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The association between anxiety and cardiac interoceptive accuracy: A systematic review and meta-analysis

Kiera Louise Adams[1], Alexandra Edwards[2], Charlotte Peart[2], Lyn Ellett[3], Inês Mendes[2], Geoffrey Bird[1] & Jennifer Murphy[2]

[1] Department of Experimental Psychology, University of Oxford, Oxford, UK

[2] Department of Psychology, Royal Holloway, Egham, UK

[3] Department of Psychology, Southampton University, Southampton, UK

* corresponding author: kiera.adams@univ.ox.ac.uk; Anna Watts Building, Radcliffe Observatory Quarter, Woodstock Road, Oxford, OX2 6GG

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Abstract

Anxiety is often conceptualised as the prototypical disorder of interoception (one's perception of bodily states). Whilst theoretical models predict an association between interoceptive accuracy and anxiety, empirical work has produced mixed results. This manuscript presents a pre-registered systematic review (https://osf.io/2h5xz) and meta-analysis of 55 studies, obtained via a Pubmed search on 9th November 2020, examining the relationship between state and trait anxiety and objectively measured cardiac interoceptive accuracy as assessed by heartbeat counting and discrimination tasks. Potential moderators of this relationship - the age, gender and clinical diagnoses of participants, the anxiety measures used and the study design - were also explored. Overall, we found no evidence for an association between cardiac interoceptive accuracy and anxiety, with none of the factors examined moderating this finding. We discuss the implications these findings have for future research, with a particular focus on the need for further investigation of the relationship between anxiety and other facets of interoception.

Keywords: interoceptive accuracy, cardiac interoception, anxiety, panic disorder, meta-analysis

1. Introduction

Interest in interoception, the perception of the body's internal state (including gastric, respiratory and cardiac signals; Craig, 2002), has increased exponentially in recent years (Khalsa & Lapidus, 2016). Such interest is arguably driven by theoretical and empirical work that implicates interoception in the aetiology of several psychiatric conditions (Khalsa & Lapidus, 2016; Brewer et al., 2016). Of all conditions, anxiety is most often thought of as the prototypical disorder of interoception (Khalsa & Lapidus, 2016). Indeed, physiological symptoms, such as a racing heart rate and rapid breathing, are included in the diagnostic criteria for anxiety disorders (American Psychiatric Association, 2013; World Health Organisation, 2019). Ehlers (1993) suggested that in panic disorder specifically, increased sensitivity to (e.g., accuracy of perceiving) cardiac signals may lead to increased catastrophising when interpreting changes in heart rate, resulting in panic attacks (Ehlers & Breuer, 1992; Ehlers, 1993). More recently, Garfinkel and colleagues suggested that anxiety may instead be characterised by poor interoceptive accuracy, coupled with increased attention to interoceptive signals (Garfinkel et al., 2016). Similarly, Paulus and Stein posit that both anxiety and depression may be caused by the combination of reduced interoceptive accuracy and an exaggerated response to aversive somatic signals (Paulus & Stein, 2010). Although each of these theories differ in the direction of the predicted association, all predict a relationship between interoceptive accuracy and anxiety.

Despite good theoretical reasons to expect that anxiety should relate to atypical interoceptive accuracy, empirical evidence is equivocal (for a review see Domschke et al., 2010). With regard to cardiac interoceptive accuracy, some studies suggest that higher anxiety relates to greater interoceptive accuracy (Ehlers & Breuer, 1992; Ehlers 1995; van der Does et al., 2000; Dunn et al., 2010; Pollatos et al., 2007), while other studies have observed either no relationship (Antony et al., 1995; Barsky et al, 1994; Palser et al., 2018),

or the opposite pattern of results (De Pascalis et al., 1984; Garfinkel et al., 2016; Sugawara et al., 2020).Given such mixed results and the considerable disease burden of anxiety disorders (Baxter et al., 2013; Mojtabai et al., 2015; Scott et al., 2016), it is important to establish whether a relationship exists between anxiety and cardiac interoceptive accuracy, the direction of this association, and which, if any, specific moderators may explain the mixed results in the literature. Such understanding is necessary in order to establish the clinical relevance of interoceptive accuracy for anxiety disorders, which in turn may provide new opportunities for intervention.

Previous studies have identified a number of factors that appear to influence the direction of the association between anxiety and cardiac interoceptive accuracy. In one commonly used task, the heartbeat counting task (HCT), participants are required to count their heartbeats over a series of intervals which are then compared to an objective estimate to determine accuracy (Schandry, 1981). Although a recent meta-analysis found no overall relationship between anxiety and HCT performance (Desmedt et al., 2020), this review only considered two potential moderators (clinical diagnosis and the anxiety measure used), neither of which had an effect. One additional moderator could be the instructions given to participants; when participants are explicitly told not to guess, individuals with panic/anxiety disorders appear to perform similarly to controls, with superior performance in panic/anxiety patients only observed when more liberal instructions are utilized (Ehlers et al., 1995; Smith et al., 2021). This may suggest that reports of superior performance in those with anxiety are driven by factors other than interoceptive accuracy, such as a greater knowledge of their typical heart rate or a bias towards over-reporting.

