed, a yellow square would symbolise a task that needs to be completed within 24 hours, clear boxes indicate future tasks and a grey square indicates no scheduled activities for that day. Using this key, we can see in Figure 21 that the participant is on "Day 1 of Week 1" and is required to complete *two* tasks within 24 hours as denoted by the *two* yellow boxes. Upon completion these two yellow boxes will turn green in colour. The progress feature will also aid the investigator to know which days the participant completed tasks and how many days participants were absent.

The box for that particular day would be colour coded whereby Green = "Completed"; Red = "Did not complete", Yellow = "Must complete today" and Clear = "A future days event" (Fig. 21).

Figure 21 Progress made by a study participant as seen in the dynamic timetable feature

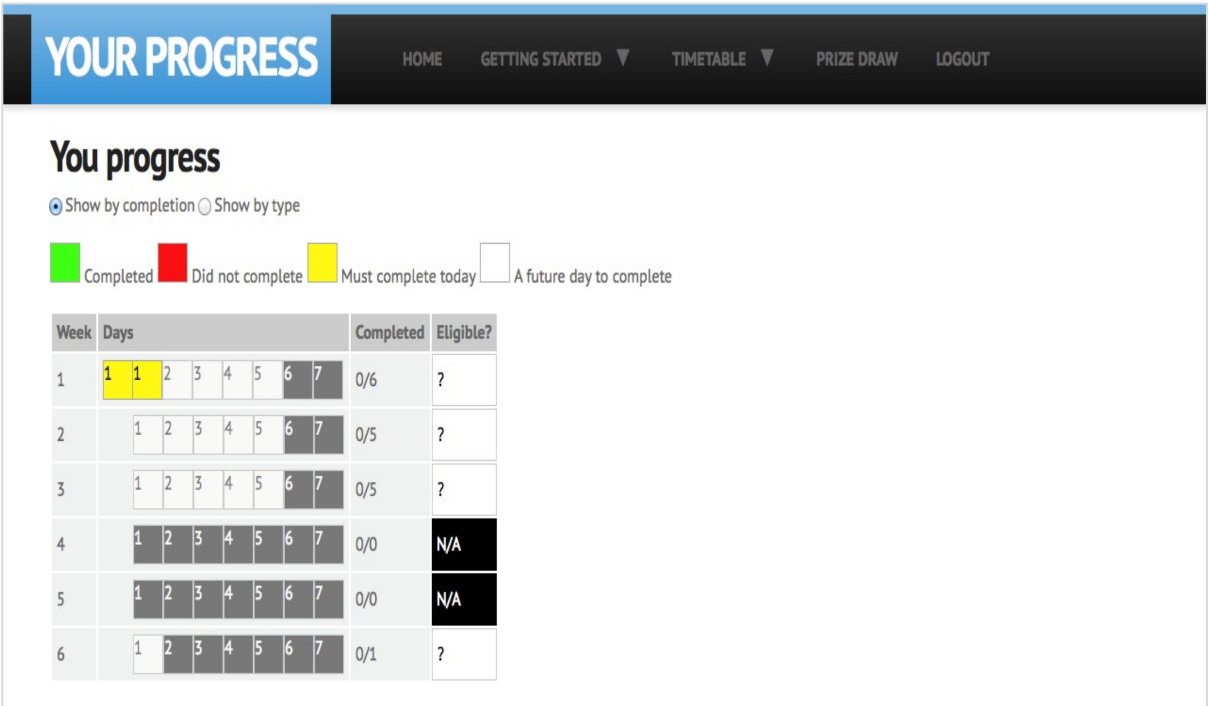
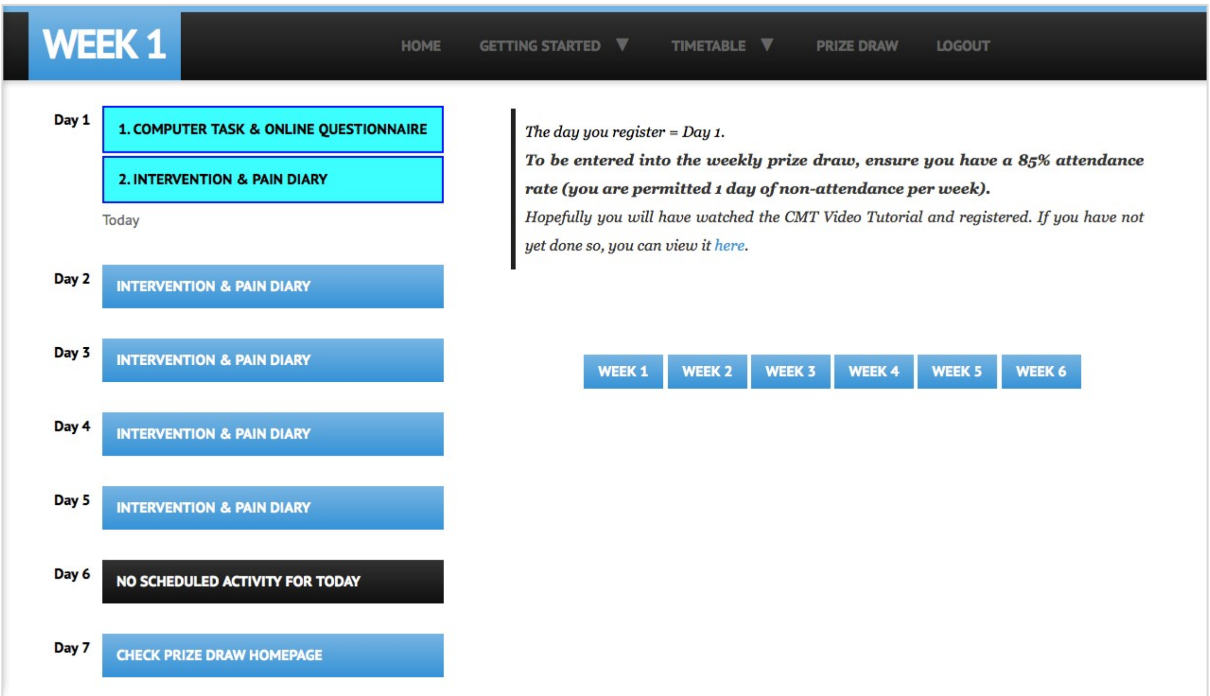


Figure 22 Daily schedule of activities for a study participant as seen in the dynamic timetable



In Fig. 22 above, the tasks to complete for the current day, Day 1, will be highlighted in a turquoise box with blue outline and black font. Future tasks such as on Days 2 to 5 are shown in blue boxes and no scheduled activities are shown in black boxes as on Day 6. On days when task completion will be required, automated reminder e-mails were sent to participants 24 hours before, at 0200 GMT.

5.13.2. New addition (2): Personal Pain Diary

All future participants will be automatically redirected to their personal online pain diary after engaging with the CMT intervention or listening to relaxation music. This feature aims to enhance acceptability. This optional feature provided an "e-Journal" feature in which participants could enter their private thoughts and look through at a future date. The pain diary served as a repository for self-critical thoughts, from which self-critical thoughts could later be added into their database.

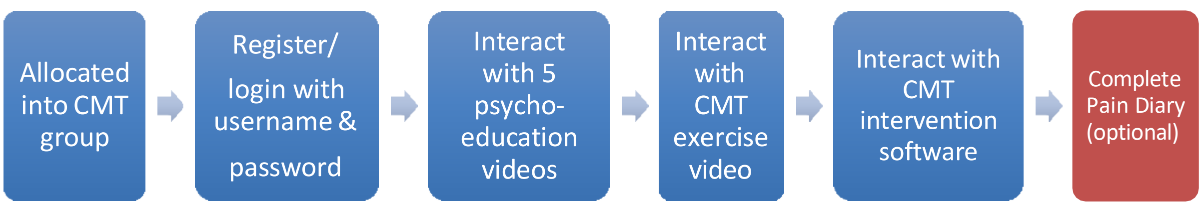
5.13.3. New addition (3): Restructuring of Pain Intensity and Pain Frequency self-report measure

The Pain Frequency and Pain Intensity measure was restructured following participant feedback to allow for ease of data entry and accuracy of information provided by study participants. This feature aims to enhance both acceptability and feasibility.

5.14. Revised flow chart for participants with addition of Pain Diary

Figure 23 below shows an example of the new flow of activities for participants. These changes were made to align with feedback received from the pilot study which requested a place to store their thoughts.

Figure 23 Revised flow of activities for participants



After engaging with CMT exercises or listening to the relaxation music participants would then be automatically redirected to their personal pain diary (Appendix AA), which is optional. To establish this group as a control group, RM group participants did not watch any videos pertaining to CMT, partake in any form of CMT exercises nor did they interact with any CMT software.

To conclude the web-platform was well received by all participants as the positive feedback suggests. To meet the aims of this study, scores from the feedback questionnaire were analysed. Mean scores for most questions in the feedback questionnaire were above the threshold score of 5 and so was deemed acceptable. Questions which were below 5 or on the cusp of the threshold were taken into consideration and new features were added to ease navigation and remind participants exactly what was required of them on each day.

Although the data obtained from the self-report measures and the DD task were not analysed in depth due to low sample size they do, however, show a promising nature. Scores for LDQ (psychological dependence to painkillers) had decreased between baseline and post-intervention for those in CMT group. The same trend can be seen in CMT group for daily prescription painkiller consumption, OTC painkiller consumption, IS, RS and HS. Thus, it can be concluded that the outcomes were not cause for immediate concern and that future studies would aim to replicate with larger a sample size and apply further statistical analysis to detect changes in study variables.

Chapter 6. Implementing a web-based RCT applying a CMT intervention to reduce painkiller dependence in those with chronic pain.

6.1. Introduction

One complication in the treatment of chronic pain is the lack of specialist psychological services available. Thus, increasing the range of short-term therapies available whilst making them easily accessible is one way to remedy this (Fonagy & Target, 2006). Research findings in the field of Compassion have highlighted several possible ways to aid vulnerable populations by helping them bring balance to the three circles model and increase self-reassurance. In turn, this could help them develop and activate the soothe system to promote well-being, cope with difficult life events and cope better with adverse mental health (Neff, 2003; Gilbert 2005; 2009).

A specific population deemed highly self-critical and who may have difficulties with self-soothing are those with chronic pain (Costa & Pinto-Gouveia, 2011). However, the relationship between self-reassurance, self-hate and self-inadequacy with impulsivity and with painkiller addiction has not been extensively explored.

6.2. Aims

This third study follows on from the second study and incorporates the changes that were derived from participant feedback. This study aims to:

Aim 1: Assess the effects of a web-based CMT intervention in reducing psychological dependence to painkillers (LDQ scores); and changes in accompanying study variables (Data sets 1 - 4).

Aim 2: Assess any associations between changes in variables over time. This will lead to an explanation on how study variables may have affected painkiller dependence. An accompanying section on analytic strategy to address these aims is provided below in section 6.6.

6.3. Rationale

Study 1 demonstrated the impact of impulsivity, self-reassurance, self-hate and self-inadequacy towards painkiller addiction (Dhokia et al., 2014). Results from this study were encouraging as it showed painkiller dependence did exist in the study population, potential risk factors were identified and meta-cognitive risk factors (HS, RS and IS) were shown to moderate psychological dependence to painkillers in those with varying levels of pain frequency with self-reassurance acting as a protective buffer (Fig. 14-16).

Principles of CMT propose that internal thoughts and images activate similar neural circuits as externally generated stimuli. This is exemplified by saliva production and stomach contractions when we are hungry and also when we see a favorite meal in front of us (external stimulus). Similarly, imagining our favorite meal to be in front of us (internal stimulus) produces comparable physiological arousal. In a similar vein, seeing a sexual image on a screen will stimulate hormone release and vasodilation. Likewise, using our imagination will result in predictable physiological outcomes (Gilbert, 2009). Therefore, if participants construct and continually employ compassionate images and self-reassuring thoughts, it may be possible to revive and progress the soothing and safeness system while reducing activity in the drive and threat systems (See section 4.5. which describes the potential role of the three circles model in reducing painkiller dependence). The notion of exercising neural circuits to think and feel in a specified manner to stimulate physiological systems is well supported by empirical evidence (Begley, 2007). CMT is not simply remedial action towards threat-based processing or developing various strategies such as learning to be assertive rather than submissive; it also aims to stimulate positive affect processing. Empirical evidence has shown application of CMT to be a highly effective strategy for reducing self-critical thoughts by instilling self-reassurance in the individual (Gilbert, 2005). Furthermore, the effect of CMT to reduce the consumption of addictive substances has been successfully demonstrated (Kelly et al., 2010), however CMT has not been applied to a population prescribed addictive painkillers. Moreover, the effect CMT may have on reducing impulsivity has not been investigated and also needs clarification. Relaxation music was deemed to play a suitable control condition as it does not incorporate any form of CMT or CFT and no training or specialist skills were required to partake in the activity.

Therefore, this study intends to produce a revised web-platform to deliver a CMT intervention which aims to (1) reduce painkiller dependence and (2) investigate associations between study variables. The latter of which will provide a framework for explaining how painkiller dependence may have changed over time.

6.4. Predictions and Hypotheses

It was hypothesised that at the end of the study, those participants within the CMT group would show (i) a significant reduction in the number of painkillers consumed and consequently (ii) a lesser severity for psychological dependence to painkillers when compared to those in the control group.

6.5. Methods

6.5.1. Design

This study was a two-arm prospective randomised controlled trial (RCT) to assess the effects of a Compassionate Mind Training (CMT) intervention on study variables. Prior to this, a pilot study (n=6) was conducted to assess acceptability and feasibility and then to obtain participant feedback on the web-platform. This allowed for *post-hoc* production of a refined web-platform to suit those with chronic pain. Feedback received from participants concerned the aesthetics of the web-platform, changes to font size and the addition of a dynamic timetable. These changes were implemented in the final version of the web-platform used in this study (Study 3).

This study incorporated a between-groups and within-subjects design. Groups had two levels (CMT and RM). The CMT group was the experimental group while the RM group was the control group (Fig. 24). One within-subjects factor, *Time*, had three levels (Baseline, Post-intervention and Follow-up).

6.5.2. Ethical Issues

All participants provided informed consent and were made aware of what the study involved and were then debriefed at the end of the study. The study was approved by the Ethics Committee at the University of Derby, UK. Qualtrics was used to replace any 3rd party data-capturing service. All data was saved to an encrypted web server.

6.5.3. Participants and Recruitment Strategy

Participants were recruited from various internet forums and social media groups. All participants received general study information (Appendix H) and an invitation to participate (Appendix O). Those who met inclusion criteria (section 6.5.3.1. – 6.5.3.2.) were briefed (Appendix X). Those participants who wished to continue were required to complete an informed consent form (Appendix K) in order to proceed with the study and obtain the instruction sheet (Appendix Y). Participants who did not meet inclusion criteria were thanked, debriefed and released from the study (Appendix Z). Additionally, there were weekly prize draws (Weeks 1, 2, 3 and 5) for a single e-Retailer voucher worth £50(GBP). Those who completed at least 70% of their weekly tasks were deemed eligible and one winning participant was chosen at random.

Following this, an automated email was sent to a secure (2-way encrypted) email account with a notification that a participant had been recruited while the participant would be redirected to a specific webpage belonging to one of the groups, either CMT or RM. A total of 442 participants expressed interest in the study and 79 participants (17.9%) were enrolled after meeting eligibility criteria. Of this, 363 participants were excluded due to not meeting inclusion criteria (n=255) or not wishing to progress further (n=108). The 79 participants who met eligibility criteria were randomly allocated into one of two study groups (Fig. 24). The CMT group was allocated 39 participants of which 1 participant withdrew. No participants in the CMT group were lost at follow-up and data from 38 participants was analysed. The RM group was allocated 40 participants, of which 4 people withdrew with no reason given, and one participant withdrew as their symptoms became too severe to continue further. No attrition occurred in the RM group at follow-up and data from 35 participants was analysed. Baseline characteristics in both groups were not significantly different (Tables 6-9). All participants who completed the study were debriefed (Appendix R). The flow of participants who entered into the study from enrolment to follow-up is presented in Fig.24 below.

6.5.3.1. Inclusion criteria

(1) Minimum age for participation = 18 years; No maximum age limit.

(2) Have experienced some form of pain at least 15 days per month for the last 3 months.

(3) Have consumed at least one over-the-counter (OTC) or prescription painkiller in the last 30 days.

(4) Must be literate and able to provide informed consent.

6.5.3.2. Exclusion criteria

(1) Have consumed an illegal substance in the last 30 days.

(2) Currently consuming psychotropic medication; or have in the last 30 days.

(3) Unable to provide informed consent.

(4) Diagnosed with ADD/ADHD.

(5) Currently undergoing any form of CBT/psychotherapy.

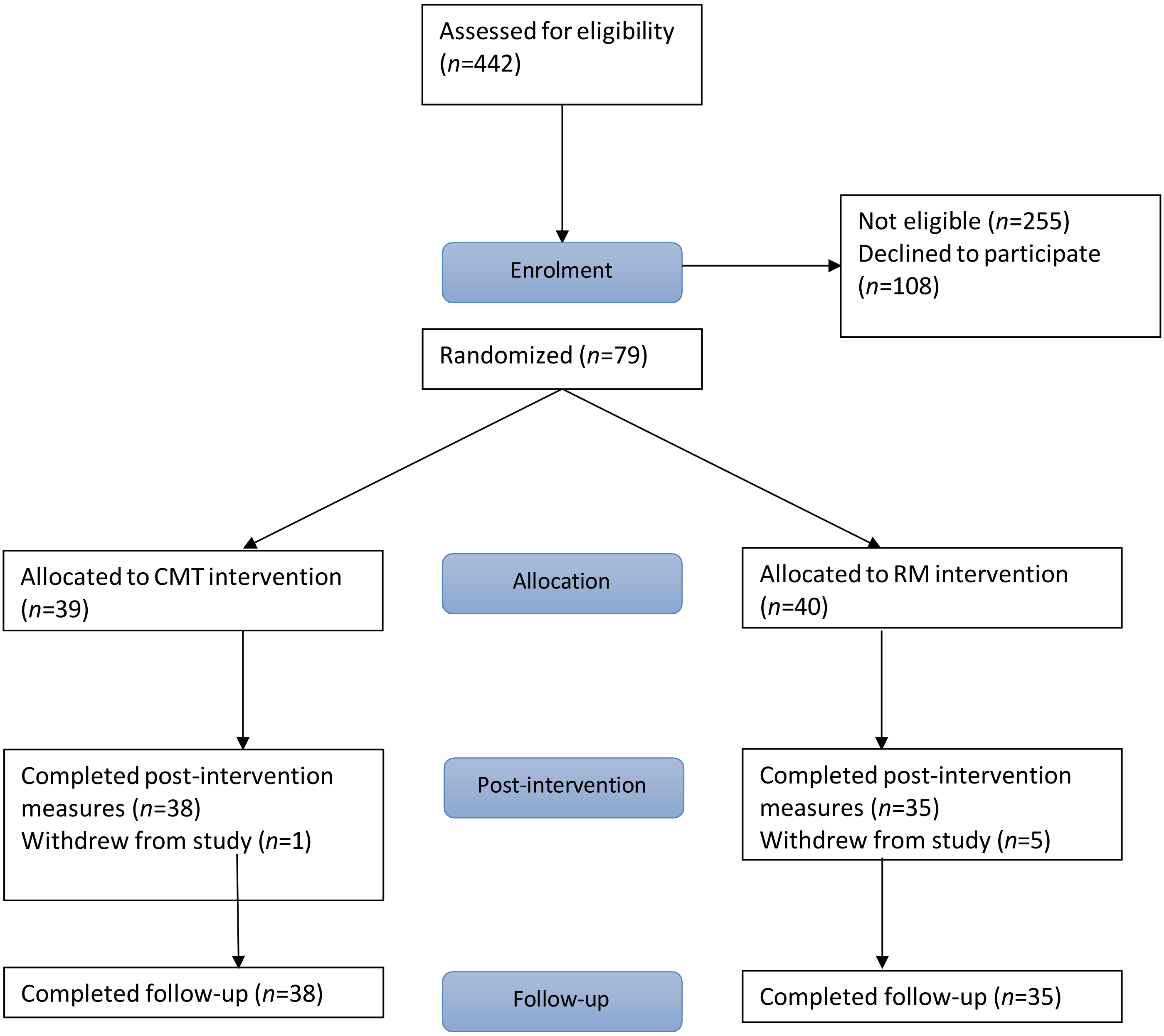
(6) Have a friend or family member in the study.

(7) Suffering from a terminal illness (e.g. Cancer).

6.5.3.3. Participant randomisation

Randomisation of participants in to groups took place when inclusion criteria for participants was met and participants had agreed to take part in the study. Participants were randomly assigned in a ratio of 1:1, with the use of balanced blocks of four, to either CMT Group (Experimental) or RM Group (Control). An algorithm for block randomisation (Kim & Shin, 2014) was adapted to suit a web browser and applied to the web-platform. Once randomised, participants were given a unique URL for their allocated group (CMT or RM) so they could log in. Study coordinators were blind to participant group assignment.

Figure 24 Consort flow diagram for Study 3



6.5.4. Measures

Measures used in this study consisted of self-report measures and one behavioural measure (DD task). All self-report measures and the DD task were placed on a web-platform where participants entered their responses. Detailed descriptions of all measures used in this study are provided above in Chapter 2 as these are the same measures used in previous studies. A brief overview is provided below.

6.5.4.1. Psychological Dependence

Psychological dependence to painkillers was captured using the Leeds Dependence Questionnaire (LDQ; See section 2.4.).

6.5.4.2. Painkiller consumption

Self-report measures on Painkiller Consumption captured data on their daily prescription painkiller consumption (DPPC), daily OTC painkiller consumption (OTCPD) and included the questions “How many prescription painkillers do you consume on a daily basis?” and “How many OTC painkillers do you consume on a daily basis?”. Participants provided a numerical answer. The number of times a participant consumes painkillers of any sort for longer than the prescribing period (LTP) and greater than the recommended daily allowance (RDA) was also quantified whereby participants chose from one of the options: “Never”, “Sometimes”, “Often” or “Always”.

6.5.4.3. Cognitive impulsivity

Cognitive impulsivity was measured using the UPPS-P. This self-report measure had six sub-scales: Negative Urgency (NU), Lack of Perseverance (LOPERSEV), Lack of Premeditation (LOPREMED), Sensation Seeking (SS) and Positive Urgency (PU). Delay Discounting (DD) scores, which quantified impulsive decision-making, were measured by participants completing an online behavioural task.

6.5.4.4. Self-criticism and Self-reassurance

Self-criticism and Self-reassurance were measured using the Forms of Self-Criticising/Self-Reassurance (FSCRS), which had 3 subscales: Self-Inadequacy (IS), Self-Reassured (RS) and Self-Hate (SH). IS and HS were deemed to be self-critical while RS scores quantified the participants level of self-reassurance. The self-criticism scale is comprised of two subscales: (i) Self-inadequate, which is a sense of feeling internally put-down and inadequate (e.g., ‘I can't accept failures and setbacks without feeling inadequate’), (ii) Self-hate, which is a sense of self-dislike and aggressive/persecutory desires to hurt the self (E.g., ‘I have become so angry with myself that I want to hurt or injure myself’). In contrast to being self-critical, people can be reassuring of themselves in these contexts. Self-reassurance is the ability to be encouraging and supportive for self when things go wrong (e.g., ‘I am gentle and supportive with myself’). The original scale had good reliability with Cronbach's alphas of 0.90 for IS, 0.86 for HS and 0.86 for RS (Gilbert et al., 2004).

6.5.4.5. Behavioural impulsivity

A behavioural measure for quantifying behavioural impulsivity (online DD task) was used as in Study 1 (See section 2.8.).

6.5.4.6. Pain Intensity and Pain Frequency

Self-report measures on Pain Intensity (PI) and Pain Frequency (PF) were altered since study 1 and only included the questions “On average, how intense is your daily pain?” measured on an 11-point Likert scale (0 = “Not intense at all”; 10 = “As intense as I could possible imagine”) and “On average, how frequent is your daily pain?” measured on an 11-point Likert scale (0 = “Not frequent at all”; 10 = “Very frequent”). This was because (1) this study did not concern itself with pain *typology* or pain *duration* so were not included and (2) feedback from study 2 revealed *“I don’t always count how often I have pain”* and *“tricky to know how many times I have had pain in the last 30 days”.* The revised version made it easier for participants to enter accurate information which will be used in the analysis of study data. Furthermore, retaining data on Pain Frequency compliments the moderation analysis in study 1 (section 3.13).

Table 8 Data sets used in analysis

Set number	Dependent variables within set	Theme
1	LDQ, DPPC, OTCPD, LTP and RDA	Painkiller consumption & Psychological dependence
2	NU, LOPERSEV, LOPREMED, SS, PU and DD	Impulsivity
3	IS, RS, HS	Self-Compassion
4	PI and PF	Perceived Pain

6.5.5. Procedures

All measures used in this study are shown in Table 8 above. They were organised in themes and are referred to as "Data Sets" (1 to 4) throughout this thesis.

