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The compassionate vagus: A meta-analysis on the connection between compassion and heart rate variability

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Highlights

- Compassion is positively linked with vagally-mediated heart rate variability (HRV)
- The size of the effect is medium and not influenced by publication bias
- The size of the association is mediated by the specific method used to assess HRV
- Results are limited by the high heterogeneity and poor methodological rigor

ABSTRACT

In recent years, increasing interest has been devoted to the physiological basis of self and other-oriented compassion. Heart rate variability (HRV) represents a promising candidate for such a role, given its association with soothing emotions and context appropriate prefrontal inhibitory control over threat-defensive responses. The aim of this study was to meta-analyze available studies on the association between compassion and HRV. Random-effect models were used. The analysis performed on sixteen studies that met inclusion criteria, yielded a significant association with a medium effect size (g = .54 95% CI [.24, .84], p < .0001). Results were not influenced by publication bias. After an extreme outlier's exclusion, the size of the association was still larger in studies that used time or frequency-domain indices of vagally-mediated HRV compared to those that used peak to trough estimates of respiratory sinus arrhythmia. Results are limited by the small number of studies included in the meta-analysis (n = 16) and are discussed in terms of indications for future research, given that existing data are highly heterogeneous and of poor methodological rigor.

Keywords: meta-analysis; compassion; vagally-mediated heart rate variability; parasympathetic nervous system; respiratory sinus arrhythmia.

Contents

1. Introduction

Approximately 2 million years ago humans began to evolve a complex array of cognitive competencies (Barrett et al., 2002). These ranged over competencies for language, new forms of reasoning and systemic understanding, and forms of self-awareness that give rise to knowing intentionality. For example, we can think about the consequences of our behavior on others but also for ourselves months, even years in the future. We have new types of self-awareness and new types of self-consciousness. Our theory of mind allows us to attribute mental states —intents, desires, emotions, etc.— to oneself and to others, and to recognize that others have desires, intentions, and emotions that are different from (or similar to) one's own (Luyten et al., 2020). Thus, what turns caring into human compassion is the utilization of recent cognitive competencies for caring motivation. This conceptualization helps to distinguish compassion from other forms of mammalian caring behavior (Gilbert, 2017; Gilbert et al., 2019).

Compassion has many definitions. It has been viewed as an affective state (Goetz et al., 2010), as a multidimensional construct (Jazaieri et al., 2013; Strauss et al., 2016), and as a motivational system rooted in mammalian caring (Gilbert, 2014). As a motivation, compassion has been defined in terms of a basic stimulus-response algorithm: *"the sensitivity to suffering in self and others, with a commitment to try to alleviate and prevent it"* (Gilbert, 2017). Here, we take an evolutionary approach arguing that compassion evolved from caring behavior and caring behavior evolved (partly) as a mammalian K-selected reproductive strategy of parental investment in offspring (K-selected species invest heavily in fewer offspring, each with a high probability of survival; Gilbert, 1992; Pianka, 1970). This strategy evolved with an algorithm that enabled the mother to be attentive to the needs and distress of her infant and then take appropriate action to rescue, feed or offer thermal regulation (Brown and Brown, 2015). This algorithm facilitated the evolution of a range of physiological processes including the hormone interplay of oxytocin and vasopressin (Carter, 2014;

Carter et al., 2017) and myelination of part of the 10th cranial nerve of the parasympathetic system, referred to as the vagus nerve (Porges, 2017). Research has shown that compassion is different from kindness because kindness does not require a sensitivity to suffering nor the courage of compassion (Gilbert et al., 2019). It differs from sympathy, which is simply an automatic reaction to another's distress that does not involve deliberate engagement or motivation to do something; e.g., Eisenberg et al., 1989). It differs from empathy because empathy is a competency (not an emotion) to understand the emotions of another but empathy can be used manipulatively to support deception or even cruelty (Bloom, 2016). Compassion belongs to the family of prosociality, but prosociality involves cooperation and does not specifically address suffering (Gilbert, 2015).

Thus, compassion can be considered the expression of the "extended" caregiving system which has emerged from ancient motivations to detect and respond to the need of dependent offspring. Although there are many inhibitors of compassion along dimensions such as ingroup-outgroup, liking-disking, trust-distrust, (e.g., we are more likely to be compassionate to people we like than people we don't, to friends and family rather than strangers), with effort and intention, caring motivation can be extended to the welfare of all living beings, including the self (Gilbert, 2019; Wang, 2005).

In recent years, a growing body of evidence has started to link compassion with the function of the vagus nerve, the longest cranial nerve, which richly innervates the entire body, including the face, the vocal apparatus, the heart, and the digestive tract (Porges, 2017; Thayer et al., 2012). There is now very good evidence that vagal tone plays a salient role in the ability for people to both be caring and respond to being cared for (Petrocchi and Cheli, 2019).

The calculation of heart rate variability (HRV), which is the fluctuation of instantaneous heart period over time, provides a non-invasive proximal measure of cardiac vagal modulation (Laborde et al., 2017). Commonly reported measures of vagally-mediated HRV (vmHRV) include the root mean square of successive differences (RMSSD) – a time-domain measure – and the high frequency HRV (HF-HRV) (Laborde et. al, 2017). Moreover, the peak-to-trough (P2T) algorithm is frequently employed to estimate respiratory sinus arrhythmia (RSA, the HRV in synchrony with respiration), although the efficacy of using P2T as a dynamic index of cardiac vagal tone remains questionable (Lewis et al., 2012).

VmHRV has been used in many studies as a psychophysiological substrate of prosocial behaviour (e.g., Bornemann et al., 2016), and, more specifically, compassion (Kim et al., 2020). Indeed, it is now relatively well established that by measuring cardiac vagal tone via HRV analysis, we can estimate the activity of specific brain areas, due to the bidirectional communication between the heart and the brain. Using transneuronal retrograde viral labeling and spinal cord transection, Ter Horst and Postema (1997) were able to trace the vagus nerve in brain structures mostly belonging to the so-called Central Autonomic Network (CAN; Bennaroch, 1993), whose output goes to the heart via the stellate ganglia. Moreover, two meta-analyses of existing studies combining neuroimaging techniques with vmHRV assessment (Beissner et al., 2013; Thayer et al., 2012) found that higher resting vmHRV is associated with greater activity in prefrontal and CAN brain regions. Further, a recent meta-analysis suggested that non-invasive brain stimulation of the dorsolateral prefrontal cortex (dlPFC) can significantly increase vmHRV (Makovac et al., 2017). Hence, vmHRV may serve as an indicator of the degree to which the PFC provides context-appropriate control over the periphery. This is also supported by brain functional connectivity studies, in which higher vmHRV was associated with increased PFC functional connectivity with the amygdala and other subcortical regions involved in autonomic control (e.g., Chang et al., 2013; Jennings et al., 2016; Makovac et al., 2016; Sakaki et al., 2016; Thome et al., 2017). Notably, the same brain regions that have been associated with vmHRV also constitute the neurobiological basis of compassion (Lamm et al., 2019 for a recent review). For example, Weng et al. (2013) found that a compassion training increased altruistic behavior, and this was associated with altered activation in the inferior parietal cortex, dlPFC, and its connectivity with the nucleus accumbens.

In light of the reviewed evidence, compassion is less likely to be activated in conditions of low vmHRV, a state characterized by reduced availability of perceived safety (such as when threatened or engaging in perseverative cognition), and associated with hypoactive prefrontal regulation, hyperactive subcortical structures and the release of the default physiological defensive responses (Brosschot et al., 2017). In the context of interpersonal motivations, higher vmHRV has been associated with greater engagement in social interactions (Shahrestani et al., 2014) and willingness to approach novelty (Shook et al., 2007), less extreme evaluation of other-blame reducing anger reactions (Leon et al., 2009), pronounced fear inhibition (Wendt et al., 2015), and adaptive functioning in close relationships (Beffara et al., 2016), including increased metacognitive awareness and mind reading (Lischke et al., 2017; Meessen et al., 2018), and reduced alexithymia (Lischke et al., 2018b). Moreover, individuals with high vmHRV are more likely to recognize (Lischke et al., 2017; Quintana et al., 2012) and remember facial expressions of others (Mattarozzi et al., 2019; Smith et al., 2011, Wendt et al., 2018) and to regulate emotional responses towards others (Geisler et al., 2010, 2013; Eisenberg et al., 1996; Lischke et al., 2019; Williams et al., 2015), including children's ability to express sympathy to other children in need (Fabes et al., 1993).

There is now considerable evidence that vmHRV is an indicator of prosocial behavior (Kogan et al., 2014; Kok and Fredrickson, 2010; Stellar and Keltner, 2017). For example, cooperative behavior can be predicted by the interaction between resting vmHRV and the environmental context (Beffara et al., 2016 and Lischke et al., 2018a albeit only in males). Furthermore, Bornemann and colleagues (2016) showed that training individuals in various techniques that improve vmHRV has an impact on prosocial behavior. This assumption is at the core of Porges' Polyvagal Theory, which postulates that social engagement and trust are emerging properties of the mammalian autonomic nervous system and conceptualizes vmHRV as a biomarker of social engagement capacities (Porges, 1998, 2003). Indeed, infant vmHRV appears to be a predictor of mother–child interactions, with lower infant vagal tone associated with more disruptive interaction patterns (Porter, 2003). In line with these findings, Svendsen et al. (2016) found higher levels of dispositional (trait) self-compassion in individuals with higher vmHRV, and the induction of a compassionate state triggers an increase in vmHRV which is proportional to the increase in soothing positive affect (Petrocchi et al., 2017b; Rockliff et al., 2008).