Concerns regarding the validity of the heartbeat counting task (for an overview, see Murphy et al., 2018) have prompted an increased focus on other measures of cardiac interoceptive accuracy. A commonly used alternative is the heartbeat detection task

(Whitehead, 1977; Clemens, 1984; Yates et al, 1985; Brener et al., 1993), in which participants are required to judge whether an auditory or visual stimulus is synchronous with their heartbeat. As performance in the HDT is not confounded by prior knowledge of one's heart rate, it is less likely than the HCT to provide false positives (i.e., to suggest a participant can detect their heart beat during the task when they can in fact not). Importantly, although both the HCT and HDT are measures of cardiac interoceptive accuracy, a previous meta-analysis suggests only a small relationship between these two tasks (4.4% of shared variance; Hickman et al., 2020). Unsurprisingly given this small association, the measures also often show different relationships with outcome variables; for example, Garfinkel and colleagues found that whilst trait anxiety was negatively correlated with performance on the HDT, this relationship was not observed with the HCT (Garfinkel et al., 2016). Conversely, Ewing and colleagues found that those with a clinical diagnosis of anxiety were significantly poorer than controls on the HCT, though no difference was found with the HDT (Ewing et al., 2017). Given such discrepancies, coupled with evidence for lack of correspondence between the HCT and HDT, it remains an outstanding question whether the relationship between anxiety and interoception varies as a function of the cardiac interoceptive accuracy task employed, as previous meta-analyses have only focused on the HCT (Desmedt et al., 2020)

The inclusion of clinical groups and the measurement of anxiety may also moderate relationships between anxiety and cardiac interoceptive accuracy. Indeed, some have argued that a relationship between anxiety and cardiac interoceptive accuracy is only observed in clinical samples, who demonstrate the most extreme manifestations of anxiety symptoms (Domschke et al., 2010; but see Desmedt et al., 2020 for conflicting evidence using the HCT). Others have highlighted the possible influence of depression on the relationship between anxiety and interoceptive accuracy (Desmedt et al., 2020). Despite

strong associations between anxiety and depression (Lamers et al., 2011; Dobson 1985), depression and anxiety are often reported to have different relationships with cardiac interoceptive accuracy- depression is thought to be associated with worse interoceptive accuracy and anxiety is often thought to be associated with better interoceptive accuracy (Dunn et al., 2010; Pollatos et al., 2009; but see Garfinkel et al., 2016). The influence of depression on the relationship between anxiety and cardiac interoceptive accuracy may be particularly important to consider where anxiety is assessed by self-report measures as evidence suggests such measures may be non-specific and pick up on negative affect and symptoms of depression (Clark & Watson, 1991; Lovibond & Lovibond, 1995).

The demographics of participants may also alter the strength of the association between cardiac interoceptive accuracy and anxiety. Both interoceptive accuracy and anxiety change across development, with some evidence that interoceptive ability decreases in adolescence (Murphy et al., 2017) around the time that anxiety disorders typically have their onset (Kessler et al., 2007). As such, one might expect to see a stronger relationship in adults compared to children, after the point where anxiety disorders typically emerge. Additionally, considering evidence for sex differences in interoception, with males showing superior accuracy on cardiac tasks (Prentice & Murphy, 2021), the gender ratio of participants could also be a moderator. As recent evidence suggests that interoceptive accuracy relates to certain emotion regulation strategies in men only (Lischke et al., 2020), it may be that the association between cardiac interoceptive accuracy and anxiety is greater in males. Finally, there is suggestion that any association between interoception and psychopathology may manifest more prominently during states of cardiac perturbation, meaning that a greater relationship may be observed if participants' heart rates are manipulated to be either higher or lower than baseline (Paulus et al., 2019).

Given mixed results in the literature regarding the relationship between anxiety and cardiac interoceptive accuracy, the aim of this pre-registered systematic review and meta-analysis was to confirm the presence or absence of a relationship between anxiety and cardiac interoceptive accuracy and assess the extent to which previously identified factors moderate such relationships. In terms of moderators, we focused on assessing the impact of the interoceptive accuracy task employed, the instructions used (for the HCT), the measurement of anxiety, whether clinical groups were included, depression (where anxiety was assessed using questionnaires), the age and gender of participants, and whether or not heart rate was manipulated on the pooled effect size.