When participants landed on the study website they were presented with a webpage that welcomed them and provided information on the research team. A button at the bottom of the homepage directed participants to be assessed for eligibility. This caused a new page to appear containing Participant Information, Confidentiality and ways to contact the research team. If participants wished to continue further, they clicked on "I wish to continue" and progressed with the screening to assess eligibility. Participants who were not eligible for the study were thanked and released from the study. Those who were deemed eligible for the study were randomised (simple random sampling) into one of two groups (Fig. 24) by giving them a unique URL, which they were asked to bookmark.

Once a participant was placed into a study group (CMT or RM) they were provided with a short introductory video that explained the procedure of the study for that particular group. A text-based version of the introductory video was available for both groups. To reduce placebo effects, participants were not informed at the time of testing that the study concerned the effect of CMT on painkiller addiction, but rather were told that the aim was to investigate the effect of a web-based intervention on psychological processes. All participants were shown how to register by first creating a username and password which they used each time they access the website.

Participants in both study groups were then provided with a unique and dynamic timetable (Figs. 25 & 26) that highlighted exactly which tasks they needed to do on that day. The dynamic timetable feature made site navigation simple whilst preventing participants from accessing or completing tasks specified for a day in the past or the future. Participants could also use the timetable to check their progress (Fig. 21). The progress feature of the timetable is colour coded and showed which tasks had been completed and which tasks needed completing for that day. The progress feature also calculated *how many* tasks were completed per week and was used to assess eligibility for the weekly prize draws. A red square would equate to "did not complete", a green square would be seen when a task has been completed, a yellow square would symbolise a task that needs to be completed within 24 hours, clear boxes indicate future tasks and a grey square indicates no scheduled activities for that day. Using this key, we can see in Fig. 21 that the participant was on "Day 1 of Week 1" and was required to complete *two* tasks within 24 hours as denoted by the *two* yellow boxes. Upon completion these two yellow boxes would turn green in colour. The progress feature also aided the investigator to know which days the participant completed tasks and how many days participants were absent.

6.5.1. Procedures for CMT group participants: Day 1 to Day 20.

Participants in this experimental group followed steps 1 through 4 as described below (see also Fig. 25; Appendices E and S).

6.5.2. Step 1: Registration and Schedule of Activities

Participants in the CMT group (Experimental Group) first registered for the study with a username and password and began by watching a series of five psycho-educational videos on CMT as outlined in section 5.7.1.2.1. Each participant was given access to a dynamic timetable that provided him or her with a schedule of activities, which they needed to complete for that particular day. The box for that particular day would be colour coded whereby Green = Completed; Red = Did not complete, Yellow = Must Complete Today and Clear = A future days event (Fig. 21).

In Fig. 22 above, the tasks to complete for the current day, Day 1, is highlighted in a turquoise box with blue outline and black font. Future tasks such as on Days 2 to 5 are shown in blue boxes and no scheduled activities are shown in black boxes as on Day 6. On days when task completion was required, automated reminder e-mails were sent to participants 24 hours before, at 0200 GMT.

A separate video (web-link in Appendix T) was produced to teach participants how to navigate the web-platform.

6.5.3. Computer Task (DD paradigm) and self-report measures

In Fig. 22, the "Computer Task" was the DD procedure as used in study 1 (see section 2.8) and the "online questionnaire" task consisted of all the self-report measures described in Chapter 2 with the exception of Pain intensity and Pain frequency. Participants from both groups completed the same computer task and the same online questionnaire when prompted to do so. This task was done on Day 1 (Baseline), Day 20 (Post Intervention) and at Day 28 (Follow-up) to provide three measurements for statistical comparisons.

6.5.4. Intervention and Pain Diary

When "Intervention and Pain Diary" (Fig. 22) was clicked, participants would be automatically redirected to their group-specific task. Those in the CMT group were required to complete CMT exercises (see section 4.2 - 4.2.4.) and those in the RM group listened to relaxation music. Group-specific tasks are described in detail below.

6.5.5. Step 2: CMT Exercises Video

Participants in the CMT group watched a series of psycho-educational videos on CMT. The titles of the videos are as follows:

- Chapter 1: Introduction to Self-Compassion and Self-reassurance
- Chapter 2: Soothing Rhythm Breathing
- Chapter 3: Voice Tones, Imagery & Facial Expressions
- Chapter 4: Compassionate-Self and Self-reassurance
- Chapter 5: Compassionate Coping
- Chapter 6: CMT Exercises

Content for each video is described above in section 5.7.1.2.1.

Figure 25 Flow of activities for CMT group participants

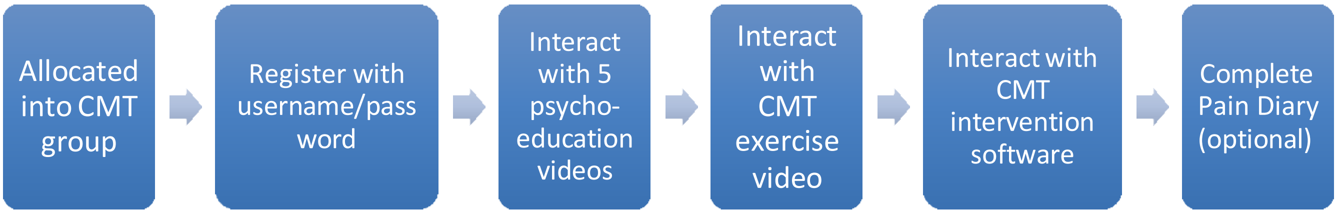
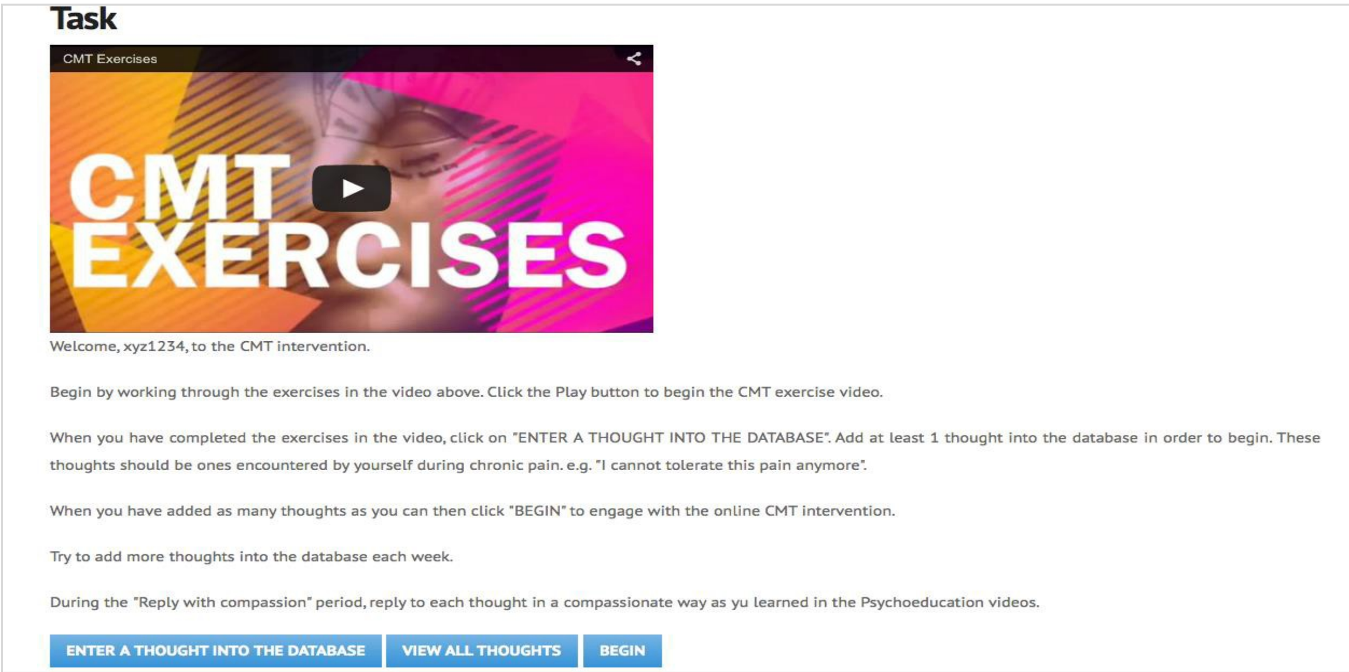


Figure 26 Preview of the stand-alone CMT exercise video homepage



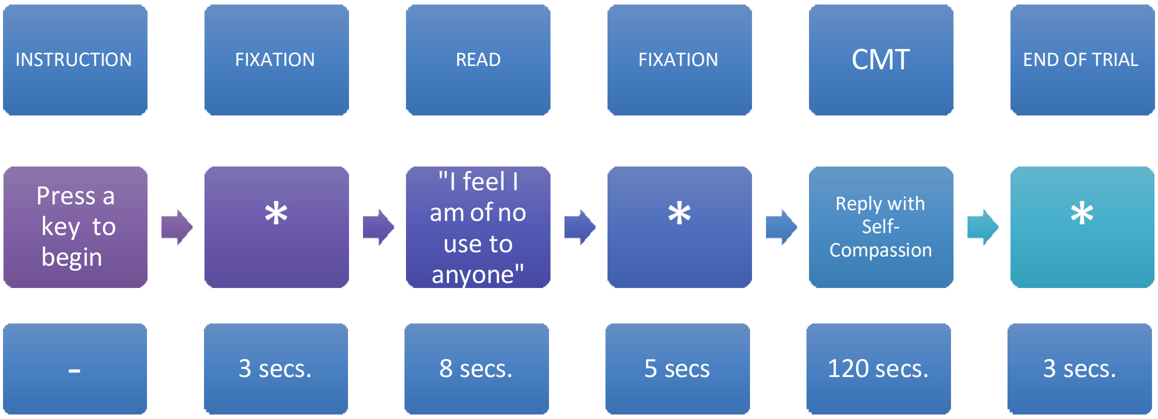
6.5.6. Step 3: CMT Software

Immediately after watching the "Chapter 6: CMT Exercises" video, participants were redirected to a web page that allowed them to engage with the bespoke CMT software.

The CMT software was designed to be interactive and aimed to (a) increase awareness of self-critical thoughts and (b) to develop the skills needed to respond to these thoughts using self-reassurance and compassion learned from the psycho-educational videos. Participants began interacting with the CMT software by entering a "thought" into their personal database. The thought entered was advised to be one that was self-critical in nature and one that would occur often and/or when enduring an episode of chronic pain. Participants had to enter a minimum of one thought into their database. There was no upper limit on the amount of thoughts that could be entered. Participants could also view which thoughts they had entered into the database and had the option to edit their personal database by adding or removing thoughts (Fig. 26). Thoughts entered into a personal database were not visible to any other persons other than the participant.

When at least one thought was entered into the database, the participant could begin interacting with the CMT intervention software by clicking the *Begin* button. The website screen would fade to a black background and participants would be instructed to "*Press a key to begin*". This would initiate the first trial. A star symbol (*) would appear on the screen for 3 seconds and then the screen would clear. Next, a thought that was entered into the participants' personal database would appear on the screen for 8 seconds. Then the screen would clear and present a star symbol for 5 seconds. The screen would then clear and the words "*Reply with Self-Compassion*" would appear on the screen for 120 seconds. It is during this period the participant would be using CMT techniques learned from the psycho-education videos to reply back to the thought they had previously read. After 120 seconds a bell sound was played to signal the end of the trial. A sound was used to allow participants to close their eyes during the self-talk process. If there was more than one thought entered into the database then they were displayed in each successive trial until all thoughts from the database had been displayed. If only one thought was entered, the software would display that one thought for 7 trials. Each trial lasted 136 seconds. When all thoughts in the database had been displayed, the CMT software prompted the participant on whether they would like to enter any further thoughts into the database. The flow of a single CMT intervention trial is shown in Fig. 27.

Figure 27 Schematic of a single CMT intervention trial



6.5.7. Step 4: Pain Diary

Finally, the participant was automatically redirected to their personal online pain diary (Appendix AA; Figs. 21 and 22). This optional feature provided an "e-Journal" in which participants could enter their private thoughts and look through at a future date. The pain diary served as a repository for self-critical thoughts, from which self-critical thoughts could later be added into their database. The software code for the website, behavioural measure and the CMT intervention software was written by myself using JavaScript, MySQL, PHP and HTML.

6.5.8. Procedures for RM group participants

Participants in this control group followed Steps 1 to 3 as described below (See also Fig 30).

6.5.9. Step 1: Registration and Introductory Video

Participants designated to the RM Group (Control Group) began by first registering a unique username and password. Participants watched a brief introductory video on what was expected of them during the study, how to navigate the website and how to make use of the dynamic timetable. Participants in this group had to complete the "Computer Task" which was the DD task and the "Online Questionnaires" which comprised of the self-report measures as outlined in section 6.5.4. above. These two tasks were identical to those completed by CMT group participants.

6.5.10. Step 2: Engaging with Relaxation Music

When participants clicked on the button labelled “Intervention and Pain Diary” they would listen to a randomly selected track from a relaxation music (copyright free) library. Track lengths varied between 6 and 9 minutes. This was done on the same days of the week and for the same number of days as when the CMT group had their scheduled CMT tasks i.e. group timetables were identical aside from the task required.

6.5.11. Step 3: Pain Diary

After listening to the relaxation music participants would then be automatically redirected to their personal pain diary (Appendix AA), which was also optional. To establish this group as a control group, RM group participants did not watch any videos pertaining to CMT, partake in any form of CMT exercises nor did they interact with any CMT software.

Figure 28 Flow of activities for RM group participants

6.5.12. Post-Intervention (Day 21)

On Day 21 (Post-intervention) all participants from both study groups completed the same computer task and the same self-report measures as were done on Day 1 (Baseline), in addition to their group-specific task i.e. engaging with the CMT Software or listening to relaxation music.

Scores from the computer task and self-report measures to allow for statistical comparisons to be made with baseline, post-intervention and follow-up scores. Participants then took a break for 6 days during which they could not engage with the website. The break was to assess whether the effects of the intervention would endure until follow-up.

6.5.13. Follow-up (Day 28)

On Day 28, all participants from both study groups were invited back for a Follow-up session. An automated email reminder was sent to them 3 days and 1 day prior to follow-up.

Participants did not engage with any group-specific tasks on this day. Instead, they only completed the computer task and the same self-report measures completed on Days 1 and 21. These were the same as those completed on Day 1 (Baseline) and Day 21 (Follow-up). This allowed for comparisons to be made with baseline and post-intervention scores. Participants were then thanked, debriefed (Appendix Z) and released from the study.

6.5.14. Summary of procedures

Below is a brief summary of the procedures used in the study.

1. Depending on their study group placing, participants would engage in a once-daily web-based CMT intervention, or listen to relaxation music, for 21 days to assess deviations in self-report-measure and behavioural measures scores from three time points (Baseline, Post-intervention and Follow-up).

2. A follow-up session on Day 28 was performed to assess maintenance.

3. Quantitative analysis was performed within and between experimental groups to assess efficacy of each experimental condition.

4. Participants were asked to provide detailed feedback on the aesthetics and usability of the web-based intervention with intent of producing a more optimal version.

6.6. Analytic strategy used to address study aims and objectives

For this study there were two aims with accompanying objectives and the analytic strategy is described below.

Aim 1: Assess the effect of a web-based CMT intervention in reducing psychological dependence to painkillers (LDQ scores) and changes in accompanying study variables (potential risk factors/protective factors for dependence).

Aim 2: Ascertain any associations between changes in variables over time. This will lend hand to an explanation by which study variables lead to painkiller dependence.

In order to address aims 1 and 2, variables were first be grouped into "data sets" as shown in tables 6-9. Following this, a linear regression with 16 independent variables (data taken from Baseline) was conducted to screen for multivariate outliers. A critical value of Mahalanobi's Distance was calculated to reveal any significant outliers. To test for multicollinearity a Pearson's Correlations was conducted between all DVs within each data sets at baseline. Results that showed correlations to be less than 0.7 were regarded as not expressing multicollinearity.

Furthermore, a doubly-multivariate MANOVA was performed on all four data sets to determine the effect of a CMT protocol on all variables within the data set. The IV always included one between-groups variable, *Groups*, with two levels (CMT and RM) and one within-subjects variable, *Time,* with three levels (baseline, post-intervention and follow-up). SPSS Ver. 20 was used for all analysis. To account for inflation of Type I error, the alpha level was set to 0.0125 (0.05/4) as four MANOVA's will be performed.

After this, a 2x3 Split-Plot ANOVA was performed on each data set to investigate univariate effects over time (Baseline, Post-Intervention and Follow-up). If a significant interaction term was present, then this would be further evaluated with simple planned contrasts. Planned contrasts would use Baseline as a reference point (Baseline vs. Post-intervention and Baseline vs. Follow-up). Independent samples t-Tests were performed on significant DVs from the ANOVA to discriminate group differences at specified time points.

To investigate data trends *within groups* a one-way ANOVA (as a follow-up to a significant interaction) with data split by Group was performed and then followed with a post-hoc test (Bonferroni correction) to assess where the significant difference occurred (between baseline and post-intervention; between baseline and follow-up; between post-intervention and follow-up) within a group. To account for inflation of Type I error, the alpha level was set such that (p = 0.05/Number of variables being tested within that data set). Bonferroni correction was also applied to assess within group differences.

This study applied an Intention-To-Treat (ITT) analysis. Participants who dropped out from the study could impose an attrition bias. This in turn would influence (1) the statistical power of the study, (2) the balance of confounders (e.g. gender) between groups and (3) weaken internal/external validity (Schultz & Grimes, 2002). To avoid the bias that can arise from this, all analysis included data from those participants who dropped out after randomization (irrespective of noncompliance or attrition). Accordingly, ITT has been introduced as a statistical solution. Missing data was handled using the "Last Observation Carried Forward" method (Mason, 1999).

6.7. Novelty and benefits of the study

The study was novel in the sense that self-critical and self-reassuring variables along with impulsive decision-making have not been investigated within this population in relation to painkiller dependence. The intervention and its delivery method were also unique. Moreover, when CMT Group participants logged in to the CMT intervention they were prompted to enter their own *personal* statements that they would have encountered during their bouts of pain thus generating an end-user driven system.

These participant-generated statements were stored in a centralised database. The software would display randomly selected statements from the database during the READ phase. Thus, participants visualised a compassionate and self-reassuring image and replied back to their own self-critical thoughts. At the end of the intervention participants would have strengthened their self-reassuring repertoire and be equipped with a psychological tool they could employ when they next encounter an episode of pain. Ideally, this would promote self-reassuring thoughts and reduce impulsive decision-making, which in turn will suppress attempts to consume painkillers and meander into addiction.

This study is a response to such needs and applied CMT with the aim of reducing painkiller dependence by way of reducing self-inadequate thoughts and impulsive decision-making. The design was novel in that it implemented a web-based CMT intervention whereby largely the target population defines the content.

6.8. Results

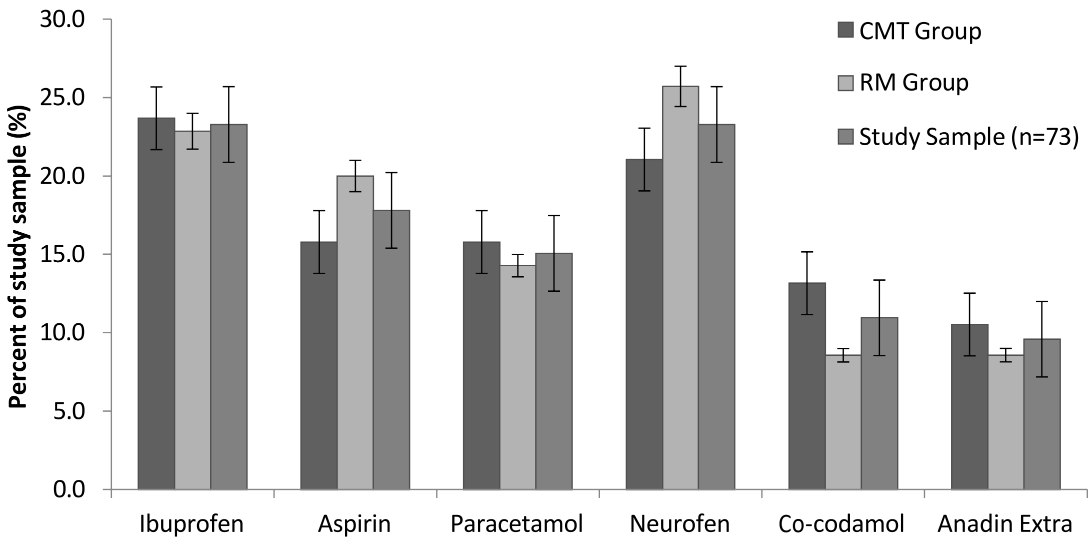
6.8.1. Descriptive Data

Demographic data on gender and location was collected and summarised in Table 9 below. Mean Age was found to be 45.63 (SD = 9.81) in the CMT group with a range of 23 to 62. The RM group had a mean age 45.43 (SD = 10.98) with a range of 25 to 66. There was a higher percentage of Females than Males in the study for both the CMT group (65.8%) and in the RM group (65.7%), although groups did not differ significantly on gender, [$X^{(1)} = 0.0$, $p = 0.995$]. The study tried to include participants from across the globe. Table 9 provides the location of participants per group as a percentage. When examining the entire study sample, the majority of participants were located in North America (50.7%) followed by Europe (23.3%), Asia (9.6%), Australasia (8.2%), South America (4.1%) and Africa (4.1%). Groups did not differ significantly on location of participants [$\chi^{(5)} = 3.27$, $p = 0.66$].

Table 9 Demographic information presented as a percentage of group membership

Category	CMT group (%)	RM group (%)
Male	34.2	34.3
Female	65.8	65.7
North America	52.6	48.6
South America	5.3	2.9
Europe	18.4	28.6
Asia	13.2	5.7
Africa	5.3	2.9
Australasia	5.3	11.4

Figure 29 Most commonly consumed OTC painkillers within groups and in the entire study sample (expressed as a percentage)

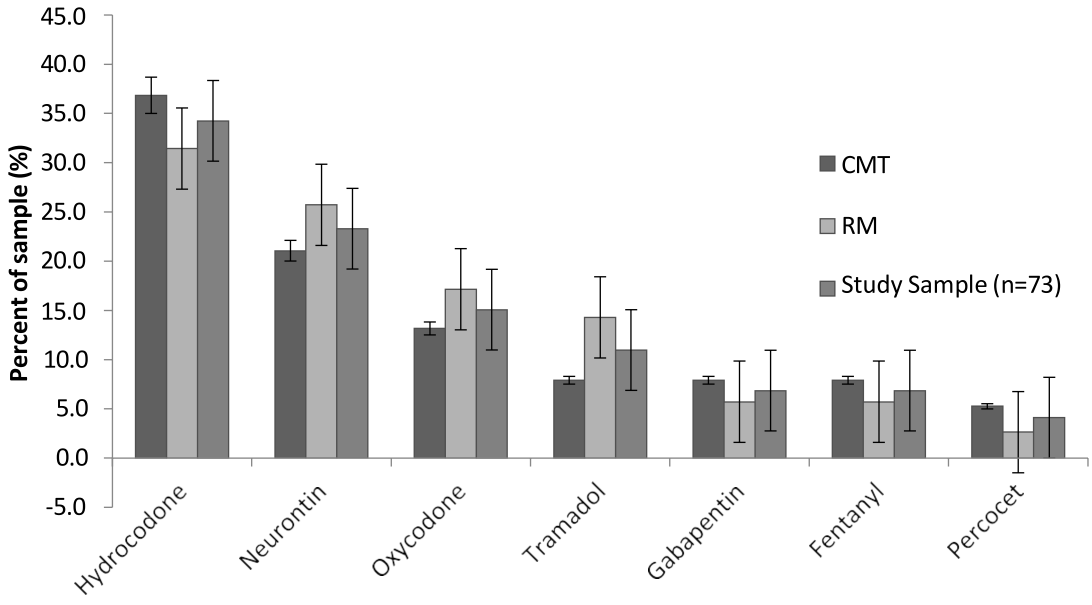


Error Bars: 95% CI

Figure 29 shows the most commonly consumed OTC painkillers as a percentage of the groups and as a percentage of the entire study. On average Ibuprofen (CMT=23.7%; RM=22.9%) and Neurofen (CMT=21.1%; RM=25.7%) were found to be the most consumed OTC painkiller for both groups. The study sample also reported consumption of several other OTC painkillers such as Aspirin (CMT=15.8%; RM=20%), Paracetamol (CMT=15.8%; RM=14.3%), Co-codamol

(CMT=13.2%; RM=8.6%) and Anadin Extra (CMT=10.5%; RM=8.6%). Upon analysing the entire sample as a whole the most commonly consumed OTC painkiller was Neurofen (23.3%), followed by Ibuprofen (23.3%), Aspirin (17.8%), Paracetamol (15.1%), Co-codamol (11%), and Anadin Extra (9.6%). A chi-squared analysis revealed there to be no statistically significant differences between groups for type of most commonly consumed OTC painkiller [$\chi^{(5)} = 1.1$, $p = 0.95$].