Such association does not occur only momentarily but increased resting vmHRV appears also after a two-week Compassionate Mind Training (Matos et al., 2017), aimed at cultivating compassion (both for ourselves and others).

Given such emerging research linking compassion to vmHRV, and in response to recent efforts to include HRV as a primary outcome measure in assessing and training compassion (Kirby et al., 2017), the present meta-analysis aims at (i) determining the existence of an association between compassion and increased HRV indices of cardiac vagal tone, (ii) quantifying the strength of this association, and (iii) identifying plausible moderators.

2. Methods

2.1. Literature search and study selection

Two search strategies were used to systematically collect empirical studies of the association between compassion and HRV indices of cardiac vagal tone. First, Medline, Web of Science, and PsychINFO databases were searched for English-language publications on human samples through January 21st 2019 using the following keywords: *(heart rate variability OR respiratory sinus arrhythmia OR vagal OR parasympathetic OR autonomic nervous system) AND compassion.* Then, to address bias in effect sizes due to the tendency of authors to fail to report nonsignificant results and editors' tendency to reject papers with many nonsignificant findings, an attempt was made to locate as many unpublished studies as possible following the recommendations of Rothstein and Hopewell (2009). To do so, the same searches were conducted on Cochrane Library, clinicaltrials.gov, controlled-trials.com, greylit.org, opengrey.eu, biomedcentral.com, ovid.com, and free Google search (adding the keyword “thesis“).

Inclusion criteria for our analysis were as follows: a) age between 18 and 65 years, b) recording of at least one time-domain or frequency-domain index of vmHRV, or P2T estimate of RSA, c) induction of compassion or compassion assessed as a trait, and d) experimental design suitable for calculating one or more effect sizes. Exclusion criteria included samples characterized by obesity, pregnancy or breast feeding, current diagnosis or history of cardiovascular disease (e.g.

hypertension), diabetes, use of medications that affect the autonomic nervous system (e.g., beta-blockers).

A total of 181 results were retrieved from database searching and 41 were identified through other sources for a total of 222 records. Comparison of the retrieved titles identified 49 studies that were duplicates, thus leaving 173 abstracts for further evaluation (see Figure 1). The current meta-analysis is based on data extracted from 16 studies that met the inclusion criteria, after examination of 47 full text (see Table 1 and references marked with an asterisk in the reference list). Among the 16 studies, additional data (not published in the reviewed article but needed to calculate effect sizes or to run moderator analyses) were received for two studies (Stellar et al., 2015; Matos et al., 2017).

2.2. Variables of interest

Time-domain indices of HRV included the standard deviation of R-R intervals (SDNN, ms), and the RMSSD (ms). Frequency-domain indices of HRV included the HF-HRV (0.15–0.4 Hz, ms^2). SDNN is thought to reflect total variability (i.e., both sympathetic and vagal contribution), RMSSD and HF-HRV are considered primary indices of vagally-mediated HRV (Laborde et al., 2017). Moreover, estimates of RSA (i.e., P2T method) were considered, despite controversy surrounding their use to index cardiac vagal tone (Eckberg, 1985; Lewis et al., 2012; Laborde et al., 2017).

2.3. Coding

A standardized data coding form was developed to extract the following information from each study: a) authors and publication year; b) study design; c) characteristics of the study sample (age, sex, size, subgroups); d) measure used to assess compassion; e) measure used to assess vmHRV; f) adjusted covariates; and g) brief results. Each study (and each participant) was included only once in one of our meta-analyses (Cooper and Patall, 2009). Each research article was read and analyzed by two of the authors (MDB, LC). Any coding disagreements were resolved through group discussion.

For cardiac vagal tone assessment, when multiple indices were reported (Beck et al., 2017; Kemper et al., 2016; Kemper and Shaltout, 2011; Rycroft et al., 2016; Svendsen et al., 2016), a hierarchical inclusion was implemented to prevent conflation of effect size estimates as follows:

RMSSD only, HF power only, next RSA only, or else SDNN only. As to the assessment of compassion, we excluded other constructs that are associated with but are not the same as compassion (i.e., empathy, sympathy, kindness). When both self-compassion and compassion were assessed (Matos et al., 2017; Rycroft et al., 2016), we chose the less specific construct of compassion. To be coded as state compassion, the assessment needed to refer to the actual moment (e.g., "*right now, how much do you feel",* usually before and after an experimental induction of compassion), whereas trait (dispositional) compassion needed to be assessed by a self-report questionnaire inquiring about the usual behavior (e.g., "*how often you behave in the stated manner*" in the Self Compassion Scale; Neff, 2003). The quality of evidence was assessed with a modified version of the Newcastle-Ottawa Scale (NOS; Wells et al., 2011). In our modified NOS scale, the maximum score that could be achieved by a study was 7 stars (S1; Supplementary material).

2.4. Data analysis

For each study (or subsample of a study), we calculated a Hedges' *g* effect size. Based on conventional standards, effect sizes of *g* equal to .20, .50, and .80 were considered small, medium, and large, respectively (Cohen, 1988). The *g* coefficient represents the strength of the association between compassion and vagal indices. Calculation of effect sizes was based on means, standard deviations, difference in mean scores, *P* values, and sample sizes of the groups. When not presented explicitly, the mean change in each group was obtained by subtracting the final mean from the baseline mean. When the standard deviation (SD) of the changes was not provided, we imputed a change-from-baseline standard deviation using a correlation coefficient as indicated by Higgins and Green (2011): $SD_{change} = \sqrt{(SD^2_{baseline} + SD^2_{final} - (2 * Corr * SD_{baseline} * SD_{final}))}$. When only standard errors (SE) were provided, standard deviations were obtained by applying the following formula $SD = SE * \sqrt{n}$ (Higgins and Green, 2011). When studies did not provide raw data to calculate effect sizes and instead provided statistics (e.g., *t values*), we applied transformation formulas to convert them to *g* (Lipsey and Wilson, 2001). When a paper reported $p < .05$ or *n. s.*, we computed Hedges' *g* with *p*-values of .045 and 1 (one-tailed), respectively, which likely yielded a highly conservative estimate of the effect size.

The effect sizes were computed in ProMeta Version 2.0 (Internovi). Random-effects models were used in all the analyses as they account for the amount of variance caused by differences between associations as well as differences among participants within associations. ProMeta also computed 95% confidence intervals (*CI*) around the point estimate of an effect size. The Q and I^2 statistics were used to assess heterogeneity among studies. A significant Q value indicates a lack of homogeneity of findings among studies. I^2 values of .25, .50, and .75 correspond to low, moderate, and high between-trial heterogeneity, respectively. The problem of publication bias, due to the tendency of journals and authors to publish studies with positive results rather than those with negative or non-significant results, was estimated informally by using a funnel plot of effect size against standard error for asymmetry and formally by using Begg and Mazumdar's rank correlations, and Egger's regression intercept test.

We first ran the analysis including the entire set of studies and then subsequently re-ran it without potential outliers, to examine the impact of these specific studies. Potential outliers were excluded if they had statistically significant standardized residuals. Statistics reported in this meta-analysis conformed to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Moher et al., 2009) statement (S2; Supplementary material).

2.5. Moderator analyses

For each outcome, we examined how the size of the association varied as a function of mean age (years), sex (% of females), country where the study was performed, study design (between- vs within-subjects), adjustment for covariates (yes versus no), HRV indices (RSA, time-domain HRV, frequency-domain HRV), length of recording, type/measure of compassion (self-compassion vs compassion), sample (psychopathological vs non), and methodological quality (0–7).

Sex was examined as a moderator in light of reported prominent sex differences in both compassion (Yarnell et al., 2019 for a meta-analysis on self-compassion) and vmHRV (Koenig and Thayer, 2016; Koenig et al., 2017 for meta-analytic findings), where men have significantly higher levels of self-compassion and lower levels of vmHRV than women. Moreover, sex and age have been shown to moderate the association between self-compassion and emotional wellbeing, namely depression and anxiety (Bluth et al., 2017), therefore the relationship between compassion and vmHRV (an index of emotional wellbeing) could differ according to sex and age.

Country where the study was conducted was included in the moderation analysis because compassion can be largely influenced by cultural factors, as shown by a recent cross-cultural study (Montero-Marin et al., 2018). Therefore, it is possible that in less socially oriented and more individualistic countries, compassion is not associated with positive physiological effects. For example, a study by Arimitsu et al. (2019) found different effects of compassion and self-compassion on wellbeing in the US and in Japan. For this reason, in this meta-analysis the type of compassion (self-oriented or other-oriented) has also been examined as a potential moderator. Given that vmHRV has been associated both with adaptive emotion regulation and prosociality, we have no reason to expect a different effect of self- versus other-oriented compassion. However, it is important to note that looking at this moderator corresponds to examining the moderating role of type of assessment, i.e., self-reported questionnaire (self-compassion was almost exclusively assessed by the Self Compassion Scale (Neff, 2003), with the exception of Petrocchi et al., 2017a) versus experimental induction (compassion).

It is also important to test whether the strength of the association is weaker in individuals with psychopathological disorders, as one would expect given that several forms of psychopathology are characterized by both reduced levels of compassion (MacBeth and Gumley, 2012 for a meta-analysis) and decreased vmHRV (reviewed in Beauchaine and Thayer, 2015). Since we are examining a physiological variable, it is relevant to see if long-lasting recordings are better suited to capture the physiological correlates of compassion compared to short laboratory assessments. Similarly, given that this is a relatively new field of investigation, and that cardiac vagal tone has been indirectly assessed using various measures of vmHRV and RSA, it is important to detect if a specific vagal index can better capture the association with compassion to guide future studies and reduce methodological heterogeneity.