2. Method

2.1 Search strategy

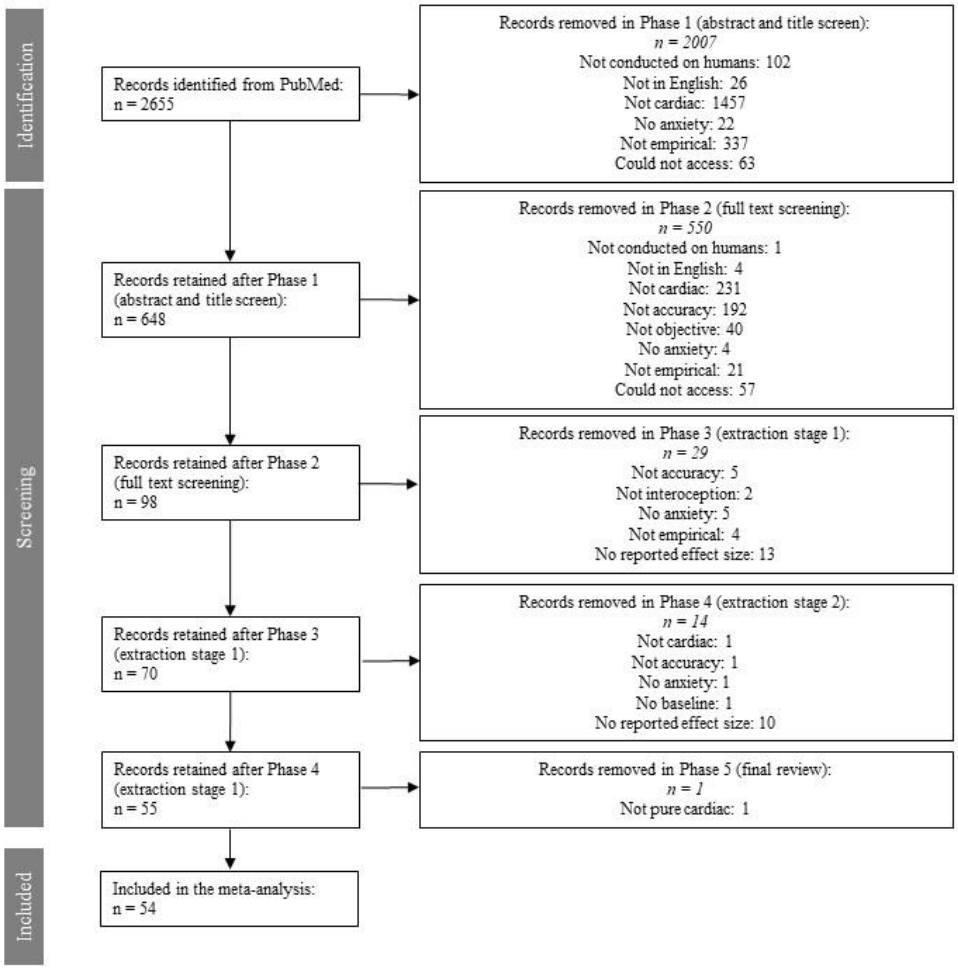
The systematic literature search was conducted following the 2020 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The PRISMA checklists and extracted data can be found at https://osf.io/gvk97/. The search strategy was pre-registered prior to the search and can be found at https://osf.io/2h5xz. Cardiac interoceptive accuracy was focused on given its primacy in the literature and because discrepant results with respect to interoceptive accuracy are common reportedly in this domain. We searched PubMed for studies that were available online before 9th November 2020 using the following search terms:

((Interoception OR viscerоception OR interoceptive OR ((awareness OR perception OR discrimination OR Detection OR tracking OR counting) AND Heartbeat OR Heart beat OR Cardiac)) AND Anxiety)

This search returned 2655 studies.

2.2 Study selection and extraction

Figure 1:



Note: This figure depicts the number of papers excluded at each phase, and the reasons why. For papers where multiple reasons were given for exclusion, just one reason is presented here for illustrative purposes.

Identified articles were screened in four phases by four reviewers (CP, AE, KA and JM). First, two reviewers (CP and AE) assessed the titles and abstracts for relevance for the meta-analysis. Interrater reliability was acceptable (80.3% agreement) and all studies where disagreement was observed were carried forward to full text screening. This initial screening resulted in the removal of 2007 articles. Studies were removed if they were not conducted on humans, were not in English, did not assess cardiac interoception or anxiety, did not present empirical data pertaining to the relationship between anxiety and cardiac

interoception or the full text could not be retrieved (Figure 1). The remaining 648 articles were submitted for full-text screening.

Second, light full text screening was completed by CP and AE. Again, interrater reliability was acceptable (70.68%). Disagreement was resolved by a third reviewer (JM), resulting in the removal of 550 articles. Reasons for removal were consistent with the abstract screening phase. Additionally, studies were removed if they did not utilise objective measures of interoception or if the measures did not assess cardiac interoceptive accuracy. Third, detailed data extraction was completed by two reviewers (CP and AE) and checked for accuracy by both JM and KA. Extracted data included details of the type and version (where applicable) of the cardiac interoceptive accuracy task employed, the type of anxiety measure used, whether strict 'no guessing' instructions were used for the HCT, whether participants' heart rates were manipulated, whether studies included participants with a clinical diagnosis of anxiety, depression, or any clinical group, the age of participants and the proportion of male and female participants. In addition to the number of participants, where correlations were reported the R value was taken as the effect size of interest. For group designs (or studies where proportions of good vs. poor perceivers were reported), F, T or X^2 test statistics were extracted or manually calculated from extracted means and standard deviations or cross tabulations. A further 43 studies were removed during the extraction stages for reasons consistent with the full text screening phase, in addition to articles that either did not report effect sizes for the simple relationship between anxiety and cardiac interoceptive accuracy, did not include assessment of anxiety directly (e.g., focused solely on disorders, such as Obsessive Compulsive Disorder, which are no longer included as an anxiety disorder in the DSM5 (American Psychiatric Association, 2013) or cortisol measurements), or did not include a baseline control condition (e.g., only scores following cardiac interoceptive training were reported). Following discussion with

GB, a further paper was removed because it involved intensity estimations of cardiac and breathing sensations simultaneously, and thus did not focus solely on cardiac interoceptive accuracy (Khalsa et al., 2015). This resulted in 54 articles that were included in the meta-analysis. We opted not to contact authors for unreported data given previous experiences of extremely poor response rates for previous meta-analyses (Prentice & Murphy, 2021). Where correlations were calculated across different participant groups (e.g., case and controls), or where both the HCT and HDT were employed, multiple effect sizes were extracted from papers.

Of the studies included, 49 utilised the heartbeat counting task (or a similar variant) and 6 utilised the heartbeat detection task (or a similar variant). 33 reported correlations between questionnaire measures of anxiety and cardiac interoceptive accuracy, and 22 utilised a case-control design and compared means across groups. In these 22 studies, 9 grouped by clinical diagnosis and 13 by other methods (e.g., questionnaire cut offs, or the occurrence of a panic attack after caffeine challenge). 26 studies included at least one clinical group, whilst 20 studies' samples were comprised solely of typically developing individuals, and sufficient detail was not reported in 8. The majority of studies focused on adult populations, with only 4 studies reporting data collected in children.