Figure 30 Most commonly consumed prescription painkillers within groups and in the study sample (expressed as a percentage)



Error Bars: 95% CI

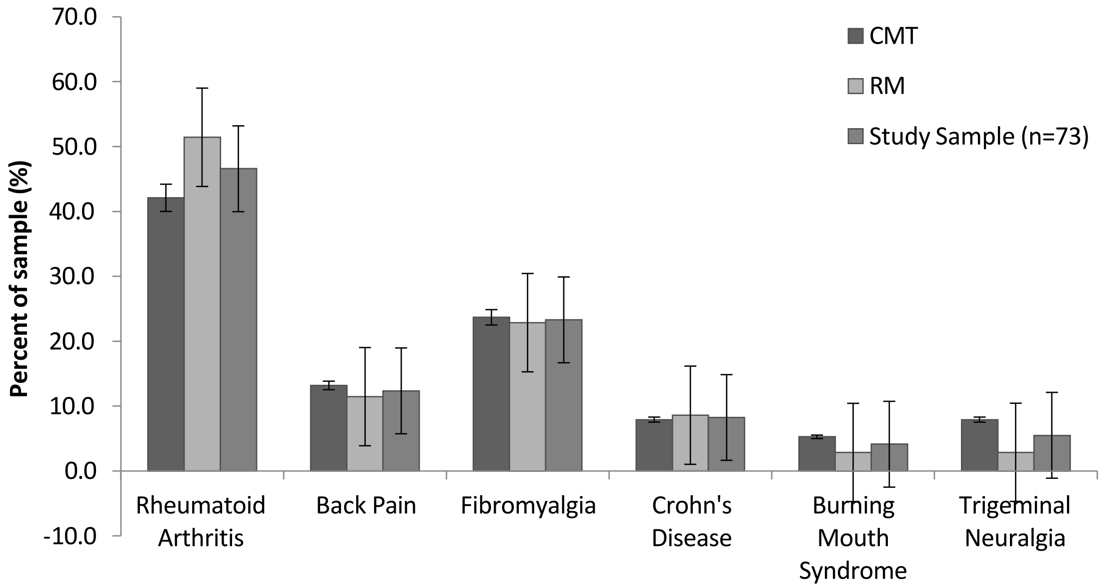
On Day 1 all participants reported their most frequently used prescription painkillers (Fig. 30). Hydrocodone was found to be the most commonly consumed in both groups (CMT=36.8%; RM=31.4%). Other powerful painkillers included Neurontin (CMT=21.1%; RM=25.7%), Oxycodone (CMT=13.2%; RM=17.1%), Tramadol (CMT=7.9%; RM=14.3%), Gabapentin (CMT=7.9%; RM=5.7%), Fentanyl (CMT=7.9%; RM=5.7%) and Percocet (CMT=5.3%; RM=2.6%). Upon analysing the entire study sample (n=73) for the most commonly consumed prescription painkillers it was found that Hydrocodone (34.2%) was the most commonly consumed followed by Neurotonin (23.3%), Oxycodone (15.1%), Tramadol (11%), Gabapentin

(6.8%), Fentanyl (6.8%), and Percocet (4.1%). A chi-squared analysis revealed there to be no statistically significant differences between groups for type of most commonly consumed prescription painkiller [$\chi^{(6)} = 3.51$, $p = 0.74$].

All participants were asked to identify their primary cause of chronic pain (Fig. 31) and groups were analysed individually for the primary cause of chronic pain. Rheumatoid Arthritis (CMT=42.1%; RM=51.4%) was the most commonly reported cause of chronic pain for both groups. Other forms of chronic pain included Back Pain (CMT=13.2%; RM=11.4%), Fibromyalgia (CMT=23.7%; RM=22.9%), Crohn's Disease (CMT=7.9%; RM=8.6%), Burning Mouth Syndrome (CMT=5.3%; RM=2.9%) and Trigeminal Neuralgia (CMT=7.9%; RM=2.9%). No significant differences were found between groups.

Analysis of the entire study sample showed Rheumatoid Arthritis (46.6%) to be the most common cause followed by Fibromyalgia (23.3%), Back Pain (12.3%), Crohn's Disease (8.2%), Trigeminal Neuralgia (5.5%) and Burning Mouth Syndrome (4.1%). A chi-squared analysis revealed there to be no statistically significant differences between groups for the most commonly experienced type of pain (Fig. 31; [$\chi^{(5)} = 1.83$, $p = 0.87$]).

Figure 31 Primary causes of chronic pain within groups and entire study sample (expressed as a percentage)



Error Bars: 95% CI

6.8.2. Organising dependent variables

A total of 16 dependent variables were assessed throughout the study. These variables were grouped into four data sets (Table 8) by grouping dependent variables that held similar properties or were subscales of questionnaires. Data set 1 included five dependent variables that captured data from the Leeds Dependence Questionnaire (LDQ), prescription painkillers consumed per day in the last 30 days (DPPC), Over-The-Counter painkillers consumed per day in the last 30 days (OTCPD), consuming painkillers longer than the prescribing period (LTP) and consuming painkillers more than the recommended daily allowance (RDA). This data set was constructed to include information on painkiller consuming behaviours and psychological dependence to painkillers. Data set 2 included six variables that targeted trait and behavioural impulsivity. The variables included in data set 2 were Negative Urgency (NU), Lack of Perseverance (LOPERSEV), Lack of premeditation (LOPREMED), Sensation Seeking (SS) and Positive Urgency (PU) which comprise the sub-scales of the UPPS-P impulsivity scale data set 2 also included results from a behavioural measure of DD. Data set 3 included three subscales from the Forms of Self-Criticising and Self-reassuring scale. They consisted of Self-Inadequate (IS), Self-Hate (HS) and Self-Reassured (RS). Data set 4 included Pain Intensity (PI) and Pain Frequency (PF). This data set aimed to capture information on perceived levels of pain and occurrence. Subsequent analyses, presented below, were performed on each set.

6.8.3. Screening data for outliers

A linear regression with 16 independent variables (at Baseline) was performed to screen for multivariate outliers. A critical value of Mahalanobi's Distance (39.25) was obtained and revealed no significant outliers. To test for multicollinearity a Pearson's Correlations was conducted between all DVs within each data sets at baseline. Results showed correlations to be less than 0.7 thus there was no multicollinearity.

6.8.4. Analysis for Painkiller Consumption & Painkiller Dependence (Data set 1)

Table 10 below presents the descriptive statistics for data set 1 within both groups at all three points of data collection. Variables in this data set aim to capture painkiller consuming behaviour and the graded severity of psychological dependence to painkillers. Generally, scores within the CMT group decrease between baseline and post intervention while in the RM group scores remained stable.

Table 10 Descriptive statistics for data set 1 variables at baseline, post-intervention and follow-up

	CMT *(n=39)*			RM *(n=40)*		
Measures	*Baseline*	*Post-intervention*	*Follow-up*	*Baseline*	*Post-intervention*	*Follow-up*
LDQ	8.5 (5.08)	6.38 (3.51)	6.56 (4.3)	8.67 (5.75)	8.75 (5.87)	8.9 (6)
DPPC	2.79 (1.67)	2.03 (1.18)	2.13 (1.22)	2.78 (1.6)	2.83 (1.6)	2.83 (1.6)
OTCPD	2.51 (1.05)	1.77 (0.9)	1.82 (1.12)	2.75 (1.81)	2.7 (1.79)	2.68 (1.73)
LTP	1.54 (0.64)	1.28 (0.6)	1.3 (0.47)	1.4 (0.67)	1.38 (0.68)	1.4 (0.63)
RDA	2.26 (1.41)	1.69 (0.77)	1.95 (0.86)	2.4 (1.15)	2.32 (1.07)	2.25 (1.1)

***LDQ** = Leeds Dependence Questionnaire; **DPPC** = Daily Prescription Painkiller Consumption; **OTCPD** = Over-the-Counter painkillers consumed per day; **LTP** = Consuming painkillers for longer than the prescribed period; **RDA**= Consuming painkillers greater than the recommended daily allowance.*

6.8.4.1. Multivariate Analysis

A doubly multivariate MANOVA was performed on data set 1 to determine the effect of a CMT intervention on the dependent variables. Results indicate there was no significant main effect for *Group* [Wilks λ = .9; multivariate F (5, 73) = 1.86, p = .11; η^2_p = .11)], however, there was a significant main effect of *Time* [Wilks λ = .69; F (10, 68) = 3.13, p = .002; η^2_p = .3], indicating significant changes in mean scores in the dependent variables across three time points. A significant *Group x Time* interaction effect, [Wilks λ = .67; F (10, 68) = 3.41, p = .001; η^2_p = .3], indicates that the difference between the CMT and RM group on the linear combination of the five dependent variables are different across time points. Because a significant interaction term was found, main effects were not considered.

6.8.4.2. Univariate Analysis

A follow-up univariate analyses was performed to deduce which variables were responsible for the significant interaction highlighted in the preliminary analysis. A 2x3 split-plot ANOVA with Greenhouse-Geisser (G-G) correction was performed on all five variables. From this set of five DVs, three DVs (LDQ, RDA and DPPC) displayed significant vales for *Time* and a *Group x Time* interaction and these were examined further.

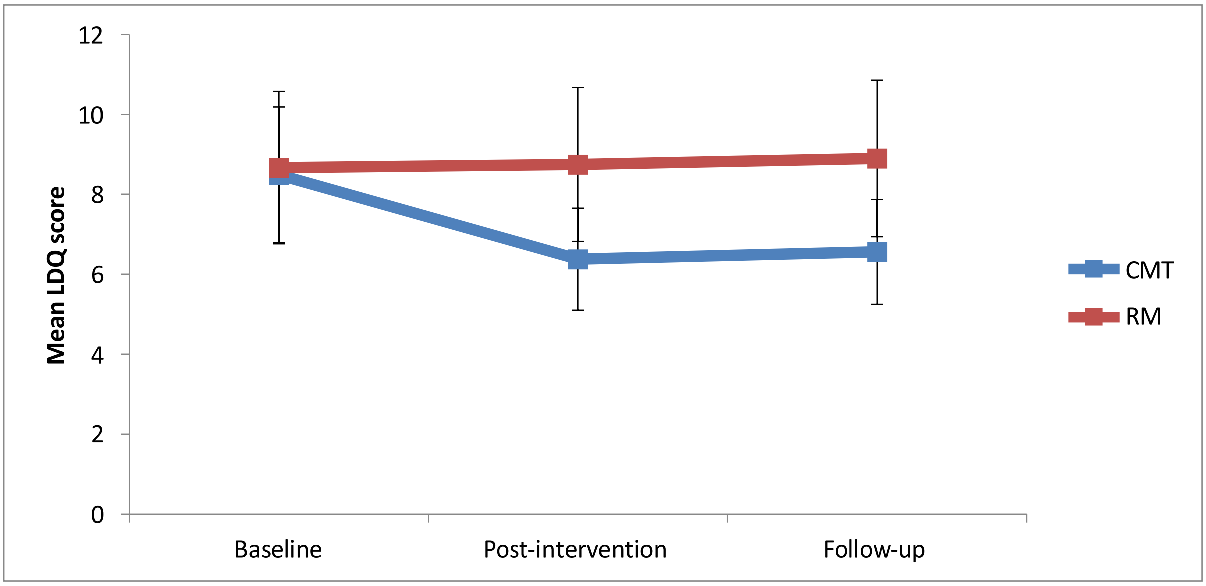
6.8.5. Psychological Dependence on Painkillers (LDQ)

Overall mean LDQ scores were higher in the RM group (8.77) than in the CMT group (7.14). Univariate analysis for LDQ scores showed there to be a significant main effect of *Time* [$F(1.7, 154) = 11.8$, $p < .01$; $\eta^2_p = 0.13$], however this was superseded by a significant *Group x Time* interaction, [$F(2, 154) = 15.58$, $p < .01$; $\eta^2_p = .17$]. This suggests that LDQ scores did differ significantly between groups but only at specific time points (Fig. 32). Planned contrasts indicated the interaction occurred between Baseline and Post-intervention [$F(1,77) = 17.57$, $p < .001$]. Mean LDQ scores at Baseline in the CMT group (8.5) differed to the RM group (8.67) by 0.18, however groups were not significantly different from each other at Baseline [$p > .05$]. At Post-intervention mean LDQ scores differed between the CMT group (6.38) and the RM group (8.75) by 2.37 [$t(77) = 2.2$, $p = .03$]. LDQ scores also differed significantly at Follow-up between participants in the CMT Group (M=6.56) and the RM Group (M=8.9) by 2.34 [$t(77) = 2$, $p = .05$].

6.8.5.1. Within groups analysis

A repeated measures ANOVA with a G-G correction showed that mean LDQ scores differed significantly between time points in the CMT group only ($F(1.6, 76.7) = 15.37$, $p < .001$). Post-hoc tests using the Bonferroni correction revealed a significant decrease ($p < .001$) in LDQ scores from baseline to post-intervention (8.49 ± 5.08 vs 6.38 ± 3.51, respectively). There was also a significant reduction ($p < .001$) from baseline to follow up (8.49 ± 5.08 vs 6.56 ± 4.3, respectively). There was no significant change over time for those in the RM group ($p > .05$) so no further analysis was performed.

Figure 32 Interaction plot of group and time on psychological dependence to painkillers



Error Bars: 95% CI

Figure 32 also shows that the statistically significant reduction in psychological dependence to painkillers within CMT group participants was maintained from post-intervention to follow-up.

6.8.6. Consuming painkillers above the Recommended Daily Allowance (RDA)

Regarding the consumption of painkillers above the RDA (Fig. 33), overall RDA scores were higher in the RM group (2.32) than the CMT group (1.97).

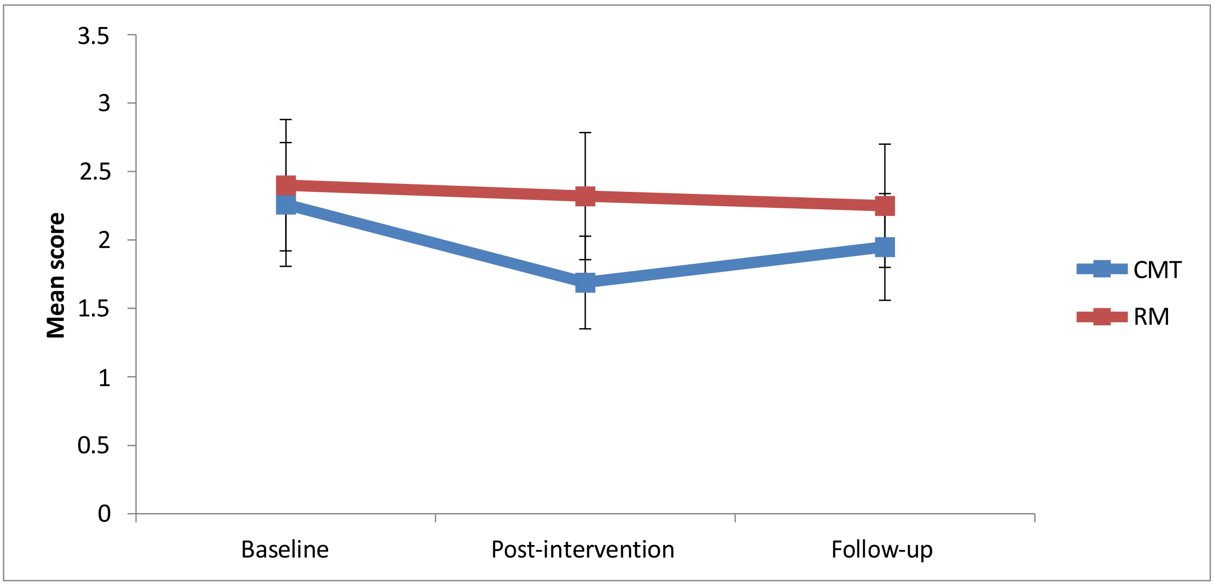
Mean RDA scores remained stable across time in the RM group while scores in the CMT group decreased from Baseline (2.26) to Post-intervention (1.69) and Follow-up (1.95). Univariate analysis results showed there to be a significant main effect of *Time* [F(1.6,124.3) = 2.7, p = .004; η^2_p = .08] and a significant interaction term [F (1.6,124.3) = 4, p= .03; η^2_p = .05]. RDA scores differed significantly between groups at specific time points.

Planned contrasts highlighted the interaction to occur between Baseline and Post-intervention [F (1,77) = 6.23, p = .02]. Mean RDA scores between groups did not differ significantly [p > .05] at baseline. At post-intervention, mean RDA scores in the CMT group (1.69) differed with the RM group (2.16) by 0.47 and scores between groups were significantly different [t (77) = 3.02, p = .03].

6.8.6.1. Within-groups analysis

A repeated measures ANOVA with a G-G correction showed that mean RDA scores differed significantly between time points in the CMT group only (F (1.6, 66.5) = 8.12, $p < .001$). Post-hoc tests using the Bonferroni correction revealed a significant decrease ($p = .003$) in mean RDA scores from baseline to post-intervention (2.26 ± 1.14 vs. 1.69 ± 0.77, respectively). Additionally, there was a significant increase in mean scores ($p < .03$) from post-intervention to follow up (1.69 ± 0.77 vs. 1.95 ± 0.86, respectively). There was no significant change over time for those in the RM group ($p > .05$) so no further analysis was performed.

Figure 33 Interaction plot of group and time on consuming painkiller for more than the RDA



Error Bars: 95% CI

Figure 33 shows that the benefits of the CMT intervention are evident at post-intervention stage but were not maintained at follow-up. The y-axis represents the possible outcomes for this self –report measure ("1 = Never", "2 = Sometimes", "3 = Usually" and "4 = Always").

6.8.7. Daily Prescription Painkiller Consumption (DPPC)

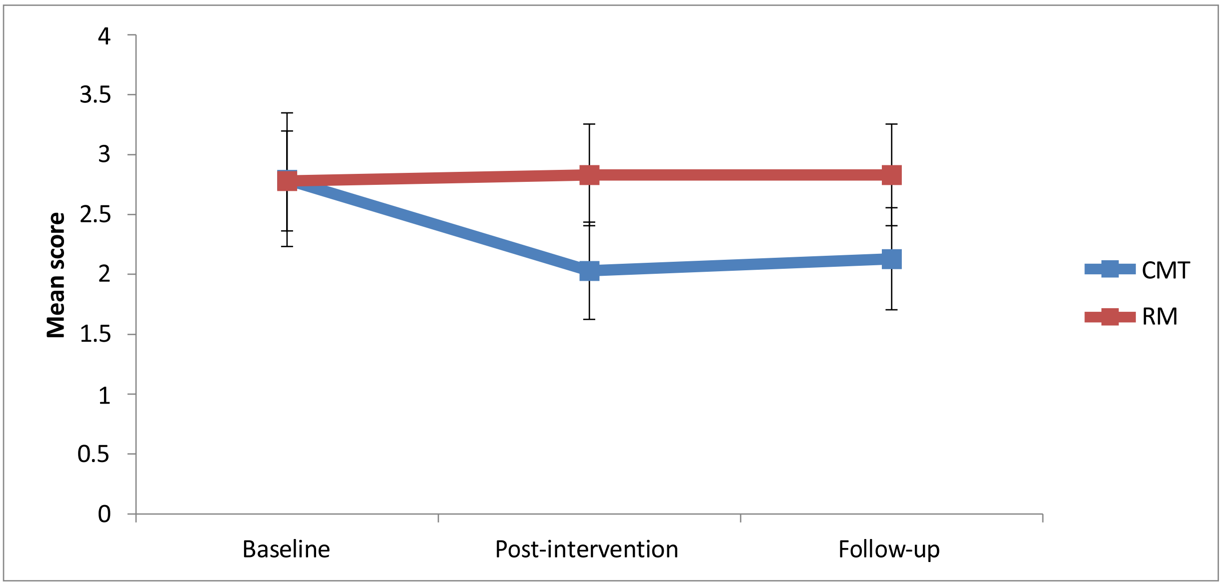
Regarding daily prescription painkiller consumption (Fig. 34), overall mean scores were higher in the RM group (2.81) than the CMT group (2.32). Mean scores in the RM group remained stable across time. Scores in the CMT group decreased from Baseline (2.79) to Post-intervention (2.03) and from Baseline to Follow-up (2.13). Univariate analysis revealed a significant main effect of *Time* [*F* (1.04, 80) = 5.1, p = .03; η^2_p = .06] and a significant interaction term [*F* (1.04, 80.1) = 6.7, p = .01; η^2_p = .08].

Planned contrasts revealed a significant interaction to occur between Baseline and Post-intervention [*F* (1, 77) = 7.46, *p* < .01] and also between Baseline and Follow-up [*F*(1, 77) = 5.98, *p* = .02]. At Baseline, mean DPPC scores (2.79) in the CMT group differed with those in the RM group (2.78) at Baseline by 0.01 and mean scores between groups were not significantly different [p > .05]. At Post-intervention, mean DPPC scores in the RM group (2.83) differed significantly with those in the CMT group by 0.71 [*t*(77) = 2.57, p = .01]. Mean scores in the RM group at Follow-up (2.83) were higher than the CMT group by 0.7 and groups differed significantly [*t*(77) = 2.22, *p* = 0.03].

6.8.7.1. Within groups analysis

A repeated measures ANOVA with a G-G correction showed that mean DPPC scores differed significantly between time points in the CMT group only (*F* (1.1, 39) = 15.03, *p* < .001). Post-hoc tests using the Bonferroni correction revealed a significant decrease (*p* = .001) in mean scores from baseline to post-intervention (2.79 ± 1.67 vs 2.03 ± 1.18, respectively). Additionally, there was a significant reduction in mean scores (*p* = .002) from baseline to follow up (2.79 ± 1.67 vs 2.13 ± 1.22, respectively). The ANOVA revealed no significant change over time for those in the RM group (*p* > .05) so no further analysis was performed.

Figure 34 Interaction plot of group and time on daily consumption of prescription painkillers



Error Bars: 95% CI

Figure 34 shows a similar trend to psychological dependence (Fig. 32) where the benefits of the CMT intervention at post-intervention were maintained at follow-up.

6.8.8. Analysis for Impulsivity and Delay Discounting (Data set 2)

Table 11 presents the descriptive statistics for data set 2 variables within both groups at all three time points of data collection. A student t-Test revealed no significant differences between groups on all six dependent variables at Baseline [*p* > .05]. DD scores were obtained from a behavioural measure of impulsivity while the remaining five variables constitute sub-scales of the UPPS-P scale for Impulsivity.

Table 11 Descriptive statistics for data set 2

Measures	CMT *(n=39)*			RM *(n=40)*		
	Baseline	*Post-intervention*	*Follow-up*	*Baseline*	*Post-intervention*	*Follow-up*
NU	27.18 (6.37)	23.85 (6.08)	23.64 (5.75)	25.98 (5.54)	26.8 (5.41)	27.5 (5.14)
LOPM	20.9 (2.61)	20.46 (4.41)	21.28 (4.56)	20.1 (3.19)	19.95 (3.85)	20.5 (3.82)
SS	24.31 (5.4)	28.23 (7.08)	30.38 (12.43)	24.85 (5.75)	29.15 (7.6)	20.65 (4.42)
LOPERSEV	19.08 (4.1)	18.1 (4.51)	18.67 (4.5)	19.6 (3.47)	23.5 (6.47)	23.92 (7.01)
PU	22.64 (5.8)	18.74 (4.12)	19.74 (5.4)	21.58 (5.28)	20.58 (5.91)	19.74 (5.4)
DD	350 (86.22)	403.46 (61.64)	412.87 (95.89)	373.25 (71.67)	372.5 (54.28)	386.13 (51.81)

6.8.8.1. Multivariate Analysis

As outlined above, the procedure and order of data analysis for data set 2 (Table 11) was the same as was performed for data set 1. Results from the doubly multivariate MANOVA indicated a significant main effect of *Group* [Wilks λ = .7) F (6, 72) = 6.32, p < .001; η^2_p = .3] and for *Time* [Wilks λ = .5) F (12, 66) = 4.73, p< .001; η^2_p = .46]. There also existed a significant *Group x Time interaction* [Wilks λ = .6) F (12,66) = 4.19, p < .001; η^2_p = .43]. Thus, mean differences in the linear composite of the six DV scores between groups did exist although this was time dependent.