We tested the role of design as a potential moderator because whereas repeated measures designs are the most commonly used in psychophysiological studies, but the debate continues about their advantages over between-subjects designs. On the one hand, a within-subjects design overcomes individual differences in physiological sensitivity; on the other it may be associated with carryover effects across conditions (Jennings and Gianaros, 2007), and this may be particularly true for variables like compassion that are intrinsically subjective in nature. Lastly, if the association is substantial, higher quality studies (i.e., using adequate samples, standardized measures) and adjusting for potential confounders should be better able to detect significant effects of compassion on indices of cardiac vagal tone. A minimum of 5 studies for each subgroup was required for the moderation analysis. Continuous moderators were evaluated using meta-regression (i.e., age, sex, length of recording, methodological quality), while categorical moderators (i.e., country where the study was performed, study design, adjustment for covariates, sample, type/measure of compassion, cardiac vagal index) were entered as grouping variables in the effect size calculations. For continuous moderators, the sign of the coefficient indicates the direction of the relation between compassion and cardiac vagal index.

3. Results

Table 1 presents the specific contrast or test that was used to extract effect sizes in the present meta-analysis. Studies marked with an asterisk in Table 1 and Figure 2 indicate potential outliers. The meta-analysis showed a significant association between compassion and increased indices of cardiac vagal tone (16 studies; 746 subjects; g = .54 95% CI [.24, .84], p < .0001), which was medium in size. Figure 2 presents the forest plot. Significant heterogeneity was shown by the Q *and* I^2 statistics, Q (15) = 117.4, $p < .0001$; $I^2 = 87.2$. Begg and Mazumdar's rank correlation test excluded the presence of a publication bias (Z = 1.26; p = .21), and this was confirmed by Egger's test (intercept = 2.36, t = 1.76, p = .10 and by the funnel plot (Fig. 3). Exclusion of an extreme outlier (Luo et al., 2018) decreased the effect size (g = .40, 95% CI [.16, .64], p = .001) but not heterogeneity

(Q (14) = 68.95; p < .0001; I^2 = 79.7). Outlier exclusion did not have any influence on publication bias.

3.1. Moderation effects

Due to an insufficient number of studies, it was not possible to test for the effects of statistical adjustment for confounders (only three studies controlled for potential confounders: Petrocchi et al. 2017a; study 1 and 3 in Stellar et al., 2015), and type of sample (only three studies included psychopathological individuals: Kemper et al., 2016; Rycroft et al., 2016; Schaflein et al., 2018; please see S3 for the results of the meta-analysis without these three studies, that is in healthy individuals only). As illustrated in Table 2, to have a comparable number of studies in each subgroup to reliably detect moderators' effects, the country where the study had been performed had to be re-coded into US versus non-US (i.e., China, Portugal, Italy, Germany, Norway, UK). Similarly, the type of measure used to assess cardiac vagal tone had to be recoded into RSA versus time- and frequency-domain vmHRV.

The type of measure used to assess cardiac vagal tone was a significant moderator, Q (1) = 6.23, p = .01, with studies examining time- and frequency-domain vmHRV measures showing a stronger association between compassion and vmHRV (g = .95, 95% CI [.35, 1.55], k = 10, n = 354) compared to those assessing RSA (g = .18, 95% CI [.07, .29], k = 6, n = 392). Only studies examining time- and frequency-domain vmHRV measures presented substantial heterogeneity, Q (8) = 80.7, p < .0001; I^2 = 88.9. Contrasting studies conducted in the Unites States versus studies conducted elsewhere yielded a marginally significant difference (Q (1) = 3.25, = p = .07), with a stronger association between compassion and high vmHRV in studies conducted outside versus within the Unites States (g = 1.03, 95% CI [.33, 1.74], k = 7, n = 304 and g = .32, 95% CI [.00, .64], k = 9, n = 442, respectively). Both subgroups showed substantial heterogeneity (ps < .0001).

The study design also played a marginally significant role as a moderator, Q (1) = 2.80, p = .07, with a stronger positive association between compassion and vmHRV in studies having a between-subject compared to a within-subject design (g = 1.06, k = 7, n = 287 vs g = .34, k = 9, n = 459) in two homogeneous sets of studies (*ps* < .0001). No other significant moderators emerged from sub-group and meta-regression analyses. Outlier removal significantly changed the results of moderation analysis: the country where the study had been performed and study design were no longer significant moderators of the association between compassion and vmHRV (*ps* > .30). The percentage of females in the sample became a significant continuous moderator, with studies having more females being characterized by a stronger association between compassion and high vmHRV (β = -.67; *p* = .07). Outlier exclusion did not influence the effect of type of vmHRV measure as a significant moderator.

4. Discussion

This meta-analysis investigated the association between compassion and cardiac vagal tone as assessed via measures of vmHRV or RSA. A significant positive association emerged, which was medium in size (*g* = .54; small-to-medium when an extreme outlier was removed from the analysis, *g* = .40). The present results suggest that cardiac vagal indices might represent a biomarker of the degree to which people feel a sense of safeness in and connectedness to the social environments, thus facilitating a crucial orientation towards "acting with intentions" (i.e., taking with intentionality the actions that will be helpful; Gilbert, 2017), which, in the case of compassion, are approach and caregiving. The size of the effects of compassion on indices of cardiac vagal tone seems comparable with that of lifestyle interventions such increased physical exercise (*d* = .46 in Sandercock et al., 2005), and superior to that of mindfulness-based interventions (rMSSD: Hedges' *g* = .02; SDNN: Hedges' *g* = −.55; HF: Hedges' *g* = -.21 in Rådmark et al., 2019). This is not surprising, if we consider mindfulness as a competency that can be used in the service of several motivations (including, for example, the goal to improve operational readiness and warfighter performance; Blacker et al., 2019), whereas compassion is considered a motivation operating through care-oriented physiological systems, biologically evolved to be threat regulators.

Interestingly, the only study that was conducted in China (Luo et al., 2018) was an extreme positive outlier (i.e., showing a disproportionately high correlation between compassion and vmHRV), which influenced the size of the effect and results of the moderation analysis. This deserves some attention, given that this study was also characterized by one of the highest scores in methodological quality, leading to some hesitance in excluding it. It is possible that the high effect size is due to cultural factors, China being a non-individualistic society, or as suggested by Shea (2014), self-compassion being a post-revolutionary response to changing opportunities and resistance to consumerism.

The only moderator that remained significant after the extreme outlier's exclusion is type of measure used to assess cardiac vagal tone. Studies assessing time- and frequency-domain vmHRV measures were characterized by a stronger positive relationship compared to those using P2T. A possible interpretation for this result is that P2T provides information about heart rate variations that specifically accompany inspiration and expiration (Laborde et al., 2017). It has been shown that estimates of RSA obtained with the P2T method are more affected by variations in respiration rate and volume than other measures of vmHRV especially when respiration slowed (Lewis et al., 2012). In comparison to HF, RMSSD has been shown to be less affected by respiratory rate (Hill et al., 2009). Thus, if compassion was associated with changes in respiratory rate and/or volume, P2T would not accurately track changes in vagal modulation anymore. Nevertheless, it has been argued that estimates of P2T are less related to vagal activity than HRV indices obtained via time- and frequency domain analysis (Lewis et al., 2012, Laborde et al., 2017), thus potentially explaining our findings.

Notably, HRV was similarly associated with being compassionate towards oneself and others. This is not a result that should be taken for granted, given that the relationship between self and other-oriented compassion has not always been reported and seems to vary based on sex and levels of training experience (López et al., 2018; Neff and Pommier, 2013). One can be very compassionate to others, but reluctant to extend compassion to oneself, or one can be very compassionate to oneself but not others (Gilbert et al., 2017). Irrespective of the weak correlation between the two constructs, it seems that both self and other-oriented compassion are significantly associated with the same physiological state of increased vagal tone. This is indirectly supported by a study showing that using a self-reflective mirror intensifies the impact of a self-compassion manipulation on vmHRV, suggesting that self-compassion recruits the same physiological mechanisms as compassion for others (Petrocchi et al., 2017a). Importantly, the element of sensitivity to suffering and caring seems to be particularly linked to increased vmHRV. For example, a very similar prosocial motivation, cooperation, is not always connected to increased vagal tone (Sariñana-González et al., 2019). In fact, cooperating with someone does not necessarily imply sensitiveness to the suffering of the other and the desire to alleviate it; nor does it imply affiliation, benevolence, or any interest in the well-being of oneself or others (Petrocchi and Cheli, 2019).

Similarly, age did not moderate the reported association between compassion and HRV. It has to be noted, however, that the studies included in the present meta-analysis did not comprise children or elderly participants. The only conclusion that can be drawn from this result is that in both adolescents and adults, higher levels of compassion are associated with increased vagal tone.

When the extreme outlier was excluded, such association was particularly true for women compared to men. Sex differences might be explained by the intrinsic and mutual physiological connection between oxytocin and vagal functioning (Carter, 2014; see also Colonnello et al., 2017 for a review). In fact, central release of oxytocin regulates output of the vagal dorsal motor nucleus, thereby regulating bodily functions associated with the parasympathetic nervous system (Thayer et al., 2012).

Lastly, both state (i.e., induced) and trait (i.e., dispositional) compassion were associated with increased vagal control of the heart. This result has relevant clinical implication, pointing to the fact that the positive consequences of compassion on the body can be achieved through practice, training, and therapeutic interventions such as Compassion-Focused Therapy (CFT; Gilbert, 2010), aimed at cultivating compassion both for oneself and others.