2.3 Measures used: interoceptive accuracy

2.3.1 HCT and Variants

In the HCT (Schandry, 1981), participants are instructed to count the number of heart beats that they believe to have occurred over a series of intervals while their heartbeat is objectively recorded. The durations used vary across trials, and participants are not told how long each interval will last. Most commonly, either an accuracy or error score is calculated from the ratio of correct responses. Four studies that used the heartbeat tapping

task (where participants tap or press a button as they feel each heartbeat; De Pascalis et al., 1984) were also included in the HCT category, as both tasks involve similar processes (Brener & Ring, 2016) and three of the four studies using the heartbeat tapping task calculated accuracy using the same equation as the majority of studies using the HCT (e.g., Schandry,1981). Two further tasks were also classed as variants of the HCT, as they both require a determination of the number of heartbeats in a given period. Steptoe and Vögele (1992) asked participants to rate the degree to which they felt their heart racing on a 10cm scale, following various tasks designed to increase heart rate. Similarly, Näring and colleagues (1995) instructed participants to rate the degree to which they felt their "pounding heart" and "fast pulse" on a five-point scale following tasks designed to increase heart rate. Accuracy was determined by correlating these ratings with actual heart rate.

2.3.2 HDT and Variants

In the 2AFC HDT (used by all studies included in this meta-analysis; Whitehead, 1977), participants are required to judge whether an external stimulus, such as a series of tones or flashes of light, is presented synchronously or asynchronously with their heartbeat. The delays chosen as synchronous and asynchronous vary across studies, with synchronous defined as between 0 to 300ms after the r wave, and asynchronous ranging from 384 to 600ms. As with the HCT, scoring of these tasks varied, and included error scores, accuracy scores, and d'.

2.4 Measures used: anxiety questionnaires

17 different anxiety questionnaires were used to assess anxiety across 48 studies (Tables 1-3).

2.4.1 Assessing the impact of depression on anxiety scores

As pre-registered, we sought to examine the extent to which depression may influence the relationship between anxiety and interoception. Specifically, we sought to examine whether the extent to which non-specific items included in anxiety questionnaires, which may tap symptoms of depression (Lovibond & Lovibond, 1995), may modulate relationships. Scoring of questionnaires was conducted by two trained clinical psychologists (IM and LE) who rated each item from each questionnaire according to the extent to which items were 1) specifically tapping anxiety symptoms 2) may pick up on symptoms of depression and 3) may pick up on symptoms of other conditions (e.g., were unlikely to be anxiety or depression). Interrater agreement was acceptable overall (74.78%), with discrepancies resolved through discussion. Scores were then summed for each questionnaire (omitting the few number of items where an 'other' response was given) and a score was provided reflecting the extent to which the majority of items assessed anxiety specifically, or may be influenced by depression. Only the STAI-T was identified as having more than 50% of items that may pick up on symptoms of depression.

Table 1:

Anxiety questionnaires

Measure	What does it assess	Number of items	Test-retest reliability	Internal consistency	Influenced by depression?
State-Trait Anxiety Inventory- State (STAI-S) *Spielberger et al., 1983*	State anxiety	20	0.70 *(Barnes et al., 2002)*	0.91 *(Barnes et al., 2002)*	No

State-Trait Anxiety Inventory- Trait (STAI-T) *Spielberger et al., 1983*	Trait anxiety	20	0.88 *(Barnes et al., 2002)*	0.89 *(Barnes et al., 2002)*	Yes
KSP-ANX			Not found	Not found	Not found
Self-consciousness scale- social anxiety subscale *Fenigstein et al., 1975*	Social anxiety (trait)	22	0.73 *Fenigstein et al., 1975*	Not found	No
Anxiety Sensitivity Index (ASI) *Reiss et al., 1986*	Anxiety sensitivity (trait)	16	0.72 *Rodriguez et al., 2004*	0.88 *Carter et al., 2009*	No
PROMIS Anxiety scale short form 4a *Pilkonis et al., 2011*	Anxiety (trait)	4	Not found	0.89 *Kroenke et al., 2014*	No
Anxiety Sensitivity Index 3 *Taylor et al., 2007*	Anxiety sensitivity (trait)	18	0.76 *Ghisi et al., 2016*	0.93 *Wheaton et al., 2012*	No
Mood and Anxiety Symptom Questionnaire Short Form- Anxious Arousal *Watson & Clark, 1991*	Anxiety (trait)	17	Not found	0.77 *Lackner & Fresco, 2016*	No

Social Anxiety Scale for Children- Revised (SASC-R) *La Greca & Stone, 1993*	Social anxiety (trait)	24	0.42 (Fear of Negative Evaluation subscale); 0.36 (Social Avoidance and Distress (New) subscale); 0.36 (Social Avoidance and Distress (General) subscale) *Storch et al., 2003*	0.86 (Fear of Negative Evaluation subscale); 0.78 (Social Avoidance and Distress (New) subscale); 0.69 (Social Avoidance and Distress (General) subscale) *La Greca & Stone, 1993*	No
Revised Children's Anxiety and Depression Scale (RCADS) – Total Anxiety Subscale *Chorpita et al., 2005*	Anxiety (trait)	37	0.75 (Separation Anxiety Disorder subscale); 0.80 (Social Phobia subscale); 0.65 (Obsessive Compulsive Disorder subscale); 0.76 (Panic Disorder subscale); 0.79 (Generalised Anxiety Disorder subscale) *Chorpita et al., 2000*	0.78 (Separation Anxiety Disorder subscale); 0.87 (Social Phobia subscale); 0.82 (Obsessive Compulsive Disorder subscale); 0.88 (Panic Disorder subscale); 0.84 (Generalised Anxiety Disorder subscale) *Chorpita et al., 2005*	No
SCARED- panic/ somatic subscale *Birmaher et al., 1997*	Panic (trait)	13	.61 *Behrens et al., 2019*	.84 *Hale et al., 2011*	Low agreement (scored for SCARED overall)
SCARED- general subscale *Birmaher et al., 1997*	General anxiety (trait)	9	.62 *Behrens et al., 2019*	.81 *Hale et al., 2011*	Low agreement (scored for SCARED overall)