6.8.8.2. Univariate Analysis

Follow-up univariate analyses with a 2x3 split-plot ANOVA with Greenhouse-Geisser (G-G) correction was performed on all six variables in order to elucidate which variable(s) were most responsible for group differences. DVs which had a significant effect of *Time* included SS [F (1.7, 150) = 7.11, p = .001; η^2_p = .09], LOPERSEV [F (1.98, 152) = 3.67, p=0.03; η^2_p =0.05] and DD [F (1.5, 116.6) = 6.5, p = .005; η^2_p = .08]. The following analysis will focus on DVs which had a significant interaction term obtained from the univariate analysis. These included DD, NU, LOPERSEV and SS and will be examined further with planned contrasts and independent samples t-Test's will be used to reveal any differences between groups at specific time points.

6.8.9. Delay Discounting (DD)

Overall mean DD scores were slightly higher in the CMT group (388.62) than the RM group (377.29) whereby a higher score equates to a greater performance on the behavioural measure. Mean scores increased across time within the CMT group from Baseline (350) to Post-intervention (403.46) and again at Follow-up (412.87). Participants in the RM group witnessed similar scores at Baseline (373.25) and Post-intervention (372.5) and saw an increase in scores at Follow-up (386.13).

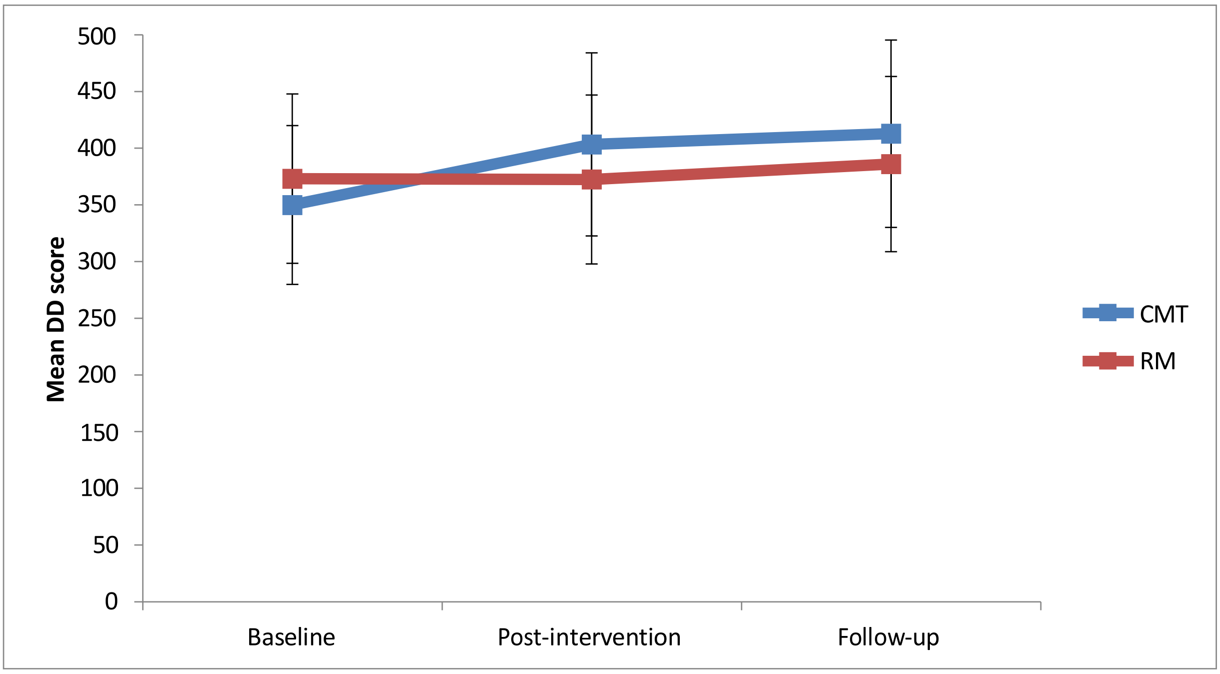
Univariate analysis on scores from the behavioural measure revealed a significant interaction term for DD scores [$F(1.5, 116.55) = 3.94$, $p< .03$; $\eta^2_p = .05$], thus DD scores differed between groups at specific time points. Planned contrasts highlighted significant interaction points to occur between Baseline and Post-intervention [$F(1, 77) = 7.3$, $p = .008$]. Mean DD scores at Baseline differed between groups by a score of 53.46 but groups did not differ significantly, [$p > .05$] as shown in Fig. 35 below. At Post-intervention, mean DD scores differed by 30.96 and allowed for a significant difference between groups to exist [$t\ (77) = 2.37$, $p = .02$]. At Follow-up, groups did not differ significantly on DD scores [$p > .05$).

6.8.9.1. Within-groups analysis

A repeated measures ANOVA with a G-G correction showed that mean DD scores differed significantly between time points in the CMT group only ($F\ (1.5, 59.9) = 6.09$, $p = .008$). Post-hoc tests using the Bonferroni correction revealed a significant increase ($p = .02$) in DD scores from baseline to post-intervention (350 ± 86.22 vs 403.46 ± 61.64, respectively) in the CMT group. There was also a significant increase in scores (p = .04) from baseline to follow up (350 ± 86.22 vs 412.87 ± 95.89, respectively). There was no significant change over time for those in the RM group ($p > .05$) so no further analysis was performed.

Figure 35 shows that the CMT intervention improved impulsive decision-making and was maintained at follow-up. The y-axis shows the mean score obtained (£ - hypothetical amount).

Figure 35 Interaction plot of group and time on Delay Discounting



Error Bars: 95% CI

6.8.10. Negative Urgency (NU)

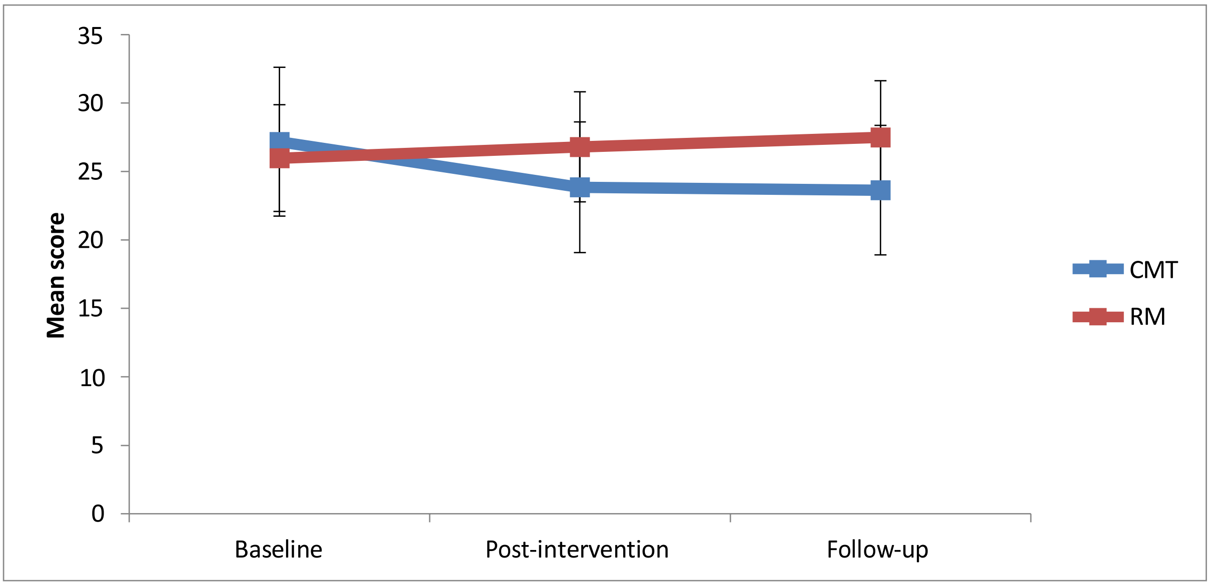
Negative urgency is described as the propensity to act impulsively when in a negative mood. Examination of overall mean scores in the CMT group (24.89) were seen to be lower when compared with RM group (26.76). Mean scores in the RM group increased from Baseline (25.98) to Post-intervention and 26.8 at Follow-up (23.64). Mean scores in the CMT group decreased across time from Baseline (27.18) to Post-intervention (23.85) and Follow-up (23.64).

Univariate analysis on the sub-scale Negative Urgency revealed a significant *Group x Time* interaction effect [$F(1.2, 92.19) = 7.65$, $p = .001$; $\eta^2_p = 0.1$], suggesting scores differ between groups at specific time points. Planned contrasts highlighted the significant interaction to occur between Baseline and Post-intervention [$F(1,77) = 6.44$, $p = .01$; Fig. 36], and between Baseline and Follow-up [$F(1, 77) = 9.5$, $p = .03$]. Mean NU scores at Baseline differed between groups by a score of 1.2 and mean scores were not significantly different between groups ($p > .05$). At Post-intervention, mean NU scores differed significantly by 2.95 between groups [$t(77) = 2.3$, $p = .03$]. Mean scores at Follow-up differed significantly by 3.86, $t(77) = 3.15$, $p = .002$.

6.8.10.1. Within-groups analysis

A repeated measures ANOVA with a G-G correction showed that mean NU scores differed significantly between time points in the CMT group only (F (1.4, 42.3) = 10.24, $p < .001$). Post-hoc tests using the Bonferroni correction revealed a significant decrease (p = .007) in NU scores from baseline to post-intervention (27.18 ± 6.37 vs 23.85 ± 6.08, respectively). There was also a significant reduction in scores (p = .004) from baseline to follow-up (27.18 ± 6.37 vs 23.64 ± 5.75, respectively). There was no significant change over time for those in the RM group (p > .05) so no further analysis was performed.

Figure 36 Interaction plot of group and time on Negative Urgency



Error Bars: 95% CI

Figure 36 shows the CMT intervention significantly reduced NU and the effect was maintained at follow-up while mean scores in the RM group remained similar over time.

6.8.11. Lack of Perseverance (LOPERSEV)

Overall mean scores of LOPERSEV (Fig. 37) differed between groups with the RM group (22.32) participants having a higher mean score than CMT group participants (18.62). Higher scores on this subscale indicate negative performance. Mean scores increased in the RM group from Baseline (19.55) to Post-intervention (23.5), and again at Follow-up (23.9). Mean scores in the CMT group decreased over time from Baseline (19.08) to Post-intervention (18.1), and at Follow-up (18.67).

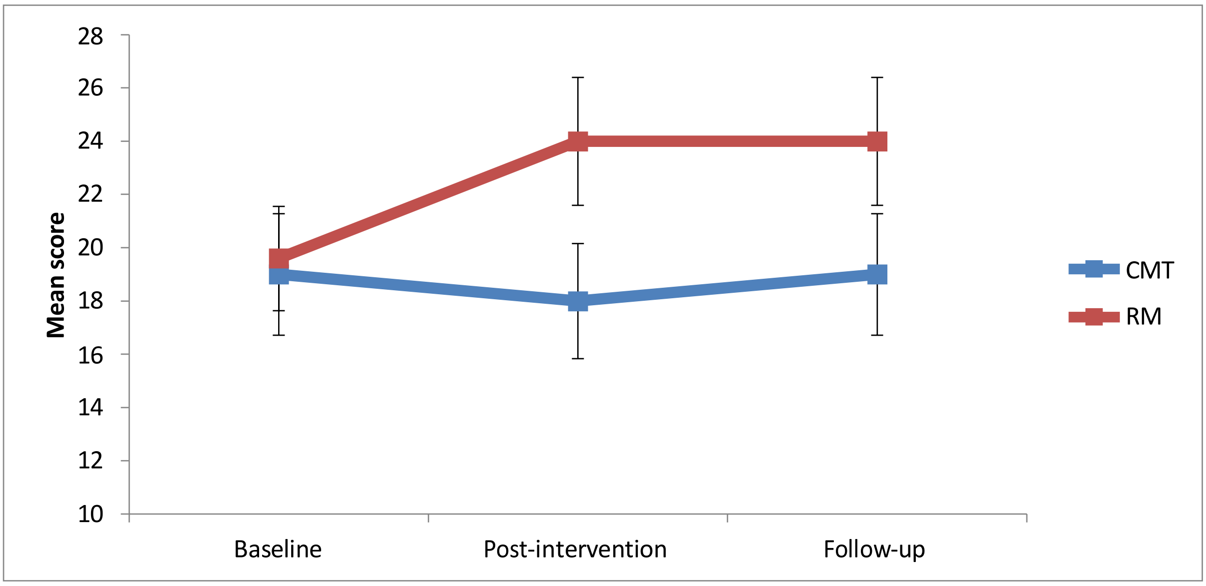
Univariate analysis on the sub-scale LOPERSEV revealed a significant *Group x Time* interaction effect [$F(2, 154) = 6.78$, $p = .002$; $\eta^2_p = .08$] suggesting that LOPERSEV scores differ significantly between groups at specific time points. Planned contrasts revealed significant interaction points to occur between Baseline and Post-intervention [$F(1, 77) = 10.19$, $p = .002$] and also between Baseline and Follow-up [$F(1, 77) = 11.07$, $p = .002$]. Mean LOPERSEV scores at Baseline differed between groups by a score of 0.47. Groups did not differ significantly at Baseline ($p > .05$). At Post-intervention, groups differed by a score of 5.4 and this equated to a significant difference between groups [$t(77) = 4.29$, $p < .001$]. At Follow-up a disparity of 5.26 in mean scores permitted a significant group difference [$t(77) = 3.95$, $p < .001$].

6.8.11.1. Within-groups analysis

A repeated measures ANOVA showed that mean LOPERSEV scores differed significantly between time points in the RM group only (F (2, 78) = 8.06, $p = .004$). Post-hoc tests using the Bonferroni correction revealed a significant increase ($p = .002$) in LOPERSEV scores from baseline to post-intervention (19.6 ± 3.47 vs 23.5 ± 6.47, respectively). There was also a significant increase in scores ($p = .004$) from baseline to follow-up (19.6 ± 3.47 vs 23.92 ± 7.01, respectively). There was no significant change over time for those in the CMT group ($p > .05$) so no further analysis was performed.

Figure 37 shows the CMT group had stable levels of LOPERSEV over time, whereas in the RM group levels of LOPERSEV increased during the intervention and the effect was maintained at follow-up.

Figure 37 Interaction plot of group and time on Lack of Perseverance



Error Bars: 95% CI

6.8.12. Sensation-Seeking (SS)

Overall mean SS scores were slightly higher in the CMT group (27.64) than the RM group (24.9) but were not significantly different. Mean scores in the RM group increased from Baseline (24.85) to Post-intervention (29.15) and then decreased at Follow-up (20.65). Mean scores in the CMT group continually increased from Baseline (24.31) to Post-intervention (28.23) and again at Follow-up (30.38).

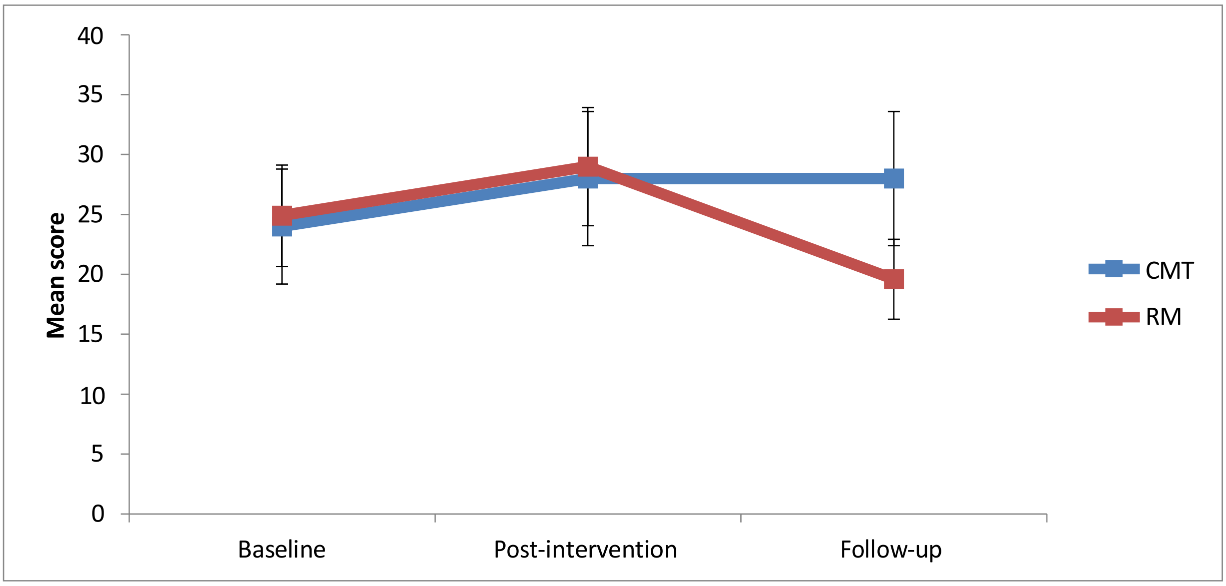
Univariate analysis on the sub-scale SS (Fig. 38) exposed a significant *Time/Group* interaction term *[F* (1.7, 152) = 14, $p < .001$; $\eta^2_p = .15$]. A planned contrast analysis revealed the significant interaction to occur between Baseline and Follow-up [F (1, 77) = 19.85, $p < .01$]. Mean SS scores at Baseline differed between groups by 0.54 and were not significantly different [$p >$ .05]. Again, groups were not significantly different at Post-intervention [$p >.05$], however, at Follow-up a disparity between groups on mean SS scores of 9.73 was substantial enough to equate to a significant difference between groups [$t(77) = 4.66$, $p < .001$].

6.8.12.1. Within groups analysis

A repeated measures ANOVA with a G-G correction showed that mean SS scores differed significantly between time points in the RM group only (F (1.5, 67.48) = 5.3, $p = .02$). Post-hoc tests using the Bonferroni correction revealed a significant **decrease** (p = .007) in SS scores from post-intervention to follow-up (29.15 ± 7.6 vs 20.65 ± 4.42, respectively). There was no significant change over time for those in the CMT group (p > .05)

Figure 38 shows the changes in mean SS scores over time for the CMT group and the RM group over time.

Figure 38 Interaction plot of group and time on Sensation Seeking



Error Bars: 95% CI

6.8.13. Analysis for Self-criticism and Self-Reassurance (Data set 3)

Table 12 presents the descriptive statistics for the DVs in data set 3. The three DVs comprise the sub-scales of the Forms of Self-Criticising/Attacking and Self-Reassuring scale (FCSRS). This self-report measure is used to ascertain participant levels of Self-Hate, Self-Reassurance and Self-Inadequacy.

Table 12 ***Descriptive statistics for Self-Compassion***

	CMT *(n=39)*			RM *(n=40)*		
Measures	*Baseline*	*Post-intervention*	*Follow-up*	*Baseline*	*Post-intervention*	*Follow-up*
IS	13.56 (6.53)	12.28 (6.36)	14.79 (5.56)	13.03 (6.53)	14.10 (6.18)	12.13 (5.59)
RS	17.62 (5.71)	21.87 (6.41)	20.36 (7.42)	19.38 (7.02)	18.58 (5.68)	19.78 (6.45)
HS	4.03 (3.38)	2.33 (2.52)	2.05 (2.59)	2.85 (3.38)	3.85 (3.79)	3.58 (3.62)

6.8.13.1. Multivariate Analysis

All three measures of the subscale (Table 12) were entered into a doubly multivariate MANOVA to deduce main effects of *Group* and *Time* and to seek an interaction effect. No main effects for *Group* (p = .61) or *Time* (p = .13) were found although an interaction effect between *Time* and *Group* did exist [Wilks λ = 0.6) F (6,72) = 7.92, p < .01; η^2_p = .4].

6.8.13.2. Univariate Analysis

A follow-up univariate analysis was performed to deduce which variables were responsible for the significant interaction highlighted by the MANOVA. A 2x3 split-plot ANOVA was performed on all three variables. Sphericity was assumed for all variables. No DV's had a significant effect of *Time* but all three had significant *Group x Time* interactions.

6.8.14. Self-Inadequacy (IS)

Inspection of the overall mean scores were slightly lower in the RM group (13.93) than the CMT group (13.97). Mean IS scores in the CMT group decreased from Baseline (13.56) to Post-intervention (12.28) and then increased at Follow-up (14.79). In the RM group, mean scores increased from Baseline (13.02) to Post-intervention (14.1) and then decreased at Follow-up (12.13).

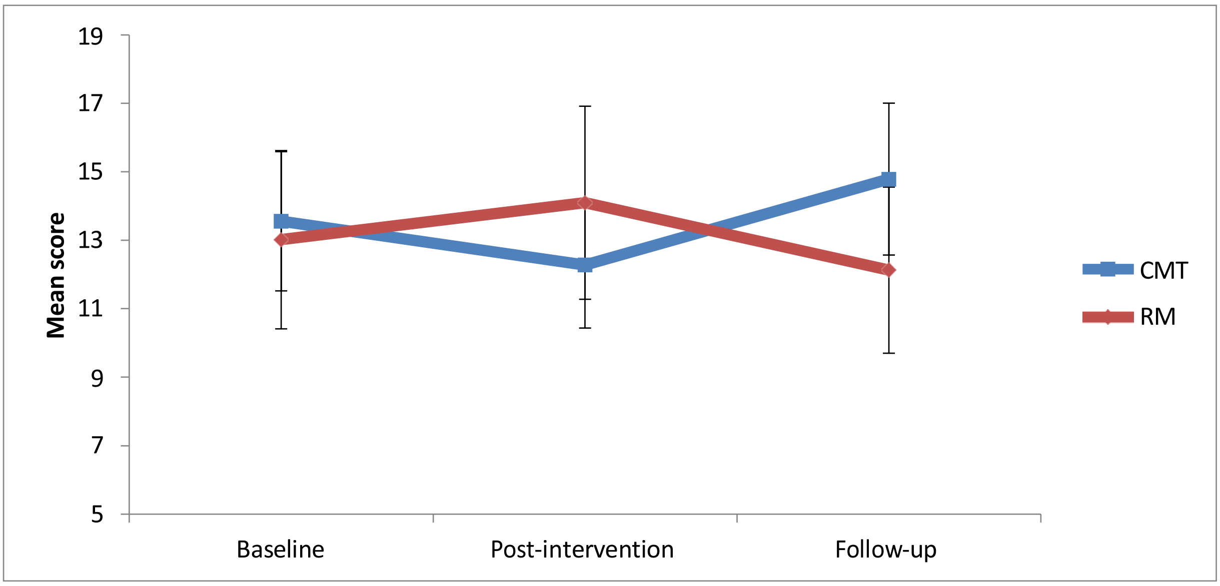
Univariate analysis revealed no significant effect for *Time*, although a significant *Group x Time* interaction was revealed for IS scores [univariate F (2, 154) = 3.24, p = .04; η^2_p = .04], ergo IS scores had differed significantly between groups but was dependent on specific time points.

IS scores were similar between CMT group (13.56) and RM group (13.03) at Baseline and groups did not differ significantly (p>.05). At Post-intervention CMT group participants had a lower mean score (12.28) than participants in the RM group (14.1) and did not differ significantly [p >.05). At Follow-up, groups differed significantly [t (77) = 2.13, p = .04] as those in the CMT group (14.79) had a higher mean score than those in the RM group (12.13). Planned contrast analysis did not reveal an interaction to occur in relation to Baseline. Therefore, in order to locate where the interaction occurred, a unique planned contrast highlighted the significant interaction to have occurred only between Post-intervention and Follow-up [F(1,71)=7.39, p = .008].

6.8.14.1. Within-groups analysis

A repeated measures ANOVA revealed no statistically significant changes between any combination of time points in both groups (p > .05). Figure 39 below shows that the CMT intervention reduced IS from baseline to post-intervention.

Figure 39 Interaction plot of group and time on Self-Inadequacy



Error Bars: 95% CI

6.8.14. Self-Reassurance (RS)

Overall mean scores were marginally higher in the CMT group (19.95) than the RM group (19.24). Results from a univariate split-plot ANOVA confirmed that no significant main effect of *Time* was present. A significant interaction term (Group/Time) was found for RS scores [F(2, 154) = 3.49, p = .03; η^2_p = .04]. Thus, the effect of time was different between the two groups.