5. Limitations and conclusion

One of the most important limitations of the present study is the small number of available studies; likely due to the fact that the inclusion of cardiac vagal indices in empirical research on compassion is a relatively new approach. Fortunately, the analysis suggests that publication bias is unlikely to have influenced our results. Although we made an effort to incorporate the so-called grey literature, only one of the studies met the requirement to be included in the present meta-analysis (Rycroft et al., 2016), mostly due to the lack of data needed to derive the effect size. Second, there was a marked heterogeneity across studies, whose source was not successfully identified in subgroup analyses. To address this limitation, random-effects models were used in the analysis. Nevertheless, there are likely to be several other important moderators that we did not consider.

Third, there is no agreed measure for compassion, and in the literature, a compassionate state has been induced in a number of different ways. This variety of measures and methods for inducing compassion is partly due to the difficulty of distinguishing between prosocial behavior, kindness and compassion despite these constructs being quite different (Gilbert et al., 2019). It is also important to keep in mind that with the exception of three studies conducted on patients with trauma (Rycroft et al., 2016) and somatic symptoms (Kemper et al., 2016; Schaflein et al., 2018), none of the other examined studies had a sample composed by patients with cardiovascular problems. Clearly, there is a need for more research in this field, not only in healthy samples but also in individuals with psychopathological disorders, preferably via analysis of cardiac vagal indices derived from ECG traces that last longer than the short assessment that characterizes existing studies. For example, none of the studies included in the meta-analysis used ecological momentary assessment with concomitant ambulatory ECG monitoring, although there are examples of studies implementing this methodological approach to study self-compassion (e.g., in response to dietary lapses; Schumacher et al., 2018). Moreover, we would recommend focusing on time and frequency domain methods of vmHRV rather than P2T for assessment of cardiac vagal tone. It would also be interesting to examine the putative protective effects of compassion on vmHRV during subsequent sleep, given evidence suggesting that the latter can be negatively influenced by daily self-critical thinking (namely rumination and worry; e.g., Brosschot et al., 2007). Altogether, the current pieces of evidence increase our insight into the relationship between compassion and vmHRV, supporting the need of including vmHRV as a primary outcome measure in assessing and training compassion (Kirby et al., 2017).

Declarations of interest

None.

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References

Arimitsu, K., Hitokoto, H., Kind, S., Hofmann, S.G., 2019. Differences in compassion, well-being, and social anxiety between Japan and the USA. Mindfulness 10, 854–862. https://doi.org/10.1007/s12671-018-1045-6.

Barrett, L., Dunbar, R., Lycett, J., 2002. Human Evolutionary Psychol. London, UK: Palgrave.

Beauchaine, T.P., Thayer, J.F., 2015. Heart rate variability as a transdiagnostic biomarker of psychopathology. Int. J. Psychophysiol. 98, 338–350. https://doi.org/10.1016/j.ijpsycho.2015.08.004

*Beck, A.R., Verticchio, H., Seeman, S., Milliken, E., Schaaba, H., 2017. A mindfulness practice for communication sciences and disorders undergraduate and speech-language pathology graduate students: Effects on stress, self-compassion, and perfectionism. Am. J. Speech Lang. Pathol. 26, 893–907. https://doi.org/10.1044/2017_AJSLP-16-0172.

Beffara, B., Bret, A.G., Vermeulen, N., Mermillod, M., 2016. Resting high frequency heart rate variability selectively predicts cooperative behavior. Physiol Behav., 164, 417–428. https://doi.org/10.1016/j.physbeh.2016.06.011.

Beissner, F., Meissner, K., Bär, K.J., Napadow, V., 2013. The autonomic brain: an activation likelihood estimation meta-analysis for central processing of autonomic function. J. Neurosci., 33:10503-10511. https://doi.org/10.1523/JNEUROSCI.1103-13.2013.

Benarroch, E.E., 1993. The central autonomic network: functional organization, dysfunction, and perspective. Mayo Clin. Proc. 68, 988–1001. https://doi.org/10.1016/s0025-6196(12)62272-1.

Blacker, K.J., Hamilton, J., Roush, G., Pettijohn K.A., Biggs, A.T., 2019. Cognitive training for military application: A review of the literature and practical guide. J. Cogn. Enhanc. 3, 30–51. https://doi.org/10.1007/s41465-018-0076-1.

Bloom, P., 2016. Against Empathy: The Case for Rational Compassion. Ecco Press.

*Bluth, K., Campo, R.A., Futch, W.S., Gaylord, S.A., 2017. Age and gender differences in the associations of self-compassion and emotional well-being in a large adolescent sample. J Youth Adolesc. 46, 840–853. https://doi.org/10.1007/s10964-016-0567-2.

Bornemann, B., Kok, B.E., Böckler, A., Singer, T., 2016. Helping from the heart: Voluntary upregulation of heart rate variability predicts altruistic behavior. Biol. Psychiatry, 119, 54–63. https://doi.org/10.1016/j.biopsycho.2016.07.004.

Brown, S.L., Brown, R.M., 2015. Connecting prosocial behavior to improved physical health: Contributions from the neurobiology of parenting. Neurosci. Biobehav. Rev. 55, 1–17. https://doi.org/10.1016/j.neubiorev.2015.04.004.

Brosschot, J.F., Van Dijk, E., Thayer, J.F., 2007. Daily worry is related to low heart rate variability during waking and the subsequent nocturnal sleep period. Int. J. Psychophysiol. 63, 39–47. https://doi.org/10.1016/j.ijpsycho.2006.07.016.

Brosschot, J.F., Verkuil, B., Thayer, J.F., 2017 Exposed to events that never happen: Generalized unsafety, the default stress response, and prolonged autonomic activity. Neurosci. Biobehav. Rev. 74, 287–296. https://doi.org/10.1016/j.neubiorev.2016.07.019.

Carter, C.S., 2014. Oxytocin pathways and the evolution of human behavior. Annu. Rev. Psychol. 65, 17–39. https://doi.org/10.1146/annurev-psych-010213-115110.

Carter, S., Bartal, I.B., Porges, E., 2017. The roots of compassion: an evolutionary and neurobiological perspective. In, Seppälä, E.M., Simon-Thomas, E., Brown, S.L., Worline, M.C., The Oxford handbook of compassion science (p. 178-188). New York: Oxford University Press.

Chang, C., Metzger, C.D., Glover, G.H., Duyn, J.H., Heinze, H.J., Walter, M., 2013. Association between heart rate variability and fluctuations in resting-state functional connectivity. NeuroImage 68, 93–104. https://doi.org/10.1016/j.neuroimage.2012.11.038.

Cohen, J., 1988. Statistical Power Analysis for the Behavioral Sciences, second ed. Erlbaum, Hillsdale, NJ.

Colonnello, V., Petrocchi, N., Farinelli, M., Ottaviani, C., 2017. Positive social interactions in a lifespan perspective with a focus on opioidergic and oxytocinergic systems: Implications for neuroprotection. Curr. Neuropharmacol. 15, 543–561. https://doi.org/10.2174/1570159X14666160816120209.

Cooper, H, Patall, E.A., 2009. The relative benefits of meta-analysis conducted with individual participant data versus aggregated data. Psychol. Methods, 14, 165-176. https://doi.org/10.1037/a0015565.

Eckberg, D.L., 1985. Human sinus arrhythmia as an index of vagal cardiac outflow. J. Appl. Physiol. 54, 961–66. https://doi.org/10.1152/jappl.1983.54.4.961.

Eisenberg, N., Fabes, R.A., Miller, P.A., Fultz, J., Shell, R., Mathy, R.M., Reno, R.R., 1989. Relation of sympathy and personal distress to prosocial behavior: a multimethod study. *J. Pers. Soc. Psychol*. 57(1), 55- 66. https://doi.org/10.1037//0022-3514.57.1.55.

Eisenberg, N., Fabes, R.A., Murphy, B., Karbon, M., Smith, M., Maszk, P., 1996. The relations of children's dispositional empathy-related responding to their emotionality, regulation, and social functioning. Dev. Psychol. 32, 195–209. https://doi.org/10.1037/0012-1649.32.2.195

Fabes, R.A., Eisenberg, N., Eisenbud, L., 1993. Behavioral and physiological correlates of children's reactions to others in distress. Dev. Psychol. 29, 655–663. http://dx.doi.org/10.1037/0012-1649.29.4.655.

Geisler, F.C.M., Kubiak, T., Siewert, K., Weber, H., 2013. Cardiac vagal tone is associated with social engagement and self-regulation. Biol. Psychol. 93, 279–286. https://doi.org/10.1016/j.biopsycho.2013.02.013.

Geisler, F.C.M., Vennewald, N., Kubiak, T., Weber, H., 2010. The impact of heart rate variability on subjective well-being is mediated by emotion regulation. Pers. Individ. Dif. 49, 723–728. https://doi.org/10.1016/j.paid.2010.06.015.

Gilbert, P., 1992. Depression: The evolution of powerlessness. Guilford Press.

Gilbert, P., 2000. Social mentalities: Internal 'social' conflicts and the role of inner warmth and compassion in cognitive therapy. In, P. Gilbert and Bailey K.G (eds.) Genes on the Couch: Explorations in Evolutionary Psychotherapy (p.118-150). Hove: Brenner-Routledge.

Gilbert, P., 2010. Compassion focused therapy: The CBT distinctive features series. London: Routledge.

Gilbert, P., 2014. The origins and nature of compassion focused therapy. Br. J. Clin Psychol. 53, 6-41. https://doi.org/10.1111/bjc.12043.

Gilbert, P., 2015. An evolutionary approach to emotion in mental health with a focus on affiliative emotions. In: Scherer K, ed. Emotion Rev. https://doi.org/10.1177/1754073915576552.

Gilbert, P., 2015. Affiliative and prosocial motives and emotions in mental health. Dialogues Clin. Neurosci. 17(4), 381–389.