SCARED-separation subscale *Birmaher et al., 1997*	Separation anxiety (trait)	8	.59 *Behrens et al., 2019*	.72 *Hale et al., 2011*	Low agreement (scored for SCARED overall)
SCARED- social phobia *Birmaher et al., 1997*	Social anxiety (trait)	7	.60 *Behrens et al., 2019*	.78 *Hale et al., 2011*	Low agreement (scored for SCARED overall)
SCARED- school phobia *Birmaher et al., 1997*	School avoidance (trait)	4	.60 *Behrens et al., 2019*	.62 *Hale et al., 2011*	Low agreement (scored for SCARED overall)
Child Anxiety Sensitivity Index (CASI) *Silverman et al., 1991*	Anxiety sensitivity (trait)	18	0.76 *Silverman et al., 1991*	0.87 *Silverman et al., 1991*	No
Fear of Negative Evaluation Scale (FNE) - German *Watson & Friend, 1969; Vormbrock & Neuser, 1983*	Social anxiety (trait)	20	0.90 *Reichenberger et al., 2015*	0.94 *Reichenberger et al., 2015*	Not found
Beck Anxiety Inventory (BAI) *Beck et al., 1988*	Anxiety (trait)	21	0.67 *Fydrich et al., 1992*	0.94 *Fydrich et al., 1992*	No
The Short Health Anxiety Inventory (SHAI) *Warwick & Salkovskis,1989*	Health anxiety (trait)	18	0.76 *Salkovskis et al., 2002*	0.95 *Salkovskis et al., 2002*	No

Sheehan Patient-Rated Anxiety Scale (SPRAS) *Kaiya, 2008*	Anxiety (trait)	35	0.91 *Mimura et al., 2011*	0.96 *Mimura et al., 2011*	No
IPAT- anxiety *Cattell, 1969*	Anxiety (trait)	40	0.94 *Levitt & Persky, 1962*	0.78 (men); 0.84 (women) *Bendig, 1966*	Not found
Depression and Anxiety Stress Scale – anxiety (DASS-A) *Lovibond & Lovibond, 1995*	Anxiety (trait)	14	0.79 *Brown et al., 1997*	0.89 *Brown et al., 1997*	No
Whitely Index (WI) *Pilowsky, 1967*	Health anxiety (trait)	14	0.90 (Medical outpatients, *Speckens et al., 1995*)	0.80 (medical outpatients); 0.78 (general practice); 0.76 (general population; *Speckens et al., 1995*)	No
Whitely Index (WI) Two factor version *Schwarz et al., 2007*	Health anxiety (trait)	10	Not found	0.63 - 0.72 *Schwarz et al., 2007*	No

Note: In some studies, the total, or an average of, the STAI-S and STAI-T was taken. For the "influenced by depression" column, two clinicians independently rated the items from these scales according to whether or not they related to anxiety specifically, may pick up on symptoms of depression, or appeared to tap other symptoms entirely. Due to the low number of items scored as "other" (one for the SASC-R, one for the SHAI, four for the RCADS, five for the WI, five for the WI 2 factor version, three for the SPRAS and three for the SCARED), these items were ignored when calculating the extent to which scales were influenced by depression.

2.5 Heart rate manipulation

Whether or not participants' heart rate was manipulated was coded as a binary variable. In two studies, participants completed a number of tasks that may increase their heart rate, including mental arithmetic, the cold pressor test or squeezing a rubber ball (Näring et al., 1995; Steptoe et al., 1992). One study induced hyperventilation in participants (Sturges et al., 1998), another played sexual and non-sexual films to participants (Suschinsky et al., 2014), and in a final study participants were told to prepare to give a public speech (Stevens et al., 2011). In all of these studies, all or the majority of the manipulations resulted in an increased heart rate.

2.6 Clinical diagnoses

For conditions other than anxiety (e.g., depression), we only classified the study as including clinical groups if the participants had received a diagnosis from a clinician. For anxiety, we took this approach in our initial moderator analyses, with follow up analyses extending inclusion to studies that classified individuals as anxious where questionnaire scores were above established clinical thresholds.

2.7 Analysis strategy

Separate meta-analyses were conducted for the HCT and HDT given evidence that the two measures are not highly correlated (Hickman et al., 2020). For the HCT, separate meta-analyses were conducted for state and trait measures of anxiety. Two studies utilised a composite score of the STAI including both state and trait anxiety (Michal et al., 2014; Stern et al., 2020). These studies were included in both state and trait models and excluded for comparisons. Separation of state and trait anxiety was not conducted for the HDT as only two studies examined the relationship between the HDT and state anxiety (Garfinkel et al., 2016; De Pascalis et al., 1991). In these initial analyses, data from both clinical groups and typically developing participants was accepted, as a greater distribution of scores

would be expected for studies including clinical populations. In primary analyses we excluded papers reporting data in child populations, which were examined later in separate meta-analyses. One study did not report the ages of participants (Watson et al., 2019), but was included in the adult group given recruitment methods focused on university students. Where pre-registered or a sufficient number of papers were identified, specific moderators were examined. As a number of studies reported the relationship between multiple measures of anxiety and cardiac interoceptive accuracy, for these studies composite scores were created using the method described by Borenstein and colleagues (2009).