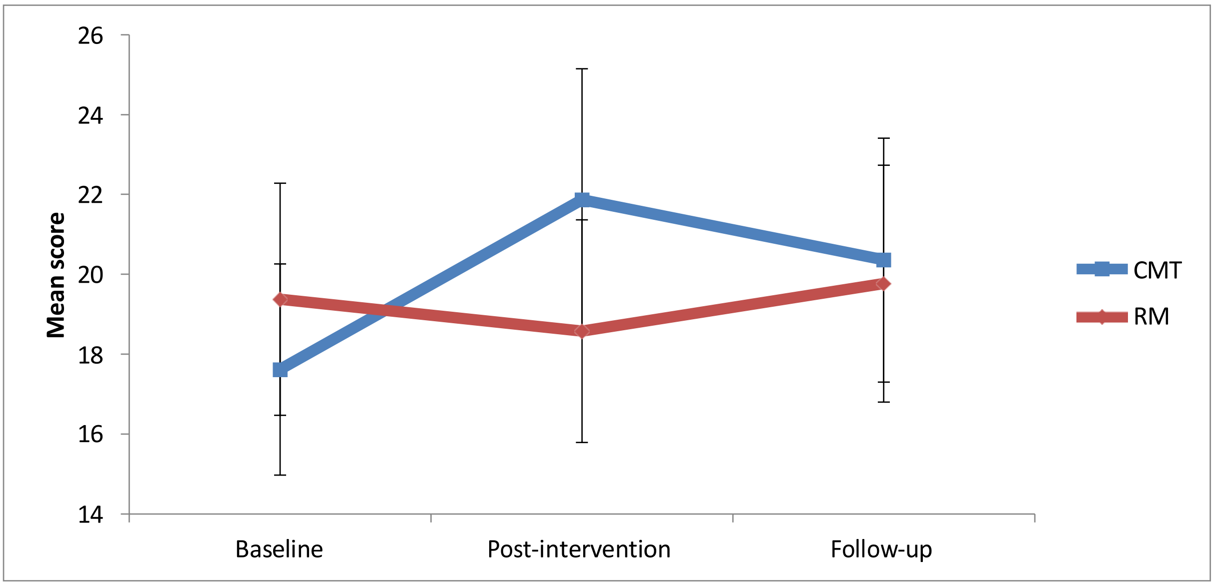
A planned contrast analysis highlighted a significant interaction to occur between Baseline and Post-intervention [F(1,77) = 7, p = .01]. RS scores at Baseline in the CMT group (17.62) were not significantly different to RM group (19.38) scores, [p > .05]. RS scores at Post-intervention in the CMT group (20.36) were higher than at Baseline and were higher than RM group participants (19.77). A difference of 3.29 in mean RS scores occurred between groups at Post-intervention and scores between groups were significantly different [t(77) = 0.27, p = .02] from each other. A comparison of scores at Follow-up revealed a higher score in the CMT group (20.36) than in the RM group (19.78), although scores did not differ significantly between groups [p > .05].

6.8.14.1. Within-groups analysis

A repeated measures ANOVA with a G-G correction showed that mean RS scores differed significantly between time points within the CMT group only (F (1.94, 76.91) = 4.23, p = .02). Post-hoc tests using the Bonferroni correction revealed a significant increase (p = .02) in self-reassurance from baseline to post-intervention (17.62 ± 5.71 vs 21.87 ± 6.41, respectively). No statistically significant changes were seen between baseline and follow-up or between post-intervention and follow-up. There was no significant change over time for those in the RM group (p = .60).

Figure 40 shows that the CMT intervention improved RS however, the effect was not maintained at follow-up.

Figure 40 Interaction plot of group and time on Self-Reassurance



Error Bars: 95% CI

6.8.15. Self-Hate (HS)

Overall mean HS scores were higher in the RM group (3.43) than the CMT group (2.80). Mean HS scores in the CMT group continued to decrease throughout the study while those in the RM group showed variance. A split-plot ANOVA revealed no significant main effect for *Time* although there was a significant *Group x Time* interaction [univariate $F(2, 154) = 12.58$, $p < .001$; $\eta^2_p = .1$].

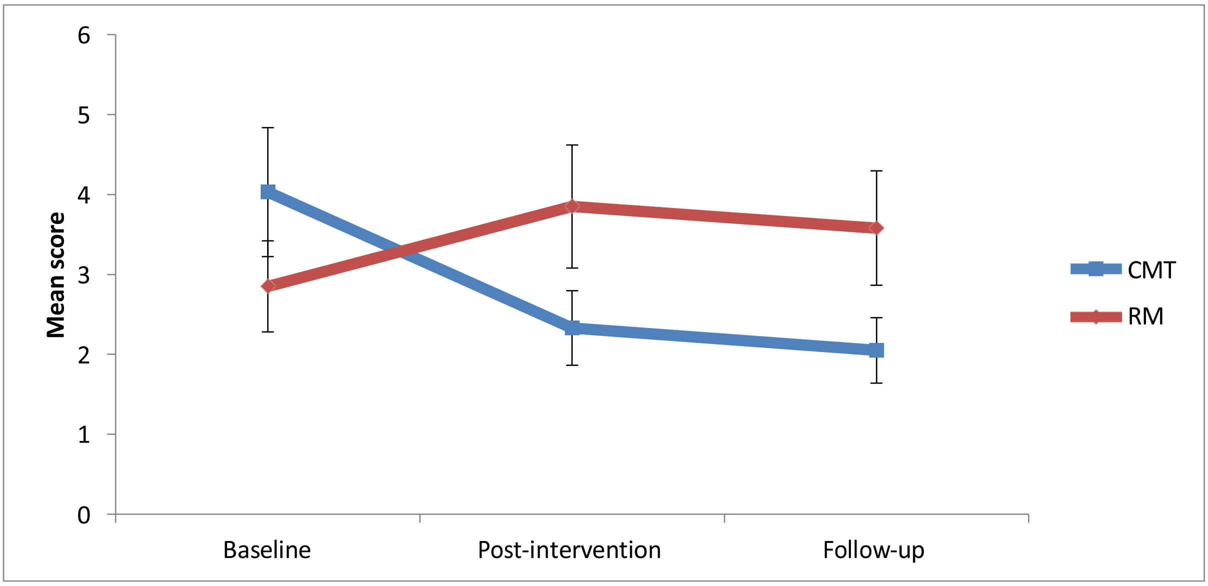
Planned contrasts presented the significant interaction to occur between Baseline and Post-intervention [$F(1, 77) = 22.3$, $p < .01$], and also between Baseline and Follow-up [$F(1, 77) = 20.71$, $p < .01$]. At Baseline the CMT group (4.03) and the RM group (2.85) had similar mean scores and did not differ significantly [$p > .05$]. At Post-intervention HS scores were lower in the CMT group (2.33) than the RM group (3.85). This difference of 1.52 in mean scores between groups meant that groups were significantly different in HS scores at Post-intervention[$t(77) = 6.7$, $p = .04$]. Follow-up scores revealed a similar pattern where CMT group (2.05) mean scores were lower than the RM group (3.58). A difference of 1.53 between groups equated to a significant difference in HS scores when the final set of measures were taken [$t(77)=3.25$, $p = .04$].

6.8.15.1. Within groups analysis

A repeated measures ANOVA with a G-G correction showed that mean HS scores differed significantly between time points in the CMT group only (F (2, 78) = 33, $p < .001$). Post-hoc tests using the Bonferroni correction revealed a significant decrease ($p < .001$) in self-hate from baseline to post-intervention (4.03 ± 3.38 vs 2.33 ± 2.52, respectively). There was also a significant reduction ($p < .001$) from baseline to follow up (4.03 ± 3.38 vs 2.05 ± 2.59, respectively). There was no significant change over time for those in the RM group ($p > .05$) so no further analysis was performed.

Figure 41 shows the CMT intervention reduced HS with benefits that were maintained at follow-up.

Figure 41 Interaction plot of group and time on Self-Hate



Error Bars: 95% CI

6.8.16. Analysis for Pain Intensity and Pain Frequency (Data set 4)

Data set 4 (Table 13) contained two dependent variables that focus on capturing information on participants perceived levels of chronic pain. The two dependent variables in this data set consist of Pain Intensity and Pain Frequency. Descriptive statistics are provided for data set 4 variables below in Table 13. Scores within the CMT group for PI remained stable across time, as did scores within the RM group. A Similar pattern of stability across time was observed for

PF within both groups. Overall scores for PI were lower in the CMT group (6.39) when compared to the RM group (7), while overall PF scores in the CMT group (5.84) were very similar to RM group scores (5.67). For both PI and PF, there was no significant difference in mean scores between groups across the three time points (p >.05)

Table 13 Descriptive statistics for data set 4 variables (Pain Intensity & Pain Frequency)

	CMT *(n=39)*			RM *(n=40)*		
Measures	*Baseline*	*Post-intervention*	*Follow-up*	*Baseline*	*Post-intervention*	*Follow-up*
PI	6.62 (2.23)	6.13 (2.5)	6.41 (2.25)	6.73 (2.23)	7.1 (1.9)	7.13 (1.8)
PF	5.82 (2.1)	5.77 (2.12)	5.95 (2.3)	5.42 (2.45)	5.9 (2.64)	5.68 (2.18)

6.8.16.1. Multivariate Analysis

Results from the doubly multivariate MANOVA revealed no significant main effect for *Group* or *Time*. No significant interaction was present either. A follow-up 2x3 repeated measure ANOVA held similar outcomes with no significant effect for time or interaction for either Pain Intensity or Pain Frequency. As a result of no significant outcomes from the MANOVA no further analysis was performed. The intensity of pain and its frequency were not influenced by the independent variables.

6.9. Discussion

This is the first study, to our knowledge, that has implemented a web-based CMT intervention with the aim of reducing opioid dependence in those with chronic pain. Feedback from a pilot study allowed for a tailored website to be created from which the study was delivered. The improved web-platform was deemed to be well accepted by the chronic pain community and since its inception has amassed 2.3 million hits (Fig. 42). When recruitment began in September 2015 the number of people the website attracted increased from an average of 551 unique visits per day to 1,217 when the study was concluded. Since then the web-platform has continued to attract almost 1,000 visits per day.

Figure 42 Summary statistics for the web-platform

Summary by Month										
Month	Daily Avg				Monthly Totals					
	Hits	Files	Pages	Visits	Sites	KBytes	Visits	Pages	Files	Hits
Mar 2016	8595	6554	6306	887	3886	2212255	13311	94598	98313	128926
Feb 2016	6745	5243	4897	960	8243	6005780	27868	142018	152070	195623
Jan 2016	7732	6277	5113	931	10094	5016241	28879	158505	194594	239698
Dec 2015	8330	6461	5375	796	7356	5591617	24684	166628	200318	258260
Nov 2015	10169	7716	6323	1217	11426	8135734	36529	189697	231497	305088
Oct 2015	7460	5736	4826	872	8785	5834116	27058	149623	177820	231285
Sep 2015	5405	3852	2872	551	5745	3252304	16532	86175	115562	162154
Aug 2015	11718	8404	4092	479	5549	9673826	14856	126861	260525	363270
Jul 2015	4251	2984	1794	332	3424	2282404	10310	55643	92506	131795
Jun 2015	3055	2320	1434	313	4712	1783571	9416	43032	69605	91663
May 2015	2692	2159	1188	354	6210	2135323	10989	36853	66936	83469
Apr 2015	1465	1228	778	207	3179	1632559	6230	23341	36860	43965
Totals						53555730	226662	1272974	1696606	2235196

Participants were recruited, assessed for eligibility and randomly allocated into one of two groups (CMT - experimental vs. RM - control). This formed the basis of a randomised controlled trial.

The control group listened to relaxation music while the experimental group engaged in a CMT intervention consisting of (a) a psycho-education syllabus (SRB, Mindfulness exercises, Compassionate Imagery exercises, Friendly Facial Tones and Friendly Voice) and (b) interacted with the novel CMT Software. The CMT psycho-education syllabus consisted of a series of videos that provided a knowledge base for participants on theory and practice in CMT and stressed the importance of "*it's not your fault*" (Gilbert, 2009). The psycho-education video series also included interactive CMT exercises that would be practised by participants and then applied during interaction with the CMT software and during their free time. The self-compassion material was based on Gilbert's (2005, 2009) CMT and CFT.

The aim of the CMT intervention (CMT psycho-education syllabus + CMT software) was to train participants to respond to their own self-critical thoughts in a soothing and self-reassured way and to eventually substitute their self-critical voice with a self-soothing and self-reassured voice. The CMT intervention had an overarching aim of increasing self-regulation (an aptitude to regulate cognitive and emotional processes) by modifying the response to negative affect in order to reduce painkiller consumption and subsequent painkiller dependence and a secondary aim to increase self-reassurance. Research outcomes describe that reduced self-regulation, particularly cognitive regulation, is correlated with an increased susceptibility to partake in health compromising risk-taking behaviour such as drug consumption (Magar, et al., 2008).

6.9.1. CMT Psycho-education Syllabus

The content of the CMT psycho-education syllabus focused on increasing participants' awareness of mental and emotional processes, improving knowledge of self-regulation and recognising when emotions become overpowering (Broderick & Metz, 2009; Gilbert, 2005; 2007). The psycho-education syllabus was composed of a 5-part video series hosted online. The video material included CMT exercises in order to cultivate and strengthen the skills of self-reassurance. Exercises consisted of SRB (See section 1.6.1.), Compassionate Imagery (1.6.1.) and the "skills of compassion" which include compassionate attention, compassionate reasoning and compassionate behaviour (section 1.5.9.2).

6.9.2. CMT software

The interactive CMT software was specifically designed to raise self-reassurance and reduce self-critical thoughts within the individual by having participants reply back to their self-critical thoughts in a more self-reassuring way. It was anticipated that over time self-reassuring streams of thought would become the default mode of processing self-critical thoughts, which may otherwise have led to states of negative affect and promoting the manifestation of NU. Additionally, endorsing a self-reassuring voice tone as default may have also have activated the soothe system which is thought to make use of endogenous opiates and OXT. By up-regulating endogenous opiates and OXT it is likely that the need for exogenous opiates (prescription painkillers) would be diminished. This is shown in the literature whereby studies show peripheral administration of OXT lead to a reduction in stress (Ring et al., 2006; Landgraf & Neumann, 2004).

Results from study 1 showed that high scores on RS may function as a protective buffer for painkiller dependence (See Fig. 14). Kelly et al., (2010) demonstrated that participants who engaged in a 3-week CMT/CFT programme had a greater rate of smoking reduction than control groups when self-reassurance was increased. Participants in the CMT group within this study displayed a significant increase in mean scores for RS between Baseline and Post-intervention and mean RS scores were significantly greater than the control group at post-intervention (Fig. 40). Therefore, if participants were better able to reduce the frequency/severity self-critical thoughts (and negative affect) by substituting them with self-reassuring thoughts then the prospect of forming a SUD may also be reduced (See Fig. 44 below on addictive loop). This change in RS scores were likely to have been achieved by the CMT software as they were trained to substitute self-critical thoughts with self-reassuring thoughts. The addition of using friendly facial expressions and self-reassuring voice tones would have helped participants cultivate a base from which self-reassurance could develop and bolstered the effects of the CMT software (Hackmann, 1998). The CMT software, in theory, has the advantage of empowering individuals with a simple concept (being attentive to and not repelling momentary experiences whilst cultivating self-reassurance) that can generally be applied to specific parts of the addiction process (Grabovac et al., 2011). The participant's interaction with the CMT intervention may, over time, progress towards the diminishment and eventual disassembly of the associative learning process of excessive painkiller consumption and so is more practical than simply removing or avoiding drug-consuming stimuli. By acclimating to attentional focus, participants soon develop an awareness of habit-associated affective states and bodily feelings such as low-level cravings and begin to "deautomate" what is principally a habitual process (Kabat-Zinn et al., 1985; Brewer et al., 2010; Teasdale et al., 1995). By instructing participants to non-judgmentally observe their self-critical thoughts, remind themselves "*it's not their fault*" and reply back to self-critical thoughts using self-reassurance, the CMT intervention may endorse the substitution of affect-induced, habituated responses with a more adaptive and healthier response such as enhanced self-regulation (Kaunhoven & Dorjee, 2017). The CMT intervention may also aid participants in forming a healthier relationship to negative affect and physical pain (Amaro, 2010). Future studies would aim to delineate the role of CMT alone in reducing such behaviours.

To be clear at this stage of the discussion, it is postulated that the mechanism of action, which led to a reduction in painkiller addiction, is the attenuation of affective biases that promote reflexive and reactive responses in addition to a change in self-related thoughts. As mentioned above, desires to consume painkillers are a result of habituated affective bias that is central to emotional reactivity. This fuels subsequent cycles of cravings and habituation. Therefore, to attenuate this affective bias by applying CMT, no further fuel is added to the fire, which leads to a reduction in painkiller consumption and ultimately a reduction in psychological dependence (Bowen & Marlatt, 2009; Brewer et al., 2010).

In addition to the above there is the role of OXT (Oxytocin). Gilbert states "*Clinical and research work suggests that some people, especially those who have experienced early histories characterised by abuse and neglect, can have great difficulty in being able to access the soothing system...in consequence they are unable to self-soothe*" (Gilbert & Irons, 2005, P4. 4; Gilbert & Proctor, 2006). Gilbert (2005; 2009) proposes that active engagement with CMT leads to activation and strengthening of the Soothe system, a system thought to be sub-served by the OXT. The OXT neuropeptide is involved in a variety of physiological functions and affiliative behaviours. Recent studies have shown that OXT can increase Dopamine release by targeting the mesocorticolimbic dopaminergic neurons via the ventral tegmental area (Melis et al., 2007). Therefore, an active engagement with the CMT intervention could have led to increased levels Dopamine, or at least maintained basal levels in the CMT group participants (Hsu et al., 2015). OXT is certainly well validated in pro-social motivation (Gordon et al., 2011) and so could play a role in other areas of motivation and perhaps explain the stable scores across time which were seen for Lack of Perseverance (LOPERSEV). Furthermore, Dopamine and OXT are known to be involved in addictive behaviour problems.

Dopamine has been shown to lead to an attitude of compulsive perseverance where sub-optimal levels of Dopamine encourage drug-seeking and drug-consuming behaviours (Salamone & Correa, 2012) while OXT has been regarded to offer protection from drug abuse and addiction (Baskerville & Douglas, 2010; Marazziti & Dell'Osso, 2008; Tops et al., 2014) and mitigate withdrawal symptoms of the opiate analgesic Heroin (Kovacs et al., 1985). Thus, if the CMT intervention kept Dopamine levels stable then there would be less motivation, or drive, for those participants to seek and consume painkillers and subsequently less propensity for psychological dependence to painkillers. The CMT intervention could have achieved this by creating positive affect (Gilbert, 2005; 2009), which stimulated Dopamine release directly, or indirectly by activating the OXT driven Soothe System.

6.9.3. Major outcomes of Study 3

Major outcomes of the study were that mean scores of known cognitive risk factors for psychological dependence to painkillers were significantly reduced in the CMT group at post-intervention. Such risk factors included self-hate, negative urgency and DD. In addition, protective factors (RS) were seen to be significantly increased in the CMT group alone. Study variables and their contributions to psychological dependence to painkillers are discussed below.

6.9.3.1. Painkiller consumption, painkiller misuse and psychological dependence decreased

A notable observation was that the mean daily consumption of prescription painkillers (DPPC; Fig. 34) and psychological dependence to painkillers (LDQ; Fig. 32) was significantly lower in the CMT group than participants in the RM group when the study concluded. Results also showed a significant reduction in mean LDQ scores from baseline to post-intervention and when comparing mean scores from baseline to follow-up in the CMT group only. LDQ scores for those in the RM group showed stable levels across time with no significant changes. Accompanying this observation, mean scores for RDA were also significantly reduced from baseline to post-intervention and from base-line to follow-up in the CMT group only while those in the RM group showed no significant changes over time. Furthermore, mean scores for DPPC were significantly lower from baseline to post-intervention and from baseline to follow-up for CMT group participants only.

These results highlight a relationship whereby (a) a reduction in the daily consumption of painkillers and (b) a reduction in RDA is significantly correlated with a reduction in psychological dependence to painkillers (r = -.419, p = < .001 and r = -.377, p < .001, respectively) but only for those engaging with the CMT intervention. It is entirely plausible to suggest that consuming an addictive substance (e.g. prescription opiates) in lower quantities and at a reduced frequency (i.e. within the RDA; Fig 35) would reduce susceptibility of developing psychological dependence to that substance. Thus, the pathway towards a significant reduction in LDQ scores observed for CMT group participants was likely due to the significant reduction in DPPC and RDA scores which in turn were due to engaging with the CMT intervention.

6.9.3.2. Cognitive and Behavioural Impulsivity

Mean scores for LOPERSEV were found to be significantly different between groups at post-intervention and follow-up. Additionally, LOPERSEV scores in the RM group were significantly greater at post-intervention and at follow-up when compared to baseline. Participants in the RM group were seen to become less persevering over time while those in the CMT group had stable levels of perseverance over time (i.e. CMT may maintain levels of perseverance). Also, within data set 2, it was observed that LOPERSEV was found to be significant in the MANOVA, not because mean scores in the CMT group changed, but because mean scores in the RM group deviated significantly from the CMT group participants at post-intervention and at follow-up. Lack of perseverance is defined as "the disposition to fail to maintain focus on tasks that are difficult or boring (Riley et al., 2015)." It is likely that scores in the RM group increased because participants may have found their group-specific task of listening to relaxation music on a daily basis as being an arduous task (Riley et al., 2015). An alternative view is that LOPERSEV scores could have increased for participants in both groups as the study endured however, the CMT intervention kept levels of perseverance stable across time for CMT group participants by providing psychoeducation which endorsed "being in the present moment" and helping to develop a greater sense of goal-achievement. This interpretation is based on results by Breines & Chen (2012), who showed participants who engaged with self-compassion had significantly greater motivation to complete tasks that aided self-improvement. Participants in this study also spent more time studying for a difficult test following an initial failure; exhibited a preference for upward social comparison after reflecting on a personal weakness and reported greater motivation to change the weakness. The authors suggest "taking an accepting approach to personal failure may make people more motivated to improve themselves."

Negative Urgency (NU) is the propensity to act impulsively in the presence of negative affect and was found to be a risk factor for painkiller addiction in study 1. These results reflect similar results that showed NU acts as a catalyst for painkiller addiction in chronic pain patients (Martel et al., 2014; Vest et al., 2016) and acts a progressive risk factor for the initiation phase of drug addiction (Pang et al., 2014). In this study mean scores for NU within CMT group participants showed a significant reduction from baseline to post-intervention and a significant reduction between post-intervention and follow-up (Fig. 36). RM group participants showed stable scores across time with no significant changes occurring over time. Between groups analysis showed only a significant difference between groups at post-intervention and this significant difference between groups was maintained at follow-up. Thus, engaging in the CMT intervention appears to have made participants less impulsive when negative emotions arise within them.

Upon inspection, it was found that significant positive correlations (Bivariate) were observed between NU and painkiller consuming behaviours (Daily consumption: DPPC; $r = .614$, $p < .01$ and Consuming above the RDA; $r = .417$, $p < .01$ which could suggest that possessing high scores on NU could influence increased drug (painkiller) consumption. This reflects a widely accepted view in the scientific literature whereby high scores on NU are seen to coincide with the severity of substance dependence (Pang et al., 2014; Verdejo-Garcia et al., 2007; Tragesser et al., 2009; Zapolski et al., 2009; Albein-Urios et al., 2011).

In addition to Negative urgency and LOPERSEV, sensation seeking scores were found to differ significantly between groups at Follow-up. Within groups analysis showed no significant change over time in the CMT group but there was a significant decrease from Post-intervention and Follow-up in the RM group.

Mean scores for DD increased significantly between baseline and post-intervention (Fig. 37) and between baseline and follow-up within CMT group participants. This suggests that those receiving the CMT intervention were making *fewer* impulsive decisions over time. At post-intervention, there was a significant difference between groups whereby those in the CMT group had significantly higher mean scores than RM group participants. High scores on the DD task indicate rational decision-making while low scores are indicative of impulsive decision making, thus achieving a high score is deemed favourable. Achieving a score higher than at baseline, as shown in the CMT group, could indicate cultivation of a more rational approach to such a task but certainly showed a less impulsive approach to the task.

Alternatively, the reduction of Ego Depletion, defined as the loss of cognitive control that arises from continuous attempts at inhibiting an impulse may play a role (Baumeister & Heatherington, 1996; Baumeister et al., 1998) in increased DD scores. Neural regions of the prefrontal cortex are responsible for behavioural inhibition. Some types of inhibition are swift, involuntary and unconscious, while some lay at the cusp of consciousness, and others are entirely conscious. Ego depletion may occur at several of these levels. When addicts in recovery say "No" to their cravings continually, this can be viewed as a cognitively demanding task requiring conscious inhibition of impulses and would lead to ego depletion. However, reframing the statement may have had a different impact on ego depletion. The tone of the internal voice may also have an impact when those high on self-criticalness and with painkiller addiction try to abstain by saying "*No! Don't have another painkiller!*" would likely have changed their tone to "*This is not good for me*" after interacting with the CMT intervention. The nature of the internal voice is often one of parental criticism that is judgmental, condemnatory, perhaps condemnatory, or threatening. Having to live with this voice on a daily basis is clearly a cause for ego depletion with potential to make one feel frustrated, isolated, anxious, and likely to cause feelings of anger making this an ideal context for consuming drugs. However, without qualitative data this remains speculative and future studies would aim to address this. Should the tone of one's voice change from self-critical to self-reassured then the way which we say "*No*" to ourselves could make a significant difference. Engaging with the CMT intervention and increasing self-reassurance could have helped participants reduce ego depletion and make it a message of sustenance and optimism, in lieu of renunciation and hindrance. One can adopt on the voice of a critical parent. Or one can adopt on the voice of a friend or a loving parent – Rather than saying "*You better not do that!*" one can apply self-reassurance and say "*Let's not do that; let's do this instead. This isn't our goal*." Even by simply adjusting the tone of the voice and by saying "*we*" instead of "*you*" there is a change in the internal dialogue to make it kind, reassured, helpful and supportive rather than penal and disciplinary. Thus, in turn, via CMT, may aid impulse control to produce the significant increase in mean DD scores as seen in the CMT group.