Gilbert, P., 2017. Compassion as a social mentality: An evolutionary approach. In Gilbert, P., Compassion, Concepts, research and applications, 31–68, London, UK: Routledge

Gilbert, P., Basran, J., MacArthur, M., Kirby, J.N., 2019. Differences in the semantics of prosocial words: an exploration of compassion and kindness. Mindfulness 1-13. https://doi.org/10.1007/s12671-019-01191-x

Goetz, J.L., Keltner, D., Simon-Thomas, E., 2010. Compassion: An evolutionary analysis and empirical review. Psychol. Bull. 136, 351–374. https://doi.org/10.1037/a0018807.

Higgins, J.P.T., Green, S., 2011. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0, Retrieved from www.cochrane-handbook.org.

Hill, L.K., Siebenbrock, A., Sollers, J., Thayer, J., 2009. Are all measures created equal? Heart rate variability and respiration. Biomed. Sci. Instrum. 45, 71-76.

Jazaieri, C.S., Jinpa, T., McGonigal, K., Rosenberg, E.L., Finkelstein, J., Simon-Thomas, E., P.R. Goldin, 2013. Enhancing compassion: A randomized controlled trial of a compassion cultivation training program. J. Happiness Stud. 14, 1113–1126. https://doi.org/10.1007/s10902-012-9373-z.

Jennings, J.R., Gianaros, P.J., 2007. Methodology. In J. T. Cacioppo, L. G. Tassinary, G. Berntson (Eds.), Handbook of psychophysiology (3rd ed., pp. 812–833). New York, NY: Cambridge University Press.

Jennings, J.R., Sheu, L.K., Kuan, D.C., Manuck, S.B., Gianaros, P.J., 2016. Resting state connectivity of the medial prefrontal cortex covaries with individual differences in high-frequency heart rate variability. Psychophysiology 53, 444–454. https://doi.org/10.1111/psyp.12586.

*Kemper, K.J., Heyer, G., Pakalnis, A., Binkley, P.F., 2016. What Factors Contribute to Headache-Related Disability in Teens? Pediatr. Neurol. 56, 48–54. https://doi.org/10.1016/j.pediatrneurol.2015.10.024.

*Kemper, K.J., Shaltout, H.A., 2011. Non-verbal communication of compassion: measuring psychophysiologic effects. BMC Compl. Alternative Med. 11, 132. http://www.biomedcentral.com/1472-6882/11/132.

Kim, J.J., Parker, S.L., Doty, J.R., Cunnington, R., Gilbert, P., Kirby, J.N., 2020. Neurophysiological and behavioural markers of compassion. Sci. Rep. 10(1), 6789. https://doi.org/10.1038/s41598-020-63846-3.

Kirby, J.N., Doty, J.R., Petrocchi, N., Gilbert, P., 2017. The current and future role of heart rate variability for assessing and training compassion. Front. Public Health 5, 40. https://doi.org/10.3389/fpubh.2017.00040.

Koenig, J., Rash, J.A., Campbell, T.S., Thayer, J.F., Kaess, M., 2017. A Meta-analysis on sex differences in resting-state vagal activity in children and adolescents. Front. Physiol. 8, 582. https://doi.org/10.3389/fphys.2017.00582.

Koenig, J., Thayer, J.F., 2016. Sex differences in healthy human heart rate variability: A meta-analysis. Neurosci. Biobehav. Rev. 64, 288- 310. https://doi.org/10.1016/j.neubiorev.2016.03.007.

Kogan, A., Oveis, C., Carr, E. W., Gruber, J., Mauss, I. B., Shallcross, A.,. . . Keltner, D., 2014. Vagal activity is quadratically related to prosocial traits, prosocial emotions, and observer perceptions of prosociality. J. Pers. Soc. Psychol. 107, 1051-1063. https://doi.org/10.1037/a0037509.

Kok, B.E., Fredrickson, B.L., 2010. Upward spirals of the heart: Autonomic flexibility, as indexed by vagal tone, reciprocally and prospectively predicts positive emotions and social connectedness. Biol. Psychol. 85, 432–436. https://doi.org/10.1016/j.biopsycho.2010.09.005.

Laborde, S., Mosley, E., and Thayer, J.F., 2017. Heart Rate Variability and Cardiac Vagal Tone in Psychophysiological Research - Recommendations for Experiment Planning, Data Analysis, and Data Reporting. Front. Psychol. 8, 213. https://doi.org/10.3389/fpsyg.2017.00213.

Lamm, C., Rütgen, M., Wagner, I.C., 2019. Imaging empathy and prosocial emotions. Neurosci. Lett. 693, 49–53. https://doi.org/10.1016/j.neulet.2017.06.054.

León, I., Hernández, J. A., Rodríguez, S., Vila, J., 2009. When head is tempered by heart: Heart rate variability modulates perception of other-blame reducing anger. Motivat. Emot. 33, 1–9. https://doi.org/10.1007/s11031-008-9112-2.

Lewis, G.F., Furman, S.A., McCool, M.F., Porges, S.W., 2012. Statistical strategies to quantify respiratory sinus arrhythmia: are commonly used metrics equivalent? Biol. Psychol. 89, 349–364. https://doi.org/10.1016/j.biopsycho.2011.11.009.

Lipsey, M.W., Wilson, D.B., 2001. Practical Meta-analysis. Sage, Thousand Oaks, CA.

Lischke, A., Lemke, D., Neubert, J., Hamm, A., Lotze, M., 2017. Inter-individual differences in heart rate variability are associated with inter-individual differences in mind-reading. Sci. Rep. 7, 11557. https://doi.org/10.1038/s41598-017-11290-1.

Lischke, A., Mau-Moeller, A., Jacksteit, R., Pahnke, R., Hamm, A.O., et al., 2018a. Heart rate variability is associated with social value orientation in males but not females. Sci. Rep. 8, 7336. https://doi.org/10.1038/s41598-018-25739-4.

Lischke, A., Pahnke, R., Mau-Moeller, A., Behrens, M., Grabe, H.J., et al., 2018b. Inter-individual differences in heart rate variability are associated with inter-individual differences in empathy and alexithymia. Front. Psychol. 9, 229. https://doi.org/10.3389/fpsyg.2018.00229.

Lischke, A., Weippert, M., Mau-Moeller, A., Päschke, S., Jacksteit, R., et al., 2019. Sex-specific associations between inter-individual differences in heart rate variability and inter-individual differences in emotion regulation. *Front. Neurosci*. 12, 1040. https://doi.org/10.3389/fnins.2018.01040.

López, A., Sanderman, R., Ranchor, A. V., Schroevers, M. J., 2018. Compassion for others and self-compassion: Levels, correlates, and relationship with psychological well-being. Mindfulness, 9(1), 325–331. https://doi.org/10.1007/s12671-017-0777-z.

Luyten, P., Campbell, C., Allison, E., Fonagy, P., 2020. The mentalizing approach to psychopathology: State of the art and future directions. Annu. Rev. Clin. Psychol. 16, 297-325. https://doi.org/10.1146/annurev-clinpsy-071919-015355.

*Luo, X., Qiao, L., Che, X., 2018. Self-compassion modulates heart rate variability and negative affect to experimentally induced stress. Mindfulness 9, 1522. https://doi.org/10.1007/s12671-018-0900-9.

MacBeth, A., Gumley, A., 2012. Exploring compassion: a meta-analysis of the association between self-compassion and psychopathology. Clin. Psychol. Rev. 32, 545–552. https://doi.org/10.1016/j.cpr.2012.06.003.

Makovac, E., Meeten, F., Watson, D., Herman, A., Garfinkel, S., Critchley, H., Ottaviani, C., 2016. Alterations in amygdala-prefrontal functional connectivity account for excessive worry and autonomic dysregulation in generalized anxiety disorder. Biol. Psychiatry 80, 786–795. https://doi.org/10.1016/j.biopsych.2015.10.013.

Makovac, E., Thayer, J.F., Ottaviani, C., 2017. A meta-analysis of non-invasive brain stimulation and autonomic functioning: Implications for brain-heart pathways to cardiovascular disease. Neurosci. Biobehav. Rev. 74, 330–341. https://doi.org/10.1016/j.neubiorev.2016.05.001.

Mattarozzi, K., Colonnello, V., Thayer J.F., Ottaviani, C., 2019. Trusting your heart: Long-term memory for bad and good people is influenced by resting vagal tone. Conscious. Cog. 75, 102810. https://doi.org/10.1016/j.concog.2019.102810.

*Matos, M., Duarte, C., Duarte, J., Pinto-Gouveia, J., Petrocchi, N., Basran, J., Gilbert, P., 2017. Psychological and physiological effects of compassionate mind training: A pilot randomised controlled study. Mindfulness 8, 1699–1712. https://doi.org/10.1007/s12671-017-0745-7.

Meessen, J., Sütterlin, S., Gauggel, S., Forkmann, T., 2018. Learning by heart—the relationship between resting vagal tone and metacognitive judgments: a pilot study. Cogn. Process 19(4), 557-561. https://doi.org/10.1007/s10339-018-0865-6.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G.; PRISMA Group, 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J. Clin. Epidemiol., 62:1006-1012. https://doi.org/10.1016/j.jclinepi.2009.06.005.

Montero-Marin, J, Kuyken, W., Crane, C., Gu, J., Baer, R., et al., 2018. Self-Compassion and Cultural Values: A Cross-Cultural Study of Self-Compassion Using a Multitrait-Multimethod (MTMM) Analytical Procedure. Front. Psychol. 9, 2638. https://doi.org/10.3389/fpsyg.2018.02638.

Neff, K.D., 2003. Development and validation of a scale to measure self-compassion. Self Identity 2, 223–250. https://doi.org/10.1080/15298860390209035.