All analyses were conducted on R version 4.1.2 (R Core Team, 2013), using the devtools, dmetar and meta packages (Wickman et al., 2021; Harrer et al., 2019; Balduzzi et al., 2019). The analysis code is available upon request. All test statistics were converted to R values, which was chosen as the majority of studies examined correlations between cardiac interoceptive accuracy and anxiety. R-to-Z transformations were implemented by the software prior to analyses. As the direction of scoring varied across studies (with differences in whether error or accuracy scores were computed), the sign on all effect sizes was adjusted such that a positive score indicates better cardiac interoception with increasing anxiety. As substantial heterogeneity was expected, random-effects models were employed (Field, 2001; Hunter & Schmidt, 2000) and the conservative Sidik-Jonkman estimator was applied (Sidik & Jonkman, 2007). Heterogeneity was investigated for each meta-analysis, and Q and I^2 statistics are reported. A Q statistic indicates whether variation is greater across or within studies, and is calculated by summing the weighted squared differences between the effect sizes of each study and the fixed-effect estimate. I^2 indicates the percentage of variation in effect sizes across studies that is due to heterogeneity rather than chance. Values of 25%, 50% and 75% indicate low, moderate, and high heterogeneity respectively. Funnel plots which mapped the relationship between

effect sizes and standard error were created as one method to explore publication bias. Additionally, Egger's tests were used to assess the asymmetry of the funnel plot. This could only be done in instances where there were 10 or more studies included (Borenstein et al., 2009). We also conducted influence analysis using the leave-one-out method to establish the influence of individual studies on the overall pooled effect sizes.

Table 2:
HCT studies

Author	N	Age	F:M ratio	Anxiety patients	Depression patients	Clinical group	Interoception task	No guessing instructions?	HR manipulation?	Anxiety measure	E.S. type	Extracted E.S.	r
Abrams et al., 2018	61	Adults	0.57	NR	NR	NR	HCT	No	No	ASI-3 and STAI-T	R	0.08 (comp)	0.08
Ardizzi et al., 2018	36	Adults	0.39 +	No	No	No	HCT	No	No	SCS - Social anxiety subscale	R	-0.25	-0.25
Borg et al., 2018	42	Adults	1.00	NR	NR	Fibromyalgia	HCT	No	No	STAI-S	R	0.07	0.07
Borg et al., 2018	42	Adults	1.00	NR	NR	Fibromyalgia	HCT	No	No	STAI-T	R	0.15	0.15
De Pascalis et al., 1984	16	Adults	0.50	NR	NR	NR	HCT - Tapping	No	No	IPAT-anxiety (Italian)	R	-0.51*	-0.51
Di Lernia et al., 2018	30	Adults	1.00	No	No	No	HCT	No	No	STAI-S (Italian)	R	-0.18	-0.18
Di Lernia et al., 2018	30	Adults	1.00	No	No	No	HCT	No	No	STAI-T (Italian)	R	-0.03	-0.03
Di Lernia et al., 2020	60	Adults	0.78	NR	NR	Chronic pain	HCT	Yes	No	STAI-S (Italian)	R	-0.28	-0.28
Dunn et al., 2010	111	Adults	0.73	Yes	Yes	Anxiety and depression	HCT	No	No	HC MASQ-S and STAI-T	R	0.18 (comp)	0.18
Ehlers et al., 1992	111	Adults	0.74	Yes	NR	PD	HCT	No	No	CD - panic	T	2.42*	0.23
Ehlers et al., 1992	96	Adults	0.73	Yes	NR	IP	HCT	No	No	CD - infrequent panic	T	0.39*	0.04
Ehlers et al., 1992	73	Adults	0.77	Yes	NR	SP	HCT	No	No	CD - phobia	T	5.10*	-0.12
Ehlers et al., 1992	65	Adults	0.74	Yes	NR	PD	HCT	No	No	STAI -T (German)	R	0.03	-0.03
Ehlers et al., 1992	50	Adults	0.72	Yes	NR	IP	HCT	No	No	STAI -T (German)	R	-0.13	0.13
Ehlers et al., 1992	27	Adults	0.81	Yes	NR	SP	HCT	No	No	STAI -T (German)	R	0.34	-0.34
Ehlers et al., 1992	46	Adults	0.74	No	NR	No	HCT	No	No	STAI -T (German)	R	0.12	-0.12
Ehlers et al., 1992	65	Adults	0.74	Yes	NR	PD	HCT	No	No	STAI-S (German)	R	-0.08	0.08
Ehlers et al., 1992	50	Adults	0.72	Yes	NR	IP	HCT	No	No	STAI-S (German)	R	-0.31	0.31
Ehlers et al., 1992	27	Adults	0.81	Yes	NR	SP	HCT	No	No	STAI-S (German)	R	0.25	-0.25
Ehlers et al., 1992	46	Adults	0.74	No	NR	No	HCT	No	No	STAI-S (German)	R	0.11	-0.11
Ehlers, 1995	169	Adults	0.75	Yes	Yes	PD, IP, SP, depression	HCT	No	No	STAI-T (German)	R	0.09	0.09
Ehlers et al., 2000	180	Adults	NR	Yes	NR	Anxiety	HCT	No	No	CD - any anxiety disorder	Chi^2	12.71	0.27
Eley et al., 2004	79	Childre n	0.57	Yes - Q	NR	No	HCT	No	No	CASI and SCARED	T	-1.13 (comp)	0.34
Eley et al., 2007	576	Childre n	0.57	Yes - Q	NR	NR	HCT	No	No	CASI and SCARED	R	0.06(comp)	0.06
Ewing et al., 2017	66	Adults	0.81	Yes	No	Anxiety	HCT	No	No	CD - any anxiety disorder	T	2.39*	-0.29