Participants in both groups completed the DD task on three separate occasions and so it is likely that participants became aware of how to achieve higher scores on the task with each attempt. However, this does not explain why participants in the CMT group achieved significantly higher scores than RM group participants at post-intervention. Delay Discounting, in addition to NU, was also found to be a risk factor for psychological dependence to painkillers (Table 4) and other drugs (Bickel & Marsh 2001). These findings suggest that not only are cognitive facets of impulsivity a risk factor for addiction but behavioural impulsivity, as quantified by the DD task, is also a risk factor and mirrors findings in the existing literature (Bickel et al., 1999; Baker et al., 2003; Kirby et al., 1999; Petry, 2001, Madden et al., 2003).

6.9.3.3. Self-hate, Self-inadequacy and Self-reassurance

A notable outcome was that within 21 days (post-intervention) participants in the CMT group had developed their skills in self-reassurance to be significantly better than the RM group. Within groups analysis for the CMT group revealed a significant increase in mean scores from Base-line to Post-intervention although this effect was not maintained at follow-up. Mean scores for RS were similar to a non-clinical (vs. clinical) population sample in other studies (M = 20.27; SD = 5.77 vs. M = 10.68; SD = 6.51; Baião et al., 2015).

For IS Scores, only at Follow-up did there exist a significant difference between groups with CMT group showing higher mean scores, although no significant differences occurred *within* the CMT group from base-line to post-intervention, base-line to follow-up or post-intervention to follow-up i.e. their mean scores were insignificantly different when comparing the mean scores throughout the study. These results could be due to the mean values for IS in this study sample at base-line (CMT: M = 13.56; SD = 6.53; n = 39 vs. RM: M = 13.03; SD = 6.53; n = 40) being lower than those observed elsewhere in the scientific literature where

Baião et al., (2015) state that IS scores in clinical patients had higher scores than non-clinical patients (M = 27.47; SD = 7.51; n= 887 compared to M = 17.72; SD = 8.29; n = 171).

Mean scores for HS at baseline in both CMT (M = 4.03; SD = 3.38) and RM group (M =2.85; SD = 3.38) were similar to non-clinical samples (M = 3.88; SD = 4.59) reported elsewhere in the scientific literature (Baião et al., 2015). An important observation is that (a) mean HS scores were significantly different between groups at post-intervention and at follow-up and (b) those in the CMT group showed significant improvements by having significantly lower scores from base-line to post-intervention and again from base-line to follow-up.

To summate, these results show that engaging with the CMT intervention results in significant improvements in increasing self-reassurance and decreasing self-criticism. Therefore, CMT group participants can be described as better at self-soothing than RM group participants when the intervention concluded. In concordance with previous research evaluating efficacy of CFT and CMT there was the decline in mean HS scores in response to a CMT intervention which emphasises participants had distanced themselves from a threat-based mentality to a more secure and self-soothing mentality (Gilbert & Proctor, 2006). The significant increase in RS scores at post-intervention within the CMT group is also an encouraging outcome and at this stage we can only speculate that participants were revising their relationship with their thoughts and being significantly better at self-soothing and, perhaps a follow-up study with qualitative analysis would be needed to investigate this directly.

To conclude we see several risk factors have been reduced at post-intervention in those who engaged with the CMT intervention and not in those who engaged with the relaxation music. These include a significant reduction in daily painkiller consumption, painkiller misuse, cognitive (negative urgency) and behavioural impulsivity (delay discounting) and painkiller dependence. Accompanying these significant reductions was a significant increase in self-reassurance. The implications these findings are discussed in detail below.

6.9.4. Reducing painkiller dependence: potential mechanisms

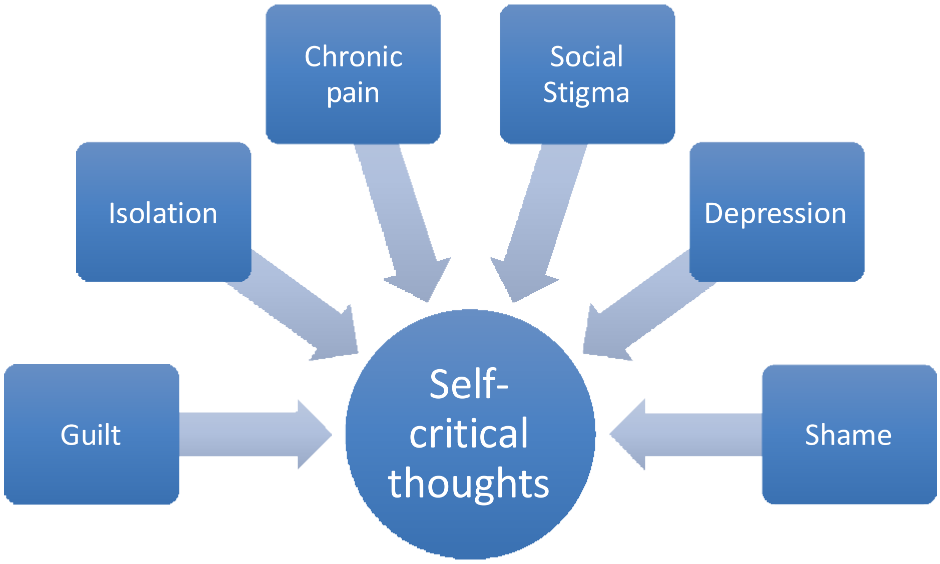
We begin to turn our attention to *how* the reduction in painkiller consuming behaviours and dependence might have occurred. Participants in the CMT group engaged with the psycho-education syllabus and the CMT software. The psycho-education syllabus included a major focus on CMT and Self-reassurance in addition to mindfulness and their roles will be discussed below.

6.9.4.1. The role of CMT towards reducing painkiller dependence

When one experiences negative affect, it can increase the likelihood that one will act impulsively (Negative Urgency; Carmody et al., 2007). Negative affect can arise within an individual via external and/or internal sources. A major contributing internal source of negative affect is the internal dialogue we have with ourselves or “the way we talk to ourselves”. This internal stream of thoughts, which we all possess, carries a “tone” which can be loosely classified as being either self-reassuring or self-critical. The dominant tone of our thoughts can become self-critical for a variety of reasons, which include shame, guilt, social stigma and isolation to name but a few (Fig. 43). All of which are prominent amongst those living with chronic pain (Waugh et al., 2014).

If an individual experiences *consistent* flows of self-critical thoughts (as measured by IS and HS scores) then this could produce a state of negative affect within the individual and it is this state which could trigger negative urgency causing certain individuals to act impulsively (i.e. prompting the individual to consume more painkillers). This could be detrimental as results from study 1 have shown negative urgency to be a progressive risk factor for painkiller dependence (Table 5; Fig. 43). Moreover, the experience of negative affect itself is known to trigger drug-seeking behaviours (Brandon et al., 1994). Therefore, it is vital that one learns to change the way one *responds* to negative affect (i.e. in a more self-reassured way) as it can trigger NU which has been shown to be a risk factor for addiction to prescription painkillers (Table 5) and other drugs of abuse (Torres et al., 2013).

Figure 43 Stimuli for Self-critical thoughts



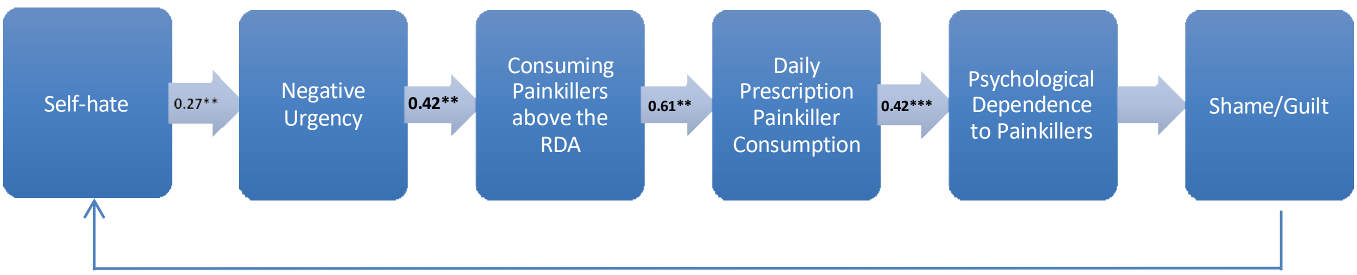
It has been reported that the repeated consumption of painkillers, or indeed other drugs of abuse, can occur in order to alleviate feelings of negative affect (Cervone et al., 2007). Opioid analgesics, such as prescription painkillers, are perfectly suited to achieve release from negative affect, albeit temporary and with negative consequences once the grip of addiction is formed (Wasan et al., 2005).

Therefore it was proposed that self-critical thoughts, as demonstrated by elevated scores on Self-hate, promote and progress painkiller dependence by producing a state of negative affect in the individual which heightens activation of NU (r = .273, p < .02; at Baseline) which in turn promotes drug consuming behaviours (r = .417, p < .01; at Baseline) and subsequent dependence (Fig. 32) by increasing daily consumption of prescription painkillers (DPPP). Interestingly, at post-intervention, the correlation between Self-hate and NU had been reduced in CMT group participants (r = .284, p = .08) and during follow-up (r = .31, p = .06). Evidence from the field of Neuroscience also lend hand to this relationship between HS and NU where Heatherington et al., (2011) and Zhao et al., (2017) show that NU originates in the same neural region (dorsolateral prefrontal cortex) that activates thoughts of self-hate, as shown by fMRI studies (Longe et al., 2010).

When examining the correlations between study variables in the CMT group, an interesting observation was that mean scores at baseline for NU showed significant positive correlation with DPPC (r = .281, p < .05). However, at post-intervention the correlation was no longer significant (r = .128, p > .05). Simultaneously, at post-intervention RS scores within the CMT group had increased significantly from base-line and showed a significant negative correlation with NU (r = -.224, p <.05) and LDQ (r = -.336, p <.05). Thus, it is plausible that RS could act as a protective buffer against the sequence of events leading to painkiller dependence.

In regard to the role of CMT in reducing painkiller consumption and addiction it could be seen to play an indirect role whereby the main input of CMT is providing a healthier, more self-reassuring response to negative affect and so offering less opportunity for NU to arise in the first instance. This could have been achieved by the CMT software, which aimed to substitute self-critical thoughts with self-reassuring thoughts.

Figure 44 The addictive loop of Self-criticism



Any wilful attempt at modifying a behavioural response to negative affect would in turn reduce manifestation of negative urgency. This would prove to be highly beneficial as negative affect, NU and impulsivity in general are antecedents for drug consuming behaviours and consequently, development of a substance use disorder (Brandon et al., 1990). NU has been shown to be a risk factor for heightened painkiller consumption in chronic pain patients (Martel et al., 2014). Therefore, in order to prevent reaching the stage of dependence it would be highly relevant to reduce feelings of negative affect in the first instance. The CMT intervention aims to fulfil this need by fostering self-reassurance and endorsing self-soothing which protects and buffers against emotional distress and stimulates well-being (Gilbert, 2005; Neff, 2003). At baseline there was a significant negative correlation between RS and NU (r = -.486, p = .02) and at post-intervention (r =-.326, p = .04) and follow-up a negative correlation was found but not significant. These results reflect those observed by Petrocchi et al., (2018) who showed that high levels of self-reassurance buffered self-criticism and depressive symptoms within study participants which support the buffering hypothesis.

Furthermore, any attempt to self-regulate can be limited by negative emotions (Baumeister & Heatherton, 1996). Living with chronic pain involves frequent visits to pain management teams, a plethora of medical tests, rehabilitation regimens and healthy lifestyle changes which can be stressful and challenging to maintain. Those who are better able to manage negative emotions are better equipped to regulate health-promoting behaviours than those who become overwhelmed by negative affect. Emotional regulation is a principal component of self-compassion (Neff, 2005) and it can be a drain on the ability to self-regulating (Baumeister et al., 1998). Studies have shown that participants who suppressed or amplified their emotions had less self-regulatory resources available for a challenging task, however those who score sufficiently high on self-compassion do not suppress their emotions (Neff et al., 2007) and instead experience their negative affect in a more mindful and less reactive manner thus not depleting their self-regulatory resources in trying to manage negative emotions. Because of this they then have sufficient resources available for other self-regulatory tasks e.g. adhering to the prescribing schedule of painkillers and not consuming more than the RDA. Self-regulation appears to have improved in the CMT group as shown by the significant rise in DD scores.

6.9.4.2. Reducing painkiller dependence - The Three Circles Model

Empirical evidence has shown that when one experiences distress and the resulting emotional fluctuations they may resort to the consumption of addictive substances in order to alleviate the distress (Khantzian, 1997; Weiss et al., 2015). This is commonly seen in those who consume drugs; alcohol and cigarettes being typical examples. As an example, a self-critical individual (High IS and/or High HS) who has been abstaining from smoking may receive harsh criticism from a colleague and resort to smoking in order to calm themselves. CFT and CMT have been shown to reduce SUD promoting behaviours such as cigarette smoking (Kelly et al., 2010). In those living with chronic pain the consumption of painkillers would be a relevant example. In times of distress, the threat protection system would become active and generate feelings of wanting to protect the individual from pain and keep it safe and pain free. In turn this would feed into the drive system and generate feelings of "wanting, pursuing and consumption" being targeted towards painkiller consumption in order to alleviate the pain and distress. When the painkillers have been consumed and their effects begin to take place and the individual is pain free then the soothe system may become active and generate feelings of the desired outcome i.e. safe, calm, warmth and pain free. This loop of positive reinforcement is clearly detrimental in some individuals as their strategy to become pain free is to continually consume painkillers. Painkillers by their very nature possess addictive compounds and so if one were to continually engage in such behavior then substance dependence will quickly ensue.

A study by Phelps et al., (2018) showed that when participants are classified as either Low, Medium or High for risk of developing a SUD then those who were classified as low risk had higher scores on self-compassion and differed significantly to those classified as high risk. The research authors conclude by acknowledged the benefits of compassion in reducing a SUD.

Gilbert (2005; 2009) states that a chief aim of CMT is to help balance the three entities within the three circles model. Taking the above into consideration, if it were possible to create an alternative way (opiate free) to stimulate the soothe system (e.g. by imagining receiving compassion from a compassionate other; compassionate imagery) then the need for excessive painkiller consumption would not be necessary and dependence would be reduced or eliminated. This statement is formulated from empirical evidence in that stimulating the soothe system will result in release of OXT which in turn can decrease analgesic tolerance and withdrawal (Kovacs et al., 1985; Sarnyai & Kovacs, 1994) and reduce drug seeking behaviors (Carson et al., 2010; Cox et al., 2013; Zhou et al., 2014). Demirci et al., 2016 also showed that impulsivity scores were significantly higher and serum oxytocin levels were significantly lower in a sample of participants with ADHD vs. non-ADHD participants (52.5 ± 18.1 and 37.62 ± 9.0, respectively, $p < .001$) and low levels of OXT are correlated with high scores of Impulsivity. Plessow et al., (2016) showed that after a single dose of OXT, subjects proactively exert control over their behavior in a behavioural task of impulsivity (go/no-go) and had longer reaction times. Moreover, self-administered OXT has been shown to reduce methamphetamine and cocaine-seeking behaviours (Carson et al., 2010; Cox et al., 2013; Zhou et al., 2014) which may explain the reduction in DPPC and RDA scores.

Additionally, reducing the drive system, a decision-making system, could also be a potential target particularly if the majority of decisions made are impulsive and not optimally constructed. Results from study 1 showed strong significant correlations between impulsivity and severity of dependence to painkillers and consumption of painkillers. If those with high levels of impulsivity also had a hyperactive/highly responsive drive system, then they may be more prone to impulsive behaviors and impulsive decision making. Therefore, if the soothe system was to become more engaged then this could dampen the drive system should the drive system be deemed responsible for impulsivity and subsequent psychological dependence to painkillers.

Furthermore, should the threat and protection system be constantly on high alert then a great majority of signals entering the mind would be perceived as threatening. However, if one were to better filter these incoming signals (by mindfulness; SRB) and see them as they are rather than reflexively responding to them then this system would feed less signals into the drive system. One such strategy to manipulate the entities in the three circles model was via CMT exercises and engaging with the CMT intervention.

The contents of the CMT intervention consisted of two parts and include the (1) CMT Psycho-education syllabus and the (2) CMT software. The hypothesised effects of these components are discussed below in section 7.2.

6.9.5. Retention rates, Acceptability and Feasibility

Rates of retention for this study were generally good. After randomisation, 1 participant from the CMT group dropped out after giving data at baseline thus 97.4% of participants provided data for the entire duration of the study. The RM group had an 87.5% compliance rate with 5 participants dropping out of the study after giving data at baseline.

The high rates of study retention could be associated with changes made to the web-platform after suggestions were made from those who participated in the accompanying pilot study which would explain high acceptability. While acceptability was not directly measured, the high rate of retention and examination of daily logins by participants would suggest participants found the web-platform easy to navigate and acceptable to use.

6.9.6. Clinical implications

The results from this study have shed light on the application of a psychotherapy being delivered from the internet for those who are susceptible to painkiller dependence. Participant's self-report measures present them as being self-critical (threat focused system) however when interacting with the CMT intervention they were proficient in the skills of CMT and were able to develop kindness and self-reassurance (activation of the soothing system), which would foster a healthier means for affect regulation. This would have given participants a tool in which to master their emotions and the intervention designed was likely to be a key facilitator for this. The study also provides data that those with chronic pain do suffer from self-criticism that needs to be addressed in treatment programs. It should also be noted that participants in this study, did not differ much from the general population in terms of scores on IS, RS and HS (IS: 13.55 vs. 12.32; RS: 17.42 vs. 23.85; HS: 3.79 vs. 2.70; Gilbert & Irons, 2006).

The web-based CMT intervention provided a novel means of disseminating therapy worldwide to an under-studied population and to those unable to leave their homes due to immobility caused by their chronic pain condition. CMT presents itself as a fresh and innovative vector for theorising psychological maladies in those with chronic pain as it includes neuroscientific and neuropsychological facets in its model of affect regulation. This model translates well for those with chronic pain and with substance use disorders. Therefore, CMT with its acknowledgement of neurobiological importance of affect regulation can aid the course of development when trying to comprehend the association between addiction and impulsivity which are often absent in other leading psychotherapeutic models.

Regarding the CMT intervention itself there are a few issues upon which to direct our attention. Primarily, shame, guilt, a sense of not belonging, feeling purposeless and self-hate are threatening in nature. Due to this nature, an individual's threat system may become hyperactive resulting in resistance. Reducing or combatting resistance in a therapeutic setting is paramount in reducing self-criticism. In addition to this, the CMT intervention provides an organised and controlled methodology, which is an asset when trying to achieve such a goal.

6.9.7. Conclusions and Future Directions

The clinical implications of treating addiction by reducing impulsive behaviors are of great benefit as are the socioeconomic advantages. Thus, the development of efficacious treatment options for impulse control disorders is critical. Compassionate Mind Training may prove to be a useful instrument towards treatment of such disorders, and so further research and study of CMT-based approaches as a cognitive therapy is warranted.

Over the past century, much has been discovered about the addictive process and its underlying neurobiology (Goldstein et al., 2009; Kalivas & Volkow, 2005). From these findings, psychological models have been put forward that have been instrumental in the development of novel treatments that directly target core components of this process. These models show remarkable similarities to ancient models aimed at describing the causes of human suffering. Modern treatments, such as CMT, that are based on these Buddhist models are beginning to show preliminary efficacy in the treatment of addictions and may be doing so through changing one's relationship to core addictive elements such as craving. By adopting a lifestyle structured around CMT one may manifest their newly learned skills behaviorally, in that individuals may develop new habits such as monitoring for unskillful thought processes and automatic behaviors and objectively observing them rather than being "sucked in" by them and smoking, using prescription painkillers, or engaging in other unhealthy behaviors: the more individuals are able to decouple craving from behavior through practicing mindfulness, the less they foster the addictive loop (Fig. 44), leading to the later dying away or cessation of craving itself. Ultimately, with practice, this may lead to more adaptive choices with concomitant decreases in stress and suffering.

The field of CMT for the treatment of addictions is a young one. As highlighted in this chapter, current work is promising but preliminary, and models developed are only useful if they provide tangible and testable hypotheses and, more importantly, inform and improve the delivery of treatment. CMT may, at least in theory, confer advantages over other approaches for addictions, especially in cases of comorbid disorders and when individuals are particularly stuck in negative (or positive) reinforcement loops. Going forward basic caveats, such as the use of active comparison conditions for randomization, therapist training, and safety issues that uniquely relate to these populations (e.g. trauma history), will continue to need attention (Lustyk et al., 2009). For example, further studies are needed to rigorously compare CMT to "gold-standard" treatments to determine if it provides any additional benefit with regards to abstinence rates and reduction of painkiller consumption.

With working models of addiction in place, several questions can now be addressed by researchers in the field to both test and improve the models, and to inform treatment:

(1) As most studies of addiction thus far have been conducted using different treatment protocols, is there a single, manualised delivery of CMT that can be agreed upon that can be vetted and used for standardized comparison across sites? Can this be developed with input from clinicians who are "in the trenches" to ensure that CMT can be readily and feasibly disseminated, because current standards (e.g., 8-week linear frameworks) may be suboptimal from a patient retention and clinical delivery standpoint (Brewer et al., 2009). This will allow for a vastly accelerated and iterative process for establishing an evidence base, optimising delivery, and maximising clinical effect.

(2) Is it time to separate CMT from other cognitive and behavioral frameworks (e.g., disentangle CMT from Relapse Prevention), such that we are better able to measure components that are CMT specific?

(3) Are there accepted laboratory and/or other behavioral measures that can be uniformly used across different substances? For example, measuring cue reactivity using dot probe and/or substance-specific Stroop tasks pre- and post-intervention and the relationship of these tasks to subjective craving and substance use may test their hypothesized relationship in proposed models. Also, measuring resting-state functional connectivity or specific relationships between regions of the brain that are implicated in self-identity (PCC) and self-monitoring (dACC) and their relationship to CMT (and home practice) may test whether these networks are indeed changed with training, as hypothesized by these models (Frewen et al.,

2008a; 2008b). Given the theoretical promise of CMT, its early supporting evidence, and the convergence of modern behavioral and brain probes, we hope to see hypothesis-driven and collaborative efforts emerge to rigorously test this “new” treatment over the next few years that will show tangible improvements in the lives of those who suffer from substance use disorders. Future studies will aim to address these points and are discussed within Chapter 14.

To summate, although the literature regarding CMT based treatments is at a nascent stage, the results are promising. Future directions in the field must concentrate on isolating the specific effects of CMT skills beyond the more global effects of cognitive therapy. The cultivation of self-reassurance appears to be a useful way in which to attenuate emotional reactivity and the treatment of impulse-related disorders and SUDs may depend upon such techniques.

Chapter 7. General Discussion

7.1. Summary and integration of findings from all studies

This section will provide a summary of findings from the three studies and explain how they are integrated with each other. Implications of findings will be explored and related to relevant fields of research as well as theoretical and empirical contributions.

7.1.1. Summary of major outcomes from Study 1

Study 1 aimed to ascertain the level of psychological dependence to painkillers within the study sample to investigate the role of Impulsivity towards (a) psychological dependence for painkillers and (b) Self-reassured (RS), Self-hate (HS) and Inadequate-self (IS) and finally to investigate the roles of self-criticism (IS and HS) and self-reassurance towards psychological dependence to painkillers. It was hypothesised that there will be some degree of dependence to painkillers occurring in this sample as the problem is widespread and reported in the scientific literature (Elander et al., 2014). It was also hypothesised that some facets of impulsivity would be contributory factors towards dependence as this again has been widely reported in the scientific literature (Madden et al., 1997; Reynolds et al., 2006; Kirby & Petry, 2004). The contributions of RS, HS, IS to painkiller dependence is yet unknown in this sample population as is the relationship they have with facets of impulsivity, both cognitive and behavioural aspects.