Neff, K. D., Pommier, E., 2013. The relationship between self-compassion and other-focused concern among college undergraduates, community adults, and practicing meditators. Self Identity 12(2), 160–176. https://doi.org/10.1080/15298868.2011.649546.

*Oveis, C., Cohen, A.B., Gruber, J., Shiota, M.N, Haidt, J., Keltner D., 2009. Resting respiratory sinus arrhythmia is associated with tonic positive emotionality. Emotion 9, 265–270. https://doi.org/10.1037/a0015383.

Petrocchi, N., Cheli, S., 2019. The social brain and heart rate variability: Implications for psychotherapy. Psychol. Psychother. 92, 208–223. https://doi.org/10.1111/papt.12224.

*Petrocchi, N., Ottaviani, C., Couyoumdjian, A., 2017a. Compassion at the mirror: Exposure to a mirror increases the efficacy of a self-compassion manipulation in enhancing soothing positive affect and heart rate variability. J. Posit. Psychol. 12, 525–536. https://doi.org/10.1080/17439760.2016.1209544.

Petrocchi, N., Piccirillo, G., Fiorucci, C., Moscucci, F., Di Iorio, C., Mastropietri, F., Parrotta, I., Pascucci, M., Magrì, D., Ottaviani, C., 2017b. Transcranial direct current stimulation enhances soothing positive affect and vagal tone. Neuropsychologia. 96, 256–261. https://doi.org/10.1016/j.neuropsychologia.2017.01.028.

Pianka, E.R., 1970. On r- and K-Selection. Am. Nat. 104, 592–597. https://doi.org/10.1086/282697.

Porges, S.W., 1998. Love: An emergent property of the mammalian autonomic nervous system. Psychoneuroendocrinology 23, 837–861. https://doi.org/10.1016/s0306-4530(98)00057-2.

Porges, S.W., 2003. Social engagement and attachment: a phylogenetic perspective. Ann. N. Y. Acad. Sci. 1008, 31–47. https://doi.org/10.1196/annals.1301.004.

Porges, S.W., 2017. Vagal pathways to compassion. In, Seppälä, E.M., Simon-Thomas, E., Brown, S.L., Worline, M.C., The Oxford handbook of compassion science (p. 189-202 are). New York: Oxford University Press.

Porter, C.L., 2003. Coregulation in mother-infant dyads: links to infants' cardiac vagal tone. Psychol. Rep., 92:307-319. https://doi.org/10.2466/pr0.2003.92.1.307.

Quintana, D.S., Guastella, A.J., Outhred, T., Hickie, I.B., Kemp, A.H., 2012. Heart rate variability is associated with emotion recognition: direct evidence for a relationship between the autonomic nervous system and social cognition. *Int. J. Psychophysiol*. 86(2), 168- 172. https://doi.org/10.1016/j.ijpsycho.2012.08.012.

Rådmark, L., Sidorchuk, A., Osika, W., Niemi, M., 2019. A systematic review and meta-analysis of the impact of mindfulness based interventions on heart rate variability and inflammatory markers. J. Clin. Med. 8, 1638. https://doi.org/10.3390/jcm8101638.

*Rockliff, H., Gilbert, P., McEwan, K., Lightman, S., Glover, D., 2008. A pilot exploration of heart rate variability and salivary cortisol responses to compassion-focused imagery. Clin. Neuropsychiatry J. Treat. Eval. 5, 132–139.

Rothstein, H. R., & Hopewell, S., 2009. Grey literature. In H. Cooper, L. V. Hedges, & J. C. Valentine (Eds.), The handbook of research synthesis and meta-analysis (p. 103–125). Russell Sage Foundation.

*Rycroft, C., Schroder, T., Sabin-Farrell, R., Gilbert, P., 2016. Evaluation of a brief self-practice CFT intervention: Phase Two. In "The development and evaluation of a brief self-practice Compassion-Focused Therapy (CFT) intervention as a precursor to treatment as usual (TAU) for trauma patients: A pilot randomised controlled trial (RCT)". DClinPsy thesis, University of Lincoln. http://eprints.lincoln.ac.uk/29718/.

Sakaki, M., Yoo, H.J., Nga, L., Lee, T.H., Thayer, J.F., Mather, M., 2016. Heart rate variability is associated with amygdala functional connectivity with MPFC across younger and older adults. *Neuroimage* 139, 44- 52. https://doi.org/10.1016/j.neuroimage.2016.05.076.

Sandercock, G.R., Bromley, P.D., Brodie, D.A., 2005. Effects of exercise on heart rate variability: inferences from meta-analysis. Med. Sci. Sports Exerc. 37, 433–439. https://doi.org/10.1249/01.mss.0000155388.39002.9d.

Sariñana-González, P., Romero-Martínez, Á., Moya-Albiol, L., 2019. Cooperation between strangers in face-to-face dyads produces more cardiovascular activation than competition or working alone. J. Psychophysiol. 33, 65–75. https://doi.org/10.1027/0269-8803/a000210.

*Schäflein, E., Sattel, H., Schmidt, U., Sack, M., 2018. The enemy in the mirror: self-perception-induced stress results in dissociation of psychological and physiological responses in patients with dissociative disorder. Eur. J. Psychotraumatol. 9, 1472991. https://doi.org/10.1080/20008198.2018.1472991.

Schumacher, L.M., Martin, G.J., Goldstein, S.P., Manasse, S.M., Crosby, R.D., Butryn, M.L., Lillis, J., Forman, E.M., 2018. Ecological momentary assessment of self-attitudes in response to dietary lapses. Health Psychol. 37, 148–152. https://doi.org/10.1037/hea0000565.

Shahrestani, S., Stewart, E.M., Quintana, D.S., Hickie, I.B., Guastella, A.J., 2014. Heart rate variability during social interactions in children with and without psychopathology: A meta-analysis. J. Child. Psychol. Psyc. 55, 981–989. https://doi.org/10.1111/jcpp.12226.

Shea, J.L. 2014. Revolutionary narratives of self-compassion among older women in post-Mao Beijing. Anthropol. Med. 21, 8–26. https://doi.org/10.1080/13648470.2014.880871.

Shook, N.J., Fazio, R.H., Vasey, M.W., 2007. Negativity bias in attitude learning: a possible indicator of vulnerability to emotional disorders? J. Behav. Ther. Exp. Psychiatry 38, 144–155. https://doi.org/10.1016/j.jbtep.2006.10.005.

Smith, T.W., Cribbet, M.R., Nealey-Moore, J.B., Uchino, B.N., Williams, P.G., Mackenzie, J., Thayer, J.F., 2011. Matters of the variable heart: respiratory sinus arrhythmia response to marital interaction and associations with marital quality. J. Pers. Soc. Psychol. 100, 103–119. https://doi.org/10.1037/a0021136.

Strauss, C., Lever Taylor, B., Gu, J., Kuyken, W., Baer, R., Jones, F., Cavanagh, K., 2016. What is compassion and how can we measure it? A review of definitions and measures. Clin. Psychol. Rev. 47, 15–27. https://doi.org/10.1016/j.cpr.2016.05.004.

*Stellar, J.E., Cohen, A., Oveis, C., Keltner, D., 2015. Affective and physiological responses to the suffering of others: Compassion and vagal activity. J. Pers. Soc. Psychol. 108, 572–585.

Stellar, J.E., Keltner, D., 2017. In Gilbert, P., Compassion, Concepts, research and applications, (p.120-134), London, UK: Routledge.

*Svendsen, J.L., Osnes, B., Binder, P.E., Dundas, I., Visted, E., Nordby, H., Sørensen, L., 2016. Trait self-compassion reflects emotional flexibility through an association with high vagally mediated heart rate variability. Mindfulness 7, 1103–1113. https://doi.org/10.1007/s12671-016-0549-1.

Ter Horst, G.J., Postema, F., 1997. Forebrain parasympathetic control of heart activity: retrograde transneuronal viral labeling in rats. Am. J. Phys. 273, H2926–H2930. https://doi.org/10.1152/ajpheart.1997.273.6.H2926.

Thayer, J.F., Ahs, F., Fredrikson, M., Sollers, J.J. 3rd, Wager, T.D., 2012. A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. Neurosci. Biobehav. Rev. https://doi.org/10.1016/j.neubiorev.2011.11.009.

Thome, J., Densmore, M., Frewen, P.A., et al. 2017. Desynchronization of autonomic response and central autonomic network connectivity in posttraumatic stress disorder. *Hum. Brain Mapp.* 38(1), 27-40. https://doi.org/10.1002/hbm.23340.

Wang, S., 2005. A conceptual framework for integrating research related to the physiology of compassion and the wisdom of Buddhist teachings. In P. Gilbert (Ed.), Compassion: Conceptualisations, research and use in psychotherapy (pp. 75–120). New York, NY: Routledge.

Wells, G.A., Shea, B., O'Connell, D., Peterson, J., Welch, V., Losos, M., Tugwell, P., 2011. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Wendt, J., Neubert, J., Koenig, J., Thayer, J.F., Hamm, A.O., 2015. Resting heart rate variability is associated with inhibition of conditioned fear. Psychophysiology 52, 1161–1166. https://doi.org/10.1111/psyp.12456.

Wendt, J., Weymar, M., Junge, M., Hamm, A.O., Lischke, A., 2018. Heartfelt memories: Cardiac vagal tone correlates with increased memory for untrustworthy faces. Emotion 19(1), 178–182. https://doi.org/10.1037/emo0000396.

Weng, H.Y., Fox, A.S., Shackman, A.J., Stodola, D.E., Caldwell, J.Z., Olson, M.C., … Davidson, R.J., 2013. Compassion training alters altruism and neural responses to suffering. Psychol. Sci. 24, 1171–1180. https://doi.org/10.1177/0956797612469537.