Furman et al., 2013	25	Adults	1.00	No	Yes	Depression	HCT	No	No	BAI	R	0.01	0.01
Furman et al., 2013	36	Adults	1.00	No	No	No	HCT	No	No	BAI	R	-0.22	-0.22
Gaebler et al., 2013	42	Adults	NR	Yes	Yes	SAD, PD, OCD, depression	HCT	No	No	CD - social anxiety	T	3.06	-0.44
Garfinkel et al., 2016	40	Adults	0.10	NR	NR	ASC	HCT	No	No	STAI-T	R	-0.17	-0.17
Garfinkel et al., 2016	40	Adults	0.10	NR	NR	ASC	HCT	No	No	STAI-S	R	-0.22	-0.22
Krautwurst et al., 2014	100	Adults	0.79	No	No	No	HCT	No	No	WI - 2 factor version (German)	R	-0.22	-0.23
Krautwurst et al., 2016	105	Adults	NR	Yes	No	PHA	HCT	No	No	CD - PHA	T	0.92	0.09
Lackner et al., 2016	101	Adults	0.74	Yes	Yes	Anxiety, depression, diabetes, HBP, ADHD	HCT	No	No	MASQ-S anxious arousal	R	-0.23	-0.23
Leonidou et al., 2020	60	Adults	0.80	Yes - Q	NR	Yes - unspecified	HCT	No	No	SHAI (Greek)	F	0.22	0.05
Li et al., 2020	36	Adults	0.67	Yes	No	GAD	HCT	No	No	CD - GAD	T (t-test)	1.00	-0.18
Mallorquí-Bagué et al., 2014	36	Adults	0.53	No	No	Hypermobility	HCT	No	No	STAI-S	R	0.28	0.28
Masdrakis et al., 2008	21	Adults	0.61 +	Yes	No	PD	HCT	No	No	Panic attack after caffeine challenge	Odds ratio	1.78	0.16
Michal et al., 2014	24	Adults	0.46	No	No	No	HCT	No	No	STAI-average (German)	R	-0.18	-0.18
Michal et al., 2014	26	Adults	0.46	Yes	Yes	Anxiety, depression, DPD	HCT	No	No	STAI-average (German)	R	-0.06	-0.06
Näring et al., 1995	24	Adults	0.00	Yes - Q	NR	No	HR rating		Yes	STAI-S (Dutch)	F	10.28	0.55
Pfleiderer et al., 2014	48	Adults	1.00	Yes - Q	No	No	HCT - Time1	No	No	ASI	T	1.15*	0.16
Pile et al., 2018	29	Children	0.48	NR	NR	TD, and other comorbidities	HCT	No	No	RCADS	R	0.40	0.40
Pile et al., 2018	25	Children	0.48	No	No	No	HCT	No	No	RCADS	R	-0.13	-0.13
Pollatos et al., 2007a	18	Adults	0.00	No	No	No	HCT	No	No	STAI-S	R (correlation)	-0.15	-0.15
Pollatos et al., 2007a	18	Adults	0.00	No	No	No	HCT	No	No	STAI-T	R (correlation)	0.47	0.47
Pollatos et al., 2007b	102	Adults	0.66	No	No	No	HCT	No	No	STAI-T	R (correlation)	0.28	0.28
Pollatos et al., 2007c	36	Adults	0.72	NR	NR	NR	HCT	No	No	STAI-T	R (correlation)	0.30	0.30
Pollatos et al., 2009	119	Adults	0.82	No	No	No	HCT	No	No	STAI-T	R (correlation)	0.20	0.20
Pollatos et al., 2016	23	Adults	1.00	No	No	No	HCT - control for BMI	No	No	STAI-T (German)	R (correlation)	0.50	0.50
Pollatos et al., 2016	23	Adults	1.00	Yes	Yes	Anxiety, depression, BN	HCT - control for BMI	No	No	STAI-T (German)	R (correlation)	-0.16	-0.16