Of note, correlation analysis revealed LDQ scores (a measure of psychological dependence for painkillers) to show significant positive correlations with DPPC, IS , HS, NU and LOPERSEV. NU showed significant positive correlation with HS and IS. Significant negative correlations were found between RS and NU, HS, PF and LDQ. Here we begin to see an emerging pattern of correlations between study variables where those belonging to the realms of impulsivity and self-criticism had significant positive correlations with LDQ while self-reassurance had significant negative correlations with those very same variables and with LDQ itself. Impulsivity has been well researched as being a risk factor for developing a SUD (E.g. Reynolds et al., 2006) and has been extensively associated with the initiation phase of drug dependence as outlined in chapter 1 of this thesis. Following this, a hierarchical multiple linear regression (stepwise) analysis with 5 blocks was performed with LDQ as the dependent variable. Block 5 contained three interaction terms between PF and HS, IS and RS. These three interaction terms were all significant. This allowed for a moderation analysis to be performed with HS, IS and RS as moderators of the effect of PF on LDQ. A Johnson-Neyman (JN) analysis revealed an effect of PF on LDQ scores when RS scores were between 2.89 and 29.91 (Fig. 14). For HS and IS, the JN analysis showed that when HS and IS increased then the effect of PF on LDQ is also increased but is only deemed significant when mean HS score were greater than -0.9 and when mean IS score were greater than 5.4.

Study 1 contributed to the existing empirical data as the results echo the findings that facets of impulsivity are correlated with dependence to addictive substances and also that they could function as risk factors (Ersche et al., 2006; Verdejo-Garcia & Perez-Garcia, 2007; Madden et al., 1997; Clark et al., 2006; Nielsen et al., 2012; Robles et al., 2011). Study results also add new theoretical data and provide avenues for future research as this is the first time, to our knowledge, that self-criticism (IS and HS) and RS have been investigated for their relationship with impulsivity and substance dependence. These findings allowed for studies 2 and 3 to be implemented so that the relationship between self-criticism/ RS and painkiller dependence could be further explored.

The study also showed that self-criticism (IS and HS) are risk factors for painkiller dependence which mirrors existing empirical findings (Rodrigues et al., 2014) and theoretical models of addiction which claim personality states can be vulnerability markers for SUD (Kotov et al., 2010). Those with chronic pain often live in isolation (Mort & Philip, 2014) those in isolation often harbour feelings of shame (Hartling et al., 2004) and guilt (Ferguson & Crowley, 1997). These are risk factors for addiction and are often reported by those with SUD themselves (Hien et al., 2005).

The moderation analysis adds to the theoretical model on Self-compassion (Three Circles Model; Gilbert, 2005). When self-criticism (IS and HS) was high then the chances of developing a SUD was also high in the presence of high Pain Frequency (PF). Also, when participants scored high on RS then the likelihood of developing psychological dependence in the presence of high PF was low. Thus, those high on RS are able to move away from a threat-based mentality (thought to be served by Dopaminergic/Opiatergic neural systems) to a more compassionate, reassuring and soothing mentality (thought to be served by Oxtocinergic neural systems, which dampen Dopamingergic/Opiatergic neural pathways) which allows participants to better manage emotions which would otherwise promote the initial stages of drug consumption (Nestler, 2013).

As the area of painkiller dependence is relatively new, these studies can allow for further research. Additionally, the findings bolster the wider literature of addiction studies in that the meta-cognitive risk factors identified in this study need to be taken into account when therapeutic interventions are devised and administered for those with psychological dependence to painkillers. More so, the study allows for future research that utilises CMT as a means of targeting psychological dependence to painkillers by strengthening self-reassurance and reducing self-criticism (IS and HS) and affect-driven impulsive traits such as NU. This may be of great value to practitioners who work in the substance misuse field and may want to apply CMT to patients who do not respond to more conventional treatment methods (e.g. Cognitive Behavioural Therapy).

To summate, results from this study showed various levels of psychological dependence to painkillers was present in the sample population and that study variables had significant correlations with LDQ scores which may influence the development of a SUD. Participants living with chronic pain may use opiates, to which they often have easy access, to help cope with situations when negative affect becomes too much to handle (Cervone et al., 2007). These findings prompted the onset of phase 2 which aimed to reduce painkiller dependence via a web-based CMT intervention. Prior to study 3 a pilot study (Study 2) was conducted to assess acceptance and feasibility.

7.1.2. Summary of major outcomes from Study 2

The aim of study 2 (pilot study) was to assess feasibility/acceptability of a web-based platform that delivered a version of a CMT intervention to those who consume painkillers and who live with chronic pain. In addition, the aim was also to study how appropriate and realistic the study's process and resource management would be for conducting a RCT. The web-platform was an interactive, information rich web-platform that gathers participants' data via questionnaires, behavioural measures and delivered a CMT based intervention. The web-platform was fully automated and so did not provide the participants with any contact to a therapist. The web-platform was extensive and delivered an evidence-based psycho-educational material built on a solid theoretical framework based on CMT (Gilbert, 2004; 2005).

When conducting the feasibility investigation, the important parameters for a planned, randomised controlled trial (RCT) were identified, adjusted, and further developed to improve the chances of success in a larger, costly (time and/or money) study. Feasibility studies such as this aid in the recognition of what needs to be adapted, improved, added or removed regarding the intervention as well as regarding the research methodology (Thabane et al., 2010). The justifications for performing this acceptability and feasibility study were numerous, including the ability to analyse the study process, resource management (e.g. the study participants' need for support), and evaluate the study's safety and effect on outcome measures (Thabane et al., 2010).

A convenience sample of 6 participants were recruited from adverts placed in social media outlets related to chronic pain. Participants were first screened for eligibility and then randomised into one of two groups (CMT and RM). All participants completed the study with no attrition. Those in the CMT group engaged with the CMT intervention that consisted of watching psycho-education videos based on CMT with the aim of building self-reassurance; engaged with a CMT software that asked participants to supply self-critical thoughts into a database and then reply back to these statements using Self-reassurance when their personal self-critical statements appeared on the screen and they also engaged in a behavioural measure of impulsivity (DD). RM group participants did not engage in any CMT related activities but listened to relaxation music instead. Both groups completed a series of self-report measures as in study 1 and the behavioural measure of impulsivity (DD Task). Measures were taken at three time-points (Baseline on Day 1; Post-intervention on Day 21; Follow-up on Day 28). However, this study was to assess feasibility and acceptability so results from these measures were not analysed further. Rather, a questionnaire to gather participant feedback at post-intervention was administered to those in both groups and data from this was analysed with the hope of planning a larger scale online RCT with the web-platform plus suggested improvements. Suggested improvements included:

1) Personal online pain diary for participants to record their private thoughts
2) Dynamic personalised timetable for ease of knowing what to do on each day
3) A vibrant colourful layout
4) Addition of nature-themed photos in the psychoeducation videos.

Limitations included the small sample size although, no consensus has been reached on what the minimum number of participants should be (Hertzog, 2008). The second limitation was that there were a large proportion of female participants (66.67%) which makes generalisability an issue.

Evaluation of acceptability and practicability of a web-based intervention on a small scale was advantageous as this could help detect potential problems and concerns that can be corrected to increase success rates in a large scale RCT that may cost more and take more time to produce. Thus, in the large scale RCT, the effect(s) of a previously tested CMT intervention would be the focus as concerns related to the web-platforms acceptability and practicability have already been investigated and amended. YouSoothe.com was found to be well regarded in terms of acceptability and feasibility as most responses to feedback questions had a mean well above the set cut-off score of 5. The study process and resource management (psycho-education videos and explanatory materials) were also considered to be feasible. However, suggestions from study participants exposed ways in which the web-platform could be further improved for increasing the chance for success in a large-scale RCT. The criteria for assessing acceptability were set prior to study onset which can be regarded as a strong point as the results may be less biased. The feedback obtained was applied to the web-platform and paved the way for a RCT with a larger participant group (i.e. Study 3).

7.1.3. Summary of major outcomes from Study 3

Study 3 took the same concept as study 2 with the additional amendments made to the web-platform as obtained from participant feedback. This study also sought to recruit a larger sample size than in study 2. The major focus of this study was to investigate the effects of the CMT intervention on study variables, particularly the levels of painkiller dependence, and the associations between study variables over time. Recruitment process, study procedures, inclusion/exclusion criteria, self-report measures, behavioural measures, RM music, CMT intervention, CMT psycho-education videos were used exactly as in study 2. The procedures that participant in each group underwent are outlined in section 6.5.5. above.

This study attracted a large number of participants from all over the globe (n=442) where n=255 were excluded during the screening procedure for not meeting entry criteria and n=108 declined to participate. Seventy-nine participants were randomly assigned into one of two arms (CMT group, n= 39; and RM group, n = 40). At post-intervention, 1 participant withdrew from the CMT group and 5 participants withdrew from the RM group. At follow-up no further attrition occurred in either group leaving a sample of n=38 in the CMT group and n=40 in the RM group. Thus, the rate of attrition can be regarded as very good and could be attributed to the small time-scale of the study as well as the application of changes made via feedback from the pilot study.

Within both groups some participants provided data at baseline but did not continue to follow-up. This data was used to allow for Intent-To-Treat analysis using the Last Observation Carried Forward methodology (Streiner, 2014). This design allowed for a two-arm prospective randomised controlled trial (RCT) to assess the effects of a Compassionate Mind Training (CMT) intervention on study variables. This study had a between-groups and within-subjects design. Groups had two levels (CMT – experimental group; RM – control group). One within-subjects factor, *Time*, had three levels (Baseline, Post-intervention and Follow-up). CMT group participants engaged with Psycho-education videos and the CMT software while RM group participants listed to theory-neutral Relaxation Music.

Major outcomes of the study were that CMT group participants showed significant reduction in (1) psychological dependence to painkillers (2) RDA scores (painkiller misuse) and (3) DPPC (daily consumption of prescription painkillers). Significant correlations were observed between DPPC and RDA with LDQ scores (r = .419, p = < .001 and r = .377, p < .001, respectively) suggesting increased consumption leads to higher propensity for developing psychological dependence. RDA and DPPC scores decreased significantly from baseline to post-intervention in those who engaged with the CMT intervention. This reflects empirical evidence from other studies in which patients with an addiction showed significant reduction in consumption after engaging with a CMT intervention (Kelly et al., 2010).

The study also investigated facets of impulsivity as these are well-established risk factors for developing SUD. Within groups analysis revealed mean Lack of Perseverance (LOPERSEV) scores in the RM group to be significantly higher at post-intervention and at follow-up in comparison to baseline. This indicates RM group participants to become *less* persevering over time while those in the CMT group had stable levels of perseverance over time. These findings are consistent with the literature which states compassion-based interventions promote perseverance (Riley et al., 2015) and "being in the present moment" to focus on a given task and bestows a greater sense of goal-achievement in recipients of such an intervention (Breines & Chen, 2012). SRB exercises were practiced daily by the CMT group and such exercises promote attention on the present moment.

Negative Urgency, an affect driven facet of impulsivity is one of the most well-researched components of impulsivity and is known for its progressive role towards developing SUD and these results reflect such findings (Martel et al., 2014; Vest et al., 2016) in this study and in study 1. This is shown by its significant correlation with DPPC (r = .614, p < .01) and RDA (r = .417, p < .01). Thus, it seems NU promotes increased consumption of painkillers when a participant is experiencing negative affect. These results support the notion that increased consumption of painkillers would increase the probability of developing a SUD (Pang et al., 2014; Verdejo-Garcia et al., 2007; Tragesser et al., 2009; Zapolski et al., 2009; Albein-Urios et al., 2011). Other noteworthy findings show NU to significantly reduce in the CMT group from base-line to post-intervention and between post-intervention and follow-up. Significant differences in scores were observed between groups at both post-intervention and at follow-up. This suggests that engaging with the CMT intervention can reduce the effects of NU over time. Behavioural impulsivity, as well as cognitive impulsivity outlined above is also a well-known risk factor for developing a SUD. Behavioural impulsivity was quantified in participants using the DD task. The rationale for including this measure was that it would complement the cognitive aspects of impulsivity and also that DD is a well-researched component of impulsivity known to promote SUD to common street drugs (Ohmura et al., 2005; Odum et al., 2006; Petry et al., 1998 & 2004) and to opiates (Madden et al., 1997; 1999; Odum et al., 2000). A high score showed a more self-controlled, or rational choice, and a low score implies an impulsive choice. Thus, the progressive rise in scores obtained in the CMT group participants showed that they became less impulsive over time and more self-regulated (Cherek et al., 1994; Miller & Brown, 1991) over time whilst engaging in the CMT intervention. This trend was not observed in the RM group. Furthermore, a significant increase in mean DD scores was seen in the CMT group from baseline to post-intervention and between base-line and follow-up. Significant differences also occurred between groups at post-intervention. Thus, the findings for NU and DD reflect theoretical knowledge observed in the scientific literature (Bickel et al., 1999; Baker et al., 2003; Kirby et al., 1999; Petry, 2001, Madden et al., 2003) and provide new empirical evidence in that they are also linked to painkiller dependence in those with chronic pain.

This study was quite distinctive in that it investigated the role of Self-criticism (IS and HS) and Self-reassurance for their roles towards painkiller dependence. Major observations were that Self-reassurance increased at post-intervention such that it was significantly higher for CMT participants in comparison to RM group participants. Within CMT group participants, but not RM group participants, there was a significant increase in mean RS scores from baseline to post-intervention suggesting CMT group participants became more proficient in self-soothing. Noteworthy results from a correlation analysis within CMT group participants revealed mean scores at baseline for NU to have a significant positive correlation with DPPC (r = .281, p < .05) which did not show a significant difference at post-intervention (p > .05) which could suggest attenuation of the influence NU has on painkiller consumption after one engages with CMT (i.e. increase in RS). Additionally, at post-intervention RS scores within the CMT group displayed a significant negative correlation with both mean NU scores (r = -.224, p < .05) and mean LDQ scores (r = -.336, p < .05) scores. Thus, it is conceivable that RS could function as a protective buffer (Noorbala et al., 2013) against known risk factors for painkiller dependence.

Mean IS scores seemed unaffected despite which group participants were placed in. For the CMT group there was no significant change in scores across any combination of time points. Equally, between groups analysis showed no significant differences to occur at any time point. This could be since baseline measures for all study participants were much lower than observed in the literature (Baião et al., 2015) Mean HS scores were significantly different between groups at post-intervention and at follow-up and participants in the CMT group showed improvements by having significantly lower scores from base-line to post-intervention and again from base-line to follow-up. Thus, engaging with the CMT intervention results in significant improvement in RS and significant attenuation of Self-criticism and so those in the CMT group can be described as being better at self-soothing and moving away from a threat-based mentality as described by Gilbert & Proctor, 2006.

Combined, these results support empirical research as it mirrors results such that (a) engaging in CMT interventions increases self-reassurance and reduces self-criticism (Gilbert & Proctor, 2006); (b) reduces consumption of addictive substances (Kelly et al., 2010); (c) those scoring high on RS at post-intervention were then better able at activating the soothe system (Gilbert et al., 2012) and so were better abled at applying self-reassurance on themselves which may function as a protective buffer against developing a SUD (Noorbala et al., 2013). This was also shown in the moderation analysis from Study 1 which showed that within a specified range of mean RS scores there is a reduction in the impact of pain frequency (PF) on painkiller dependence (LDQ). Novel findings were reduction in facets of impulsivity (i.e. NU, DD, LOPERSEV).

Theoretical and empirical contributions are like that of Study 1 in that they add to models of addiction (Nestler, 2013) and models of Self-compassion (Gilbert, 2005). Results from the study add their theoretical implications to the field of addiction, personality traits and self-compassion. Those with chronic pain often live in isolated conditions, carry the burden of shame, guilt and social stigma and are in continual bouts of chronic pain. Each of these serve as vulnerability markers for substance dependence. It is thought that a certain population of chronic pain patients may develop a self-critical (as seen by HS scores) inner voice over time due to such conditions. This is turn may activate NU. NU is well established in its role for the initiation phase of drug consumption, which may lead to developing a SUD over time should consumption continue (Smith et al., 2016). NU is “activated” when experiencing negative affect. Consumption of analgesics have been used to alleviate oneself from feelings of negative affect (Cervone et al., 2007). Heightened consumption of painkillers, as shown by elevated scores on DPPC and RDA, will likely lead to SUD (LDQ scores). This is depicted diagrammatically in Figure 44. To remedy this series of events, applying CMT with the aim of reducing HS scores and increasing RS scores may reduce painkiller dependence although further research is required to fully answer this. Increase in RS has already been shown to act as a protective buffer (Noorbala et al., 2013) and many studies show engaging in CMT reduce self-critical thoughts (Gilbert & Proctor, 2006).

CMT and compassion-based therapies permit for better emotional regulation (Neff, 2005). This is useful for those who score high on NU as NU is emotionally driven. Furthermore, difficulties with emotion regulation can have adverse effect on self-regulating behaviour and individuals suppressing or intentionally increasing their emotions did not fare well on tasks that required self-regulation (Baumeister et al., 1998). Thus, being better able to manage emotions may reduce the frequency of NU being activated and subsequently initiating the chain of events that lead to painkiller dependence. Neff et al., (2007) has shown that those who score high on RS do not suppress their emotions and so are better able to regulate their behaviour (e.g. not overconsuming painkillers). The rise in RS scores and DD scores in CMT group participants appears to show a significant improvement in self-soothing and self-regulation at post-intervention.

Other theoretical contributions include aligning these study findings to The Three Circles Model (Gilbert, 2005). Gilbert states the major aim of CFT and CMT is bring about balance between the three circles (Fig. 5). CMT has been shown to increase self-reassurance and self-soothing (Gilbert & Proctor, 2006) by increasing activity in the Soothe system and reducing subjective distress by reducing activation of the Threat System. In times of distress (e.g. High Pain Frequency; Figs 14-16) the Threat system becomes activated to bring about feelings of needing to protect the individual from threat (internal and/or external) and keep oneself pain free. Subsequently, the Drive system becomes active and produces feelings of "want, pursuing and consumption" with painkillers being the object of desire in order to free the individual of the threat (pain, cravings, distress). This notion is echoed in the literature where opiate consumption relieves one of negative affect (Khantzian, 1997; Weiss et al., 2015). Immediately after painkiller consumption and when the individual is pain free the Soothe system becomes activated to create feelings of warmth, tranquillity and mental quiescence. Clearly this strategy is problematic as the individual enters a vicious cycle of positive reinforcement by way of addictive substances which will lead to severe detriment in the quality of life. However, the path to addiction is not always logically thought out or “chosen”. Those high on impulsivity have difficulties in planning future events and often display a “temporal myopia” in regard to future goals and often choose a smaller-but-sooner rewards (E.g. misusing painkillers to be pain-free;) in lieu of larger-but-later rewards (E.g. satisfactory health; being addiction free; Mischel et al., 1970; Bickel et al., 2001;). This pattern of decision making can be detrimental to health. In these studies, it was shown that those who scored low on the DD task (greater impulsivity) also had higher LDQ scores (Mitchell 1999; Reynolds et al., 2004 & 2006a). However, the path to activating the Soothe system is not solely accomplished via consumption of painkillers. CMT aims to activate the soothe system and so training in such an intervention may, over time, increase activation of the Soothe system and decrease activation of the Drive and Threat systems in a more “natural” way. Increasing Self-reassurance by way of the CMT intervention is what could have resulted in the decrease in DPPC and RDA scores and subsequent LDQ scores via a reduction in NU, upon which RS acts on to quash the effects of NU (See Fig.46). In addition, there may be a neurobiological underpinning behind this notion. The Drive system (incentive and Resource seeking) is thought to be sub-served by Dopaminergic neurons while the Soothe system is thought to be sub-served by Oxytocinergic neurons (Gilbert, 2010) which release the neurohormone OXT. Studies have shown that artificial infusion of OXT in drug dependent participants showed a reduction in drug consumption (Carson et al., 2010; Cox et al., 2013; Zhou et al., 2014) and OXT is known to play a role in reducing impulsive decision making (Demirci et al., 2016; Plessow et al., 2016). Taken together, we can see the therapeutic benefits CMT may provide to a vulnerable and underserved population as CMT aims to increases levels of self-reassurance and bring balance amongst components of the Three Circles Model (Gilbert, 2010).

7.2. The role of the CMT intervention in reducing painkiller dependence

Engaging in short-term mindfulness/compassion-based exercises, such as CMT, have been shown to reduce painkiller consumption in chronic pain patients. Ninety chronic pain patients were trained in a 10-week Stress Reduction and Relaxation Program. Statistically significant reductions were observed in measures of present-moment pain, negative body image, mood disturbance and psychological symptomatology, including anxiety and depression. There was also a significant increase in self-esteem and a significant reduction in pain-medication consumption. Thus, we see that changes in affect (mood, anxiety, depression, self-esteem) have an effect on pain medication consumption (Kabat-Zinn et al., 1985). This lends support to this piece of research in that short-term interventions, such as the CMT intervention, may help reduce the way one deals with negative affect (i.e. increased feelings of warmth, kindness, self-reassurance and decreased self-hate) and subsequently reduce pain-medication consumption (i.e. consuming less than the RDA) which in turn could lead to a reduced propensity of developing a SUD. There would also be a reduced likelihood of negative urgency being activated if there is an absence of low-mood (See section 4.5. for a more detailed treatise of how CMT may reduce painkiller dependence and see also Fig. 44 below). The sections below will explain how specific components of the CMT syllabus could have reduced painkiller dependence.

7.2.1. Compassionate imagery

Compassionate imagery exercises, as used in studies 2 and 3, with an emphasis on self-compassion have been shown to be beneficial for impulse control as shown in a seminal study by Adams and Leary (2007), which investigated the effects of self-compassion on self-regulation. The study first assessed the proclivity for guilty and restrictive eating patterns. Participants were randomly allocated into groups in which they would either consume an unhealthy preload or eat nothing followed by a self-compassion induction or receiving no induction after which they took part in a tasting session of sweets. It was expected that restrictive eaters would have displayed the disinhibition effect of overeating upon breaking dietary rules (Herman & Mack, 1975), which was required by the preload condition. However, the authors discovered that restrictive eaters consumed less food after a preload if they were imbued with a self-compassion protocol. Therefore, this study suggests that poor self-regulation can be diminished with self-compassion within those participants who were thought to have difficulties in controlling their impulsive behaviour.

7.2.2. Mindfulness

Mindfulness, defined as the "*maintenance of attention on the present moment, as well as* *bringing a quality of curiosity, openness, and acceptance to that awareness*" (Erisman et al., 2005, page.1) has been hypothesised to assist individuals in a healthier engagement with their emotions and so mindfulness can also be related to affect regulation. Erisman et al., (2005) analysed results from their study on affect regulation by measuring anxiety, stress, depression, difficulties on affect regulation (Difficulties in Emotion Regulation Scale, DERS; Gratz & Roemer, 2004) and two scales of mindfulness (Mindful Attention and Awareness Scale, MAAS; Brown & Ryan, 2003, and the Self Compassion Scale, SCS; Neff, 2003). Non-judgmental, compassionate portions of mindfulness were captured by the SCS and was not directly measured by the MAAS (Erisman et al., 2005). A subscale in the DERS captures some aspects of impulsivity. Significant negative correlations were observed between this subscale of impulsivity (impulse control) and the MAAS, as well as with the SCS. Regression analysis revealed that aptitude in mindfulness may predict impulse control strategies in addition to affect regulation strategies (Erisman et al., 2005). The results provide direction for targeting affect regulation as a risk-factor for risky behavior**.** The authors also advocate mindfulness in cultivating self-acceptance and compassion as treatment options for affect regulation. Despite this, it was not concluded as to what degree impulsivity advances emotional volatility or whether impulsivity is an appropriate indicator for those with affective disorders. The study is of interest because it is one of few to suggest an association between mindfulness and affect driven forms of impulsivity (e.g. Negative urgency). The results are of clinical importance as the majority of impulse control disorders include models of affect dysregulation (Linehan, 1993). The associations between negative affect and affect dysregulation are well established (Erisman et al., 2005), however what remains unclear is which direction it occurs. It remains unknown whether impulsivity is a cause or consequence of affect dysregulation. Affect dysregulation is regarded as the inability to adequately regulate the emotions in accord to the demands of the environment (Thompson, 1994). Impulsivity could be a misaligned response to negative affect or it could inhibit the ability to effectively regulate an emotional experience.

Impulsivity has been well documented to be a progressive risk factor for addiction. Thus, it is conceivable that if aspects of impulsivity are reduced by practising mindfulness by being aware of the presence (i.e. presence of negative affect) then this could have reduced dependence on painkillers, perhaps by reducing the magnitude of prescription painkillers consumption (Dakwar & Levin, 2009; Garland et al., 2010). As stated above, mindfulness (including mindful breathing exercises) improves self-regulatory processes, which in turn may function to moderate impulsive decision-making in regard to negative affect and negative risk (Casey et al., 2008). Impulsivity has been purported to be an enduring trait. However, there is a prevailing amount of data to suggest that it can be improved with practice (Muraven et al., 1999) such as the practice Mindfulness and SRB. Data exists to suggest that self-regulation and impulsivity can be exercised in order to reduce its impact on substance abuse (Aklin et al., 2005). When self-regulatory processes and impulsivity are viewed as being malleable then it could be suggested that the extent to which CMT and self-reassurance is practiced, and incorporated into daily life, will allow participants to become proportionally better equipped at self-regulating their impulses and desires. These impulses and desires may include those that wish to manifest behaviourally as painkiller consumption.