Williams, D.P., Cash, C., Rankin, C., Bernardi, A., Koenig, J., et al., 2015. Resting heart rate variability predicts self-reported difficulties in emotion regulation: a focus on different facets of emotion regulation. *Front. Psychol*. 6, 261. https://doi.org/10.3389/fpsyg.2015.00261.

Yarnell, L.M., Neff, K.D., Davidson, O.A., Mullarkey, M., 2019. Gender differences in self-compassion: examining the role of gender role orientation. Mindfulness 10, 1136-1152. https://doi.org/10.1007/s12671-018-1066-1.

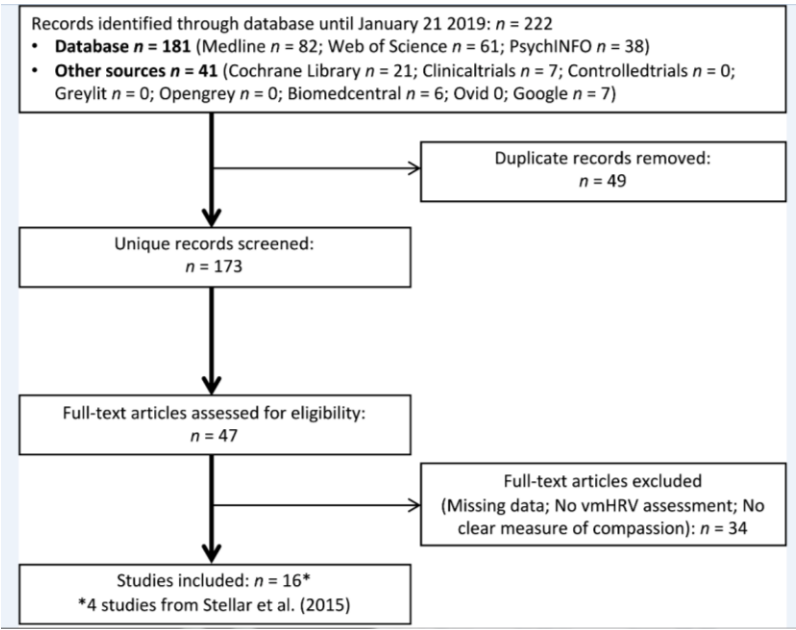

Fig. 1. Flow chart showing study selection for the meta-analysis.

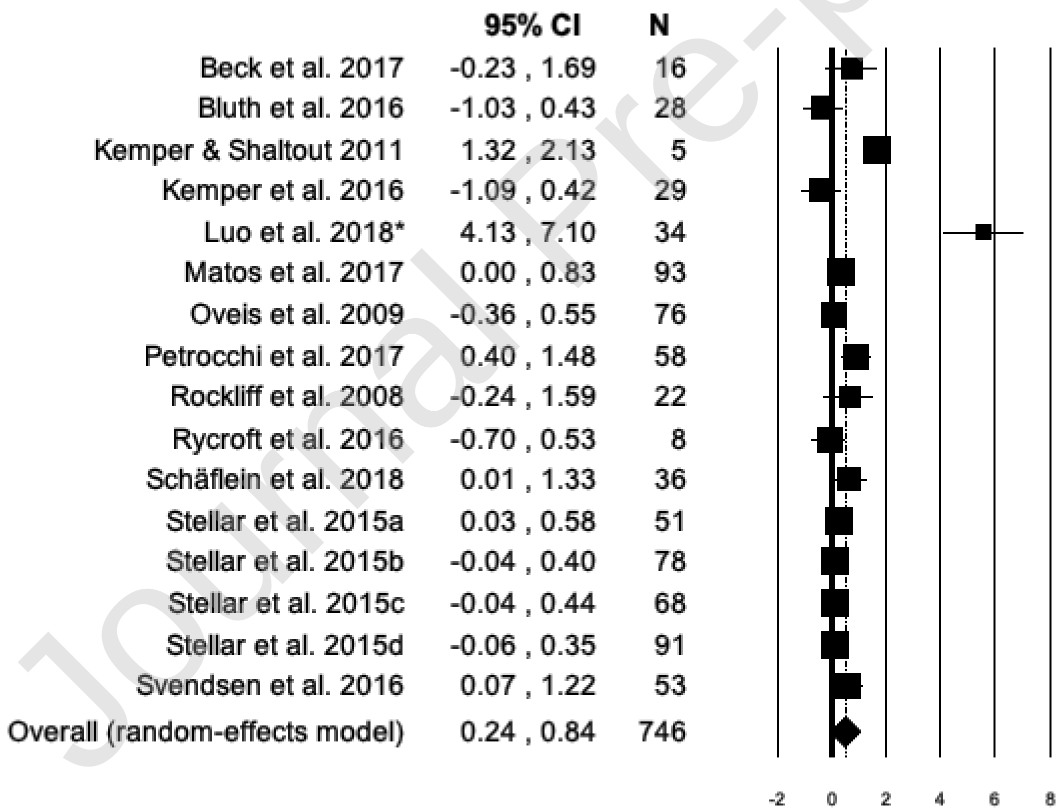

Fig. 2. Forest plot for the meta-analysis.

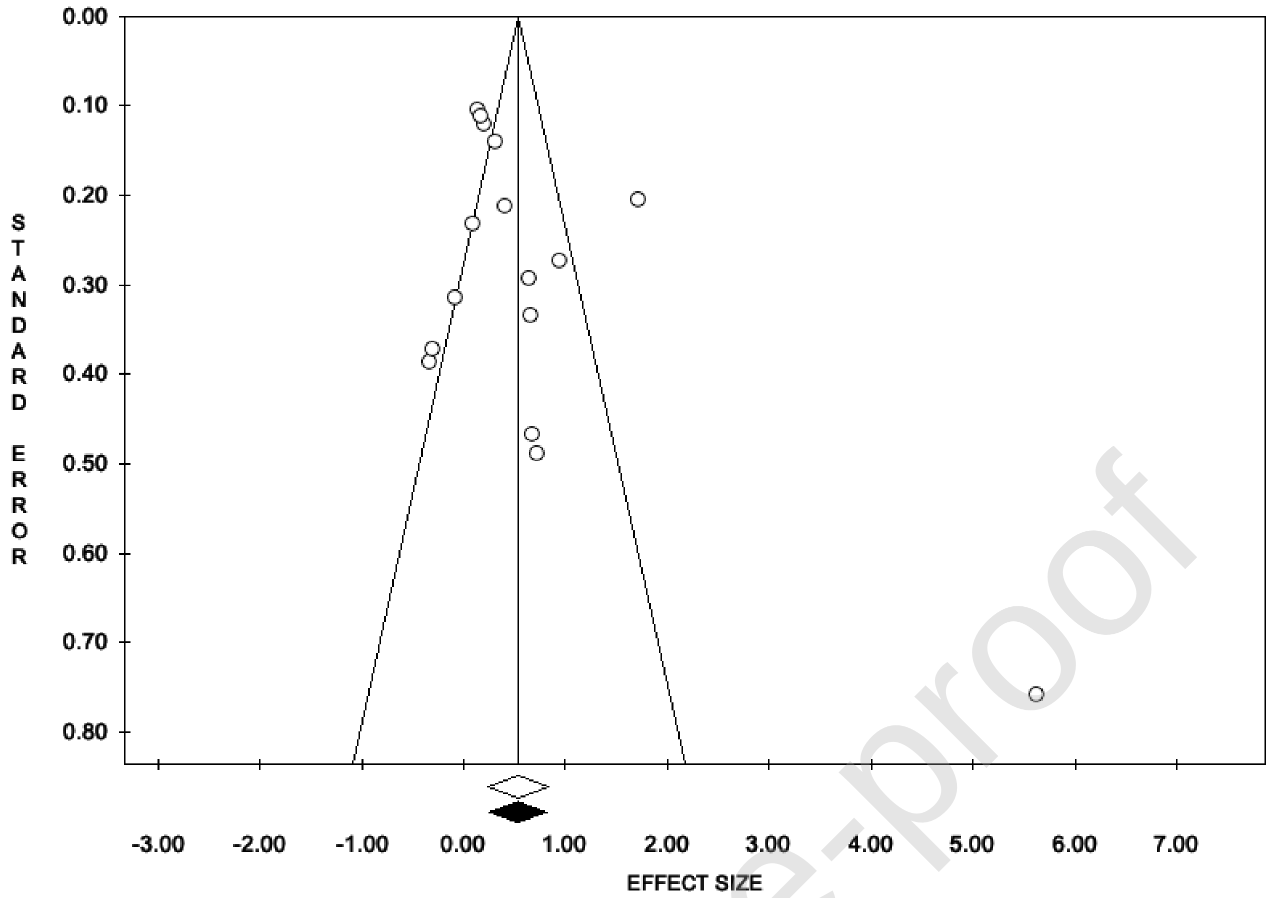

Fig. 3. Funnel plot for the meta-analysis.