Rost et al., 2017	98	Adults	0.83	NR	NR	Fibromyalgia	HCT	No	No	DASS-A	R (correlation)	0.02	0.02
Santangelo et al., 2018	43	Adults	NR	No	No	Parkinson's	HCT	No	No	BAI (Italian)	R (correlation)	0.01	0.01
Schaefer et al., 2014	52	Adults	0.73	No	NR	MUS	HCT	No	No	WI (German)	T (t-test)	2.33*	0.32
Schandry, 1981	34	Adults	0.41 +	NR	NR	NR	HCT	No	No	STAI-S (German)	T (t-test)	2.88	0.44
Schmitz et al., 2012	40	Childre n	0.53	NR	NR	High social fear + control group	HCT	No	No	SASC-R	T (t-test)	0.80	-0.13
Schultchen et al., 2019	52	Adults	0.46	Yes	Yes	OCD, depression, AN, SD, SP, PD	HCT	No	No	STAI-T	R (correlation)	-0.21	-0.21
Solano Lopez et al. 2019	76	Adults	0.71	Yes	Yes	PH, depression, anxiety, diabetes, DL, asthma, COPD, OA, obesity, cataract, glaucoma	HCT	No	No	PROMIS Anxiety scale short form 4a	R (correlation)	0.17	0.17
Steptoe et al., 1992	29	Adults	1.00	No	No	No	HR rating		Yes	STAI-T	Cohen's D	0.49*	-0.20
Stern et al., 2020	23	Adults	NR	NR	NR	NR	HCT- tapping	No	No	STAI-average	R (correlation)	-0.36	-0.36
Stevens et al., 2011	48	Adults	0.52	No	No	No	HCT	No	Yes	FNE (German)	T (t-test)	2.81	0.38
Stewart et al., 2001	30	Adults	0.70	Yes - Q	No	No	HCT	No	No	ASI	T (t-test)	3.02	0.49
Sturges et al., 1998	24	Adults	1.00	Yes - Q	NR	NR	HCT	No	Yes	ASI	F(ANOVA)	0.60	0.13
Suschinsky et al., 2014	31	Adults	1.00	Yes	NR	Anxiety	HCT	No	Yes	SPRAS and ASI	T (t-test)	1.33	-0.24
Tabor et al., 2019	38	Adults	0.50	No	No	No	HCT	Yes	No	ASI-3	R (correlation)	-0.07	-0.07
Tan et al., 2018	40	Adults	0.55	No	No	No	HCT	No	No	STAI-T (Chinese)	R (correlation)	0.28	0.28
Tan et al., 2018	40	Adults	0.55	No	No	No	HCT	No	No	STAI-S (Chinese)	R (correlation)	0.17	0.17
Watson et al., 2019	54	NR	0.85	No	No	No	HCT	No	No	STAI-T	R (correlation)	0.01	0.01
Watson et al., 2019	54	NR	0.85	No	No	No	HCT	No	No	STAI-S	R (correlation)	0.02	0.02
Yoris et al., 2015	34	Adults	0.44	Yes	NR	AD with panic in last month	HCT- tapping	No	No	Panic attack in previous month	F (ANOVA)	1.76	-0.23
Yoris et al., 2017	40	Adults	0.58	Yes	NR	PD	HCT - tapping	No	No	CD - panic disorder	T (t-test)	0.57*	-0.09
Zoellner et al., 1999	58	Adults	0.48	Yes	NR	IP	HCT	Yes	No	ASI and CD	T (t-test)	2.16	0.28

Note: F:M = female to male; NR = not reported; Q = questionnaire; PD = panic disorder; IP = infrequent panic; SP = simple phobia; PHA = pathological health anxiety; HBP = high blood pressure; BN = bulimia nervosa; MUS = medically unexplained symptoms; TD = tic disorder; SAD = separation anxiety disorder; OCD = obsessive compulsive disorder; SD = somatic disorder; AD = anxiety disorder; GAD = generalised anxiety disorder; COPD = chronic obstructive pulmonary disease; OA = osteoarthritis; PH = primary hypertension; DL = dyslipidaemia; CD = clinical diagnosis; + = ratio calculated before exclusions; * = effect size calculated from data provided in the paper

Table 3:

HDT studies

Author	N	Age	F:M ratio	Anxiety patients	Depression patients	Clinical group	Interoception task	HR manipulation?	Anxiety measure	E.S. type	Extracted E.S.	r
De Pascalis et al., 1991	78	Adults	1.00	NR	NR	Not reported	HDT	No	STAI-S	R	0.08	0.08
De Pascalis et al., 1991	78	Adults	1.00	NR	NR	Not reported	HDT	No	STAI-T	R	-0.10	-0.10
Ewing et al., 2017	66	Adults	0.81	Yes	No	Anxiety	HDT	No	CD	T	-0.36	-0.16
Garfinkel et al., 2016	40	Adults	0.10	NR	NR	ASC	HDT	No	STAI-T	R	-0.47	-0.47
Garfinkel et al., 2016	40	Adults	0.10	NR	NR	ASC	HDT	No	STAI-S	R	-0.35	-0.35
Lyyra et al., 2018	50	Adults	0.54	No	No	No	HDT	No	KSP-ANX	R	0.34	0.34
Michal et al., 2014	24	Adults	0.46	No	No	No	HDT	No	STAI-T	R	-0.14	-0.14
Michal et al., 2014	26	Adults	0.46	Yes	Yes	DPD, anxiety, depression	HDT	No	STAI-T	R	0.09	0.09
Schirmer-Mokwa et al., 2015	13	Adults	0.46	No	No	No	HDT	No	STAI-T	R	-0.01	-0.01
Schirmer-Mokwa et al., 2015	12	Adults	0.50	No	No	No	HDT	No	STAI-T	R	0.37	0.37
Schirmer-Mokwa et al., 2015	13	Adults	0.54	No	No	No	HDT	No	STAI-T	R	0.43	0.43

Note: Where it says "comp" in the effect size, it means the average was taken from all reported correlations within that sample group, to avoid issues with non-independence. F:M = female:male; NR = not reported; ASC = autism spectrum condition; AN = anorexia nervosa; DPD = depersonalisation derealisation disorder; GAD = generalised anxiety disorder; OCD = obsessive compulsive disorder; MMD = major depressive disorder; E.S. = effect size; CD= clinical diagnosis