7.2.3. Soothing Rhythm Breathing

Soothing Rhythm Breathing (SRB) requires one to focus on their breath and is required to "*pay attention in a gentle and kind way*" (Gilbert, 2010. Pg. 37). It aims to make the participant aware of the present moment and focus on "*the here and now*" in a very similar way that Mindfulness exercises are performed and so SRB can be considered a form of Mindfulness that focuses on breathing (Garland et al., 2014. Pg. 451). Gilbert & Proctor (2006, Pg. 370) describe SRB as "*a brief relaxation exercise that involved being mindful of breathing.*" Thus, SRB in this context acts as a gateway to the CMT exercises that soon followed (CMT group participants only) such that participants became more aware of themselves (including their pain intensity, pain frequency and desire for opiates).

SRB is thought to activate the Vagus nerve and stimulate the neural regions responsible for the Soothe system and alter Heart Rate Variability and so helps one to self-regulate (Duarte et al., 2017). SRB exercises help participants to get a sense of calmness and allows for a gentle shift into the CMT exercises. SRB exercises that focus on breath, as used in study 2 and 3, have been shown to help manage emotions and regulate impulsive behaviour similar to Mindfulness exercises (Broderick, 2009). In addition to Compassionate Imagery exercises, SRB exercises featured throughout the CMT exercises and the possible effects on the study results are outlined below.

7.2.3.1. SRB and Substance Dependence

The effects of SRB lends hand to the information-processing aspect of substance dependence in which attention and memory have a responsibility governing positive and negative affect. Drug consumption is regarded to be directed by memory-based, repetitive stereotypical drug use and operates below the conscious level and often with minimal effort (Tiffany, 1990). SRB halts this process by reconfiguring automatic thought processes to come into awareness and simply be observed. The antithetical properties of SRB and automatic impulsive behaviours offer theoretical potential for the ability of SRB as a possible intervention for impulse control disorders. Practise of SRB functions as an exposure stratagem for negative affect and may be "incorporated as a shift in perspective from actor to observer, thus reducing the urgency inherent in an urge or emotion" (Breslin et al., 2002, pg. 17). Indeed, mindful based breathing exercises (such as SRB used in studies 2 and 3) have been used to successfully reduce addictive behaviours (Khanna & Greeson, 2013), enhance relapse prevention programmes (Vallejo & Amaro, 2009), reduce alcohol dependence (Singer et al., 2013), enhance recovery programmes for nicotine dependence (Froeliger et al., 2017) and reduce prescription painkiller dependence in chronic pain patients (Garland et al., 2014, Garland, 2014).

7.2.3.2. SRB and its effect on Impulsivity

Impulsivity has been described as rapid action without conscious forecasting or awareness and spur-of-the-moment emotional reactivity. The SRB exercise is almost the opposite as one is required to be "paying attention in a particular way: on purpose, in the present moment, and non-judgmentally" (Kabat-Zinn, as quoted in Segal et al., 2002, p.121). The engagement of a SRB induced state impedes impulsive thought and behavior by dedicating cognitive resources to the maintenance of attention on the present moment while promoting qualities of compassion, non-judgment, and wisdom. Breathing exercises have taken center stage within an array of cognitive therapies (Kabat-Zinn, 1990; Segal et al., 2002), dialectical behavioral therapy (Linehan, 1993), and Acceptance and Commitment Therapy (Hayes et al., 1999). While the literature surrounding breathing exercises views impulsivity as a key element in psychological maladies, very few studies have examined the link between aptitude in breathing exercise mastery and impulsivity. Breathing exercises such as SRB may offer individuals hope towards amelioration of impulsive control disorders due to the antithetical approach of focused awareness.

7.2.3.3. SRB and its effect on Negative Urgency

In addition to this the advantage of SRB is that it may mitigate stressors and reduce urges to act with negative urgency. A multitude of "*awareness of breath*" programmes, such as SRB, exist whereby the attentional shift towards the incoming and outgoing breath aids individuals in elevating awareness on the present-moment and helps reduce habitual engagement in self-related preoccupations concerning any other moment in time other than the present. This may include the preoccupation of drug-seeking and drug-consuming thoughts. The relationship between affect regulation and impulsivity is certainly of significance and the majority of research outcomes on impulse control disorders have highlighted fundamental complications with affect regulation (Khantzian, 1985; Brown et al., 2006; Cazenave et al., 2007; Cheetman et al., 2010; Fox et al., 2007). Negative affect incited by chronic pain and self-critical thoughts may drive individuals into acting rapidly and reflexively to quickly quash feelings of distress. This may extend to include the consumption of painkillers in order to quickly escape from both the physical onset of pain and the emotional pain associated with living with chronic pain. Therefore, a key contribution of SRB in negating the effects of negative urgency is by enforcing conscious attention and awareness of thoughts and feelings to foster detachment from negative affect before automatic behaviour has the chance to arise. This could also be enhanced by developing greater self-reassurance.

7.2.3.4. SRB and its effects on Delay Discounting

It is widely agreed that mindful based breathing exercises such as SRB affects thoughts in addition to feelings and emotions that influence *behavior* and specifically promotes paying attention to "the present moment" (Paulson et al., 2013). If CMT group participants became sufficiently competent in SRB then this could be an explanation as to why DD scores may have improved for the CMT group participants. The DD paradigm aims to delineate those who prefer a S-S reward or a L-L reward, whereby a greater preference for S-S is regarded as being impulsive. By utilising SRB, CMT group participants may have been able to foresee the benefits of choosing the L-L reward in lieu of the S-S reward by focusing on the choice available in the present moment and not "discounting future rewards". This phenomenon could have translated into a real-world situation whereby the short-term desire to consume of painkillers greater than the RDA would have been replaced by the preference of not consuming prescription painkillers above the RDA and the associated long-term health benefits. Scores on the DD task could also have improved by increasing positive affect, courtesy of the CMT intervention as increasing positive affect and self-reassurance has been shown to aid in self-regulation (Aspinwall, 1998), cognitive performance in goal relevant tasks (Ashby et al., 1999) and in decision making (Dreisbach & Goschke, 2004).

Self-regulation has been identified in the literature as an ability to resist the need for instant gratification as driven by the pleasure centers of the brain (Baumeister & Heatherton, 1996). An objective of SRB in the CMT syllabus was to bring awareness to thoughts, feelings, and emotions that influence behaviour (Broderick, 2009).

To summarise thus far it is likely that during the course of the study CMT group participants grew more aware, or *mindful*, of their self-critical thoughts, including desires (cravings and urges) to consume painkillers by engaging with the SRB exercise and then consciously choosing to act against these desires by consciously exerting self-regulation (i.e. being less impulsive) and replacing self-critical thoughts with self-reassuring thoughts. SRB provides a framework for acceptance-based techniques that work in synergy with cognitive-behavioral treatment (Breslin et al., 2002). Aptitude in SRB may reveal itself as an exposure strategy, in which participants can begin to suppress and/or interact differently with automatic reflexive actions triggered by negative affect. These negative affect states are well validated to be precursory to drug seeking and drug consuming behaviours. Careful attention to drug-associated cues or triggers combined with a conscious, non-avoidant behavioral reaction may soothe the patient to the motivating effects of negative affect. With due time, mindful cognizance of thoughts, feelings and behaviors may develop into a default method of managing negative affect (Breslin et al., 2002).

In addition, it is also highly probable that participants first became more aware of their self-critical thoughts (by practicing SRB) and when detected, participants were able to reply back to themselves with self-reassurance – a skill that was acquired through interaction with the CMT software.

7.2.4. The role of self-reassurance towards reducing painkiller dependence

It has been suggested that self-reassurance is of great benefit to those who are self-punitive (Gilbert, 2005), such as those living with the harsh reality of chronic pain and are hypothesised to have a hypoactive soothe system and a hyperactive threat system (LeDoux, 1998). The threat system exists to function as a defense against dangers and perceived threat, which then leads to the manifestation of anxiety and shame. Self-preserving behaviours can also become activated e.g. fight or flight response. It is probable that having an authoritarian attitude for oneself and having a harsh self-critical voice tone as default when accompanied by attempts of self-regulation may stimulate the threat system leading to difficulties in achieving a state of calmness that may aid the distress associated with a life lived in chronic pain. Moreover, having a Self-critical voice tone may present as a challenge towards obtaining a self-soothing and self-reassured approach to life. Therefore, those who are predisposed to self-retaliation may benefit from self-regulation obtained via the exercises in the CMT syllabus.

7.2.5. Components of the CMT intervention responsible for reducing painkiller dependence

The CMT intervention was composed of: The CMT psycho-education video library and the CMT software. The CMT psycho-education syllabus in general was constructed to better shape the affect regulation system and nourish the soothe system. This is important because the soothe system acts to moderate and subdue the threat system when a threat is detected (Gilbert 2005, 2007). A threat could be internally or externally generated. Internally generated threats such as Self-critical thoughts can lead to activation of the drive system. The drive system functions to motivate the individual to gather resources necessary for survival and sense-gratification. A likely scenario could be that a stream of Self-critical thoughts cause inner torment in the individual and is driven to procure and consume drugs in order to suppress the state of negative affect. Thus, an activated threat system, in the presence of a hypoactive soothe system, activates the drive system towards drug-seeking and drug-consuming behaviours. The effect of the drug acts as a temporary replacement of the soothe system. In healthy, non drug-addicted individuals, the feelings of self-reassurance generated by a healthy soothe system would not culminate in drug seeking/consuming behaviours.

The CMT psycho-education syllabus aims to rectify disparities within the three affect-regulation systems, aiming to aid individuals who struggle activating the soothe system in response to threat (Gilbert, 2004; 2005). This struggle may have an environmental (Belsky & Beaver, 2011), or a biological basis such as hypoactivation of the soothe system during infancy (Gilbert, 2000). The CMT psycho-education syllabus informs participants that the plethora of cognitive preconceptions/distortions are founded in biological processes fashioned from genes and the environment and reminds participants "*it's not your fault*". The CMT psycho-education syllabus and the CMT software incites self-reassurance in order to access and develop the soothe system, overcome self-criticism by boosting self-reassurance and to improve self-regulation.

To summarise thus far, the major outcomes from study 1 showed that painkiller dependence was present in the study sample and that study variables such as negative urgency were significantly correlated with painkiller dependence. Study 1 also showed that self-hate and self-inadequacy moderated painkiller dependence in the presence of the study variable Pain Frequency as did self-reassurance but offered protective characteristics against painkiller dependence. This paved the way for studies 2 and 3 which aimed to assess acceptability and feasibility of a web-platform and then the effects of a CMT intervention on reducing painkiller dependence and explore the relationship between study variables. Study 3 being a refined version of study 2 and had a larger study sample.

In study 3, participants in the CMT group underwent engagement with a CMT syllabus and CMT software showed significant reduction in painkiller dependence and a significant increase in self-reassurance in comparison to a control group when the intervention ended. The CMT syllabus was composed of a breathing exercise (SRB) akin to mindfulness and also contained compassion-based exercises grounded in the works of Gilbert et al., (2004; 2005). The effects of SRB (mindful breathing; Garland et al., 2014; See also section 7.2.3.) and CMT would both have had an effect on participants in terms of reducing painkiller dependence.

SRB would have had a positive impact on participants self-regulatory behaviours by having participants dedicate cognitive resources on the present moment instead of future events. Those who score high on impulsivity are known to lack foresight and so focusing on the "here and now" may benefit decision making in that moment (i.e. to consume more painkillers or not). Thus, SRB could have contributed to reduction in painkiller dependence by reducing impulsive tendencies (Sections 7.2.3.2 – 7.2.3.4.). Indeed, mindful based breathing exercises (such as SRB) have been shown to reduce addictive behaviours (Khanna & Greeson, 2013), and reduce prescription painkiller dependence in those with chronic pain (Garland et al., 2014, Garland, 2014).

The effect of the CMT syllabus and CMT software could have been such that self-reassurance would have increased and so offered protection against painkiller dependence (Fig. 14) in addition to cultivating an underactive soothe system which would have become strengthened by CMT and also offered protective benefits (Gilbert & Proctor, 2006). Additionally, the role of the soothe system (thought to be sub-served by Oxytocin; Gilbert, 1989; 2010) could have offered protection as activity of this system is stimulated when we "experience compassion for self and others" (Ebert et al., 2018). Evidence also shows OXT release to have an inverse relationship with impulsivity (Demirci et al., 2016; Section 4.3.4.). Oxytocin is also known to have therapeutic effects on drug dependence (Section 4.3.5.). Data from a study by Kelly et al., (2010) showed that participants who engaged with a compassion-based exercise had significantly improved their ability to reduce cigarettes smoked while the administration of Oxytocin was shown to decrease tolerance levels and withdrawal symptoms for opioid analgesics (Kovacs et al., 1985; Sarnyai & Kovacs, 1994). Thus, by engaging in CMT exercises to develop, strengthen and activating the soothe system, could prove to be a protective factor against painkiller dependence.

This section highlights the conclusion that both mindfulness-based breathing exercises (SRB) and engaging in a CMT intervention in combination both aid the reduction of painkiller dependence. Future studies could aim to determine which of the two is more responsible for painkiller dependence however, to extract a key component (SRB) from the CMT exercises would misrepresent the integrity of CMT as self-soothing by using SRB is a fundamental component of CMT.

The following section will discuss study limitations and future research.

7.3. Study limitations

While efforts have been made to ensure this piece of research were as robust as possible, some limitations were identified. The limitations identified within the studies are outlined below.

7.3.1. Obtaining a representative sample

Obtaining a sample that broadly represents those in the wider chronic pain community was of importance when designing the study and particularly during the recruitment stage. Upon analysing demographic data, it was found that study participants were not too dissimilar from those in a study by Elander et al., (2014). This is encouraging as it suggests that the study sample obtained here is representative of the chronic pain population.

7.3.2. Measures

The study made use of several self-report measures to gather participant data. A well-known flaw with this is that participants are cautious when providing personal data. This may or may not have been an advantage considering the forms were completed online and so provided some degree of privacy. Moreover, participants may not be truthful in answering questions, particularly sensitive questions such as drug consumption habits. It is also plausible that some participants do not possess sufficient insight to be able to answer questions with a high degree of reflectivity and accuracy. Living with an extremely difficult condition such as chronic pain may make it challenging to focus and concentrate on such a task. Furthermore, while they did have the option to ask for help/guidance if they did not understand a question, the option of asking another human directly is far easier and quicker than sending an email asking for help.

In spite of the above, Gosling et al., 2004 state that data collected from sufficiently motivated participants recruited from the internet can generally be regarded as reliable and generalizable when compared to randomly selected participants. These views were echoed in a separate study that compared probability samples vs. nonprobability samples who completed self-report measures (Chang & Krosnick et al., 2009). Results from this study were generally on par with data collected from Elander et al., (2014) who also explored a population of chronic pain sufferers.

In addition to self-report measures a behavioural measure (DD Task) was used. As participants would engage with this task on three separate occasions, it is possible for some degree of familiarity to evolve and a strategy to flourish in order to score as high as possible.

7.3.3. Not knowing if the participant is legitimate to be included in the study

While the advent of the internet provides anonymity to the end user, it also masks the true identify of that end user to the researcher. It can be almost impossible to deduce whether the participants were who they claimed to be. It also cannot be verified whether the end-user is the gender they claim to be, has chronic pain or whether they even consume painkillers.

7.3.4. Not knowing if a participant has registered more than once for the study

In addition to 7.3.3. it could also be possible for a participant to have more than one account. The allure of an Amazon Gift Card could provide enough impetus for an individual to create multiple accounts to increase the probability of winning the prize. This issue can be circumvented by placing additional code in the website which limits access from only one IP Address.

7.4. Improvements for Study 3

The following section describes improvements which were identified for study 3.

7.4.1. Expanding online material

Future iterations of the web-platform would include more videos in the psycho-education library, in order to cover the entire CMT syllabus. This would ensure a comprehensive application of CFT/CMT and would perhaps target those who were not responsive to the material provided by this version of the web platform. By presenting the material in a modular fashion whereby participants progress in stages from one to another would give participants a greater sense of accomplishment and motivate them to pursue the study to completion (See section 7.4.2 below).

7.4.2. Incentive system to enhance participant retention

A second improvement for the web-platform would be to divide the CMT video library into a modular system. Participants would work through each CMT module week-by-week. Upon completion of a module, participants will receive a Bronze, Silver and Gold medal which appears next to their username. Obtaining a medal will unlock new features on the website such as access to online material (e.g. videos, training material). A reward system such as this has been employed by a wide range of successful web-platforms and video games (e.g. Code Academy, Reddit, DataCamp).

7.5. Strengths of using a web-based platform for CMT combatting painkiller addiction

Despite there being limitations to the study and scope for improvement, there exists certain novelties and strengths within these studies. These are identified and presented below.

7.5.1. Ease of recruitment

A major strength of studies 2 and 3 was placing an evidence-based intervention on the internet. First, as a research tool, this offers the advantage that a large number of participants can be recruited quickly and with relative ease. The pool of participants can, if the sample is large enough, be statistically representative of the global chronic pain population. Study 3 initially drew in 442 individuals where 255 did not meet eligibility criteria and 108 declined to participate. Future studies would aim to seek reasons for participants declining to partake so solutions may be devised to increase the sample size.

7.5.2. Accessibility

Furthermore, placing the CMT intervention on the internet allows participants to access the web-platform from the comfort of their homes. Many therapeutic and psychological interventions available to those with SUD are "*face-to-face*" and requires the individual to attend an institution offering such support. The web-platform created permits end-users to access similar support from anywhere on the globe; the only requirements being sufficient motivation and an internet enabled device. Furthermore, chronic pain can be a physically debilitating condition for many and so attending an institution for treatment may not be an option. Thus, offering a web-based solution would circumvent mobility issues faced by those wanting to seek help. However, placing the resource on the internet may also be precluding those who wished to participate but do not have internet access or do not have competency in engaging with technology. Feedback from study 2 showed that participants welcomed the option of being able to engage with CMT from the comfort of their home and in their own time (e.g. *"I can do it all on my laptop and I don't need to see my doctor"; "I can learn things online and practise in my own time…I don't have to do it in a 40-minute session with a doctor."; "Amazing! Now I don't need to leave my home – I can do it in my own time")*

7.5.3. Overcoming social stigmas and providing privacy

In addition to ease-of-access and overcoming mobility issues, the web-platform overcomes the social stigma attached to substance dependent individuals wanting to seek help. The vast majority of people who need treatment for SUD do not seek it. Several barriers can discourage someone from getting help, and many people are deterred by a combination of factors (Appel et al., 2004; Luoma et al., 2007). A well-established deterrent to seeking help for drug dependence is the lack of anonymity (Cunningham et al., 1993). Existing face-to-face consultation does not provide one with much privacy however this barrier is circumvented with a web-platform, as end-users do not need to leave their homes to seek a therapeutic intervention. Users of the web-platform can remain anonymous online as they are not required to provide personally identifiable information.

7.5.4. Socio-economic impact

A notable feature of hosting a therapeutic intervention online is that treatment costs can be greatly reduced. Current expenditure on (a) manufacturing of painkillers and (b) treatment costs for painkiller dependence costs nations billions of dollars. The need to reduce consumption of powerful painkillers with addictive properties is of great benefit for patients' health and for socio-economic impact. To put this into perspective, for prescription painkillers, the mean Daily prescription painkiller consumption (DPPC) score change from baseline to post-intervention in the CMT group was 2.79 to 2, or a 28.32% decrease.

7.5.5. Malleability of a web-platform

One of the true strengths of a web-based platform is speed. Engaging and captivating digital content can be quickly created and easily uploaded to the web-platform with rapidity. Written content can also be created, changed and accessible to a worldwide audience within minutes. This is particularly useful should the web-platform become successful and the need to *scale-up* becomes a prospect.

7.6. Future research

Future research identified from studies 1 to 3 are outlined below.

7.6.1. Serial vs. Random presentation of self-critical thoughts

The CMT software displayed "thoughts" which were self-critical in nature and were provide by the participant. These "thoughts" were stored in their personal database and were only visible to that particular participant. An example of a self-critical thought would be "I am not strong enough to manage my medication intake". Thoughts were displayed to the participant in serial order. The first thought entered into the database would be the first thought displayed each time they engaged with the CMT software. It would be interesting to see what effect changing the order in which thoughts were presented might have on dependent variables. Future studies would aim to present thoughts in random order to one group and serial presentation of thoughts to a second group.

7.6.2. Current CMT methodology vs. CMT Software

Existing forms of delivering CMT have shown to be highly successful. These usually consist of one-to-one sessions of therapy and completing pen-and-paper work under the guidance of a trained professional. The novelty of this study is the implementation of CMT software. Future studies would assess the efficacy of existing CMT materials in comparison to the CMT software with the aim of reducing painkiller dependence.

7.6.3. Applying the web-platform to other areas of addiction

Results from this study show facets of impulsivity to be risk factors for substance dependence. The existing literature strongly suggests impulsivity to be a risk factor for dependence to other substances such as cocaine, heroin, alcohol and cigarettes. An exciting study would be to test the CMT software with participants dependent on substances other than painkillers.

Furthermore, dependence can occur in other forms. Frequently, it is assumed for physical dependence to be described by withdrawal symptoms as a requirement for someone to be diagnosed with a SUD, however behavioral addiction is known to exist with all the negative costs without the physical concerns seen in those who impulsively engage in drug and alcohol abuse. The impulsive nature of the behavior is suggestive of a behavioral addiction, or process addiction. The urge to continually engage in an activity or behavior regardless of the negative effect on one's ability to remain mentally and/or physically healthy and defines behavioral addiction. An individual may discover the behavior psychologically rewarding while partaking in the activity but then may later feel remorse, guilt, shame or even overwhelmed by the consequences of their decisions. A future study would quantify the impact of the web-platform on those whose lives are affected by process dependence (e.g. sex and love addition, internet addiction, gambling, shopping addiction, food addiction, video-game addiction, exercise addiction, risky behaviour addiction, porn addiction, social media addiction).

While this study was limited to a pool of participants who suffered chronic pain and were on painkiller medication, future studies would aim to reduce substance dependence to other substances of abuse as well as process addictions.

7.6.4. Exploring the role of other facets of impulsivity

Figure 4 (page 53) showed many forms of impulsivity and to have studied the effect of them all on psychological dependence to painkillers is beyond the scope of this thesis. However, to build a complete picture on the influence of impulsivity it would be imperative to use different behavioural measures in place of the DD task. One such example would be the well-documented go-/no-go task and to ascertain whether scores on this task would be a stronger predictor of painkiller dependence than DD scores.

7.7. Conclusions

The studies within this thesis attempted to explore the apertures toward painkiller dependence, specifically: impulsivity, self-reassurance, self-hate, self-inadequacy, painkiller consuming patterns and severity of pain. Research efforts exploring the link between these variables have been sparse and this thesis aims to cover the knowledge gap.

Studies have revealed that painkiller dependence does occur in the chronic pain community and that risk factors are present in individuals who may become prone to painkiller dependence. These include distinct forms of cognitive impulsivity and behaviour impulsivity. The study also revealed that for some individuals' interventions do exist which are capable of reducing the graded severity of psychological dependence on painkillers. This comes in the form of Compassionate Mind-Training. This insight is one of the key findings in this thesis and provides empirical support for compassion-based therapies in the pursuit of reducing painkiller dependence and opens the gate to test this intervention in other fields of research related to addiction, impulsivity and compassion.

Furthermore, another finding revealed that the role of affect driven-states play a key role towards drug dependence via impulsive behaviours and so the tone of our internal dialogue should be recognised as an important stimulus of impulsive behaviour, which is itself categorised by a multifaceted group of enmeshed affective and cognitive processes. Impulsive behaviour is tightly intertwined with the human experience of emotion. The tone of our internal dialogue can influence impulsivity distally, via a personal predilection to experience the extreme ends of the mood spectrum, or proximally, through the powerful experience of negative (or positive) affect altering one's cognisance to provide impetus towards participating in a particular behaviour. Definitions and measures of impulsivity that take consideration of affect, such as the UPPS-P, are therefore vital to the research field in order to understand and prevent maladaptive impulsive behaviours.

Finally, another insight arising from these studies is that those living within the chronic pain community were welcoming of web-platforms that aimed to deliver a compassion-based intervention in a novel way. This comes at a great moment in time and provides hope for many who find it difficult to speak to others, to seek help, have mobility issues, live in rural areas or are weighed down by the social stigma surrounding drug dependence.

Chapter 8. References

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