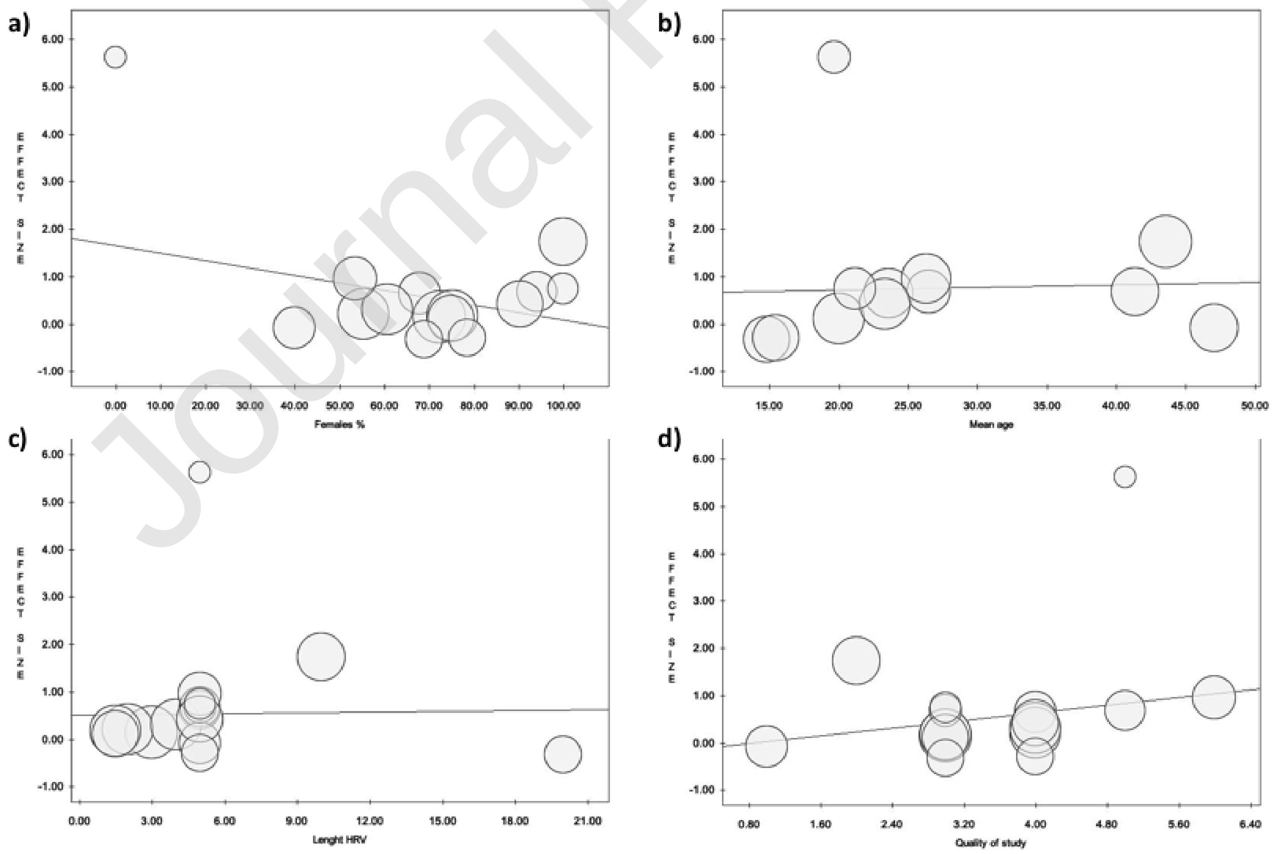

Fig. 4. Results of the meta-regression analyses for: a) % of females; b) mean age; c) length of HRV assessment; d) quality of study.

Table 1

Studies included in the meta-analysis and conditions/comparisons used to derive effect sizes.

Studies	*n*	Wo (%)	Age	Country	Induction/ Measure	HRV measure	Device used	Length HRV[1]	Position	Design	Covariates	Quality	Contrast/ Correlation	Hedges' *g*
Beck et al. (2017)	16	100	21.2	US	Mindfulness practices/SCS (Self)	HF	Biofeedback system	5	Seated	Between	No	3	Post-intervention HRV at rest in Low- (control) vs High-Compassion (experimental) groups	.73
Bluth et al. (2016)	28	78.6	15.5[2]	US	SCS (Self)	RSA	3-lead EKG	5	Seated	Between	No	4	Mean HRV (average of the two 5-min) in LSC vs HSC	-.30
Kemper et al. (2016)	29	69	14.8	US	SCS (Self)	rMSSD	2-lead EKG (Bionex)	20	Supine	Within	No	3	Correlation between SC and HRV	-.34
Kemper and Shaltout (2011)	5	100	43.6	US	LKM-NVCC induction (Comp)	HF	Belt (Biopac BioHarness)	10	Seated	Within	No	2	HRV increase from baseline after the non-tactile NVCC	1.72
Luo et al. (2018)*	34	0	19.7	China	SCS (Self)	rMSSD	HR belt (HRM)	5	Supine	Between	No	5	Baseline HRV in LSC vs HSC	5.62

Note. Wo = women; HRV = vagally-mediated heart rate variability; HF = High Frequency-Heart rate variability; RSA = Respiratory Sinus Arrhythmia; rMSSD = Root Mean Square of the Successive Differences; SDNN = Standard Deviations of Normal-to-Normal R-R intervals; US =

Matos et al. (2017)	93	90.3	23.3	Portugal	CMT/CAAS, SCS, FCS (Comp)[2]	rMSSD	2-lead EKG (eMotion)	5	Seated	Between	No	4	Increase in HRV in the CMT vs control groups	.42
Oveis et al. (2009)	76	75	20	US	Compassion-inducing slides/self-report (Comp)	RSA	2-lead EKG (VU-AMS)	1.5	Seated	Within	No	3	Correlation between slide-congruent emotional reactivity to compassion and rest HRV	.10
Petrocchi et al. (2017a)	58	53.5	26.3	Italy	Compassionate sentences at the mirror/FSCRS (Self)	rMSSD	3-lead EKG (Monitoring)	5	Seated	Between	Gender n.s.	6	HRV change scores after repeating compassionate sentences in front of a mirror	.94
Rockliff et al. (2008)	22	-	26.5[2]	UK	CFI/FSCR, SCS (Self)	SDNN	3-lead EKG (Biopac)	5	Seated	Between	No	3	Correlation between HRV change in response to CFI and SC	.67
Rycroft et al. (2016)	8	40	47.1	UK	SCS-SF, FOC, FSCR (Comp)[2]	rMSSD	HR monitor (Polar)	5	Seated	Within	No	1	Change in HRV after CFT	-.08

United States of America; Self = Self-compassion; LSC = Low Self Compassion; HSC = High Self Compassion; LKM = Loving Kindness Meditation; NVCC = Non Verbal Communication of Compassion; CMT = Compassionate Mind Training; CFI = Compassion Focused Imagery;

Schäflein et al. (2018)	36	94.2	41.4[2]	Germany	SCS (Self)	rMSSD	2-lead EKG (VU-AMS)	5	Seated	Between	No	5	Baseline HRV in Low- (patients) vs High-SC (controls) groups	.67
Stellar et al. (2015; study 1)	51	60.8	-	US	Compassion inducing video/self-report (Comp)	RSA	2-lead EKG (Biopac)	4	Seated	Within	Resp. rate	4	HRV in the compassion vs neutral condition	.31
Stellar et al. (2015; study 2)	78	75.3	-	US	Compassion inducing slides/self-report (Comp)	RSA	2-lead EKG (VU-AMS)	1.5	Seated	Within	No	3	HRV in the compassion vs neutral condition	.18
Stellar et al. (2015; study 3)	68	55.4	-	US	Compassion inducing video/self-report (Comp)	RSA	2-lead EKG (Biopac)	2	Seated	Within	Resp. rate	4	HRV in the compassion vs neutral condition	.20
Stellar et al. (2015; study 4)	91	72.3	-	US	Compassion inducing video/self-report (Comp)	RSA	2-lead EKG (Biopac)	3	Seated	Within	No	3	HRV in the compassion vs neutral condition	.14

CFT = Compassion Focused Therapy; SCS = Self Compassion Scale; CAAS = Compassionate Attributes and Actions Scales; FCS = Fears of Compassion Scale; FSCRS = Forms of Self-criticizing/attacking and Self-reassuring Scale; FOC = Fear of Compassion Scale.

Svendsen et al. (2016)	53	67.9	23.6	Norway	SCS (Self)	rMSSD	2-lead EKG (Biopac)	5	Comfort able position	Within	No	4	Correlation between resting HRV and SCS	.64

[*] Potential outlier; [1] In minutes; [2] Estimated value; [3]The study focused also on self-compassion;

Table 2

Association between compassion and increased vmHRV in different subgroups

	Random-effects model			Heterogeneity		Test of difference
	k	N	g (95% CI)	Q	I^2	Q
	16	746	.54 (.24, .84)**	117.4**	87.2	
Compassion measure[1]						1.35
Self-oriented	8	276	.92 (.16, 1.68)*	56.9**	87.7	
Other-oriented	6	369	.42 (.06, .79)*	52.6**	90.5	
Country						3.25§

Non US	7	304	.1.03 (.33, 1.74)**	50.6**	88.1	
US	9	442	.32 (.00, .64)*	58.5**	86.3	
HRV measure[2]						6.23*
RSA	6	392	.18 (.07, .29)*	2.75	0.00	
Other[3]	10	354	.95 (.35, 1.55)*	80.8**	88.9	
Study design						2.80§
Between-subjects	7	287	1.06 (.27, 1.84)**	51.6**	88.4	
Within-subjects	9	459	.34 (.04, .64)*	58.1**	86.2	

Note. Moderation analyses are presented for the full set of studies including potential outliers (see the Results section for moderation results that changed after outliers' exclusion). k = number of studies; n = number of participants; ES = Hedges' g effect size; CI = Confidence Interval; Q, I^2 = heterogeneity statistics. Q = contrast between (sub)sets of studies. [1]two studies included both self- and other-oriented compassion (i.e., Matos et al., 2017; Rycroft et al., 2017); [2] Results did not substantially change when studies assessing SDNN (n = 1) and HF-HRV (n = 2) were left out from the analysis; [3] rMSSD, SDNN, and HF-HRV; § p = .07; * p < .05; ** p < .001. US = United States of America; RSA = respiratory sinus arrhythmia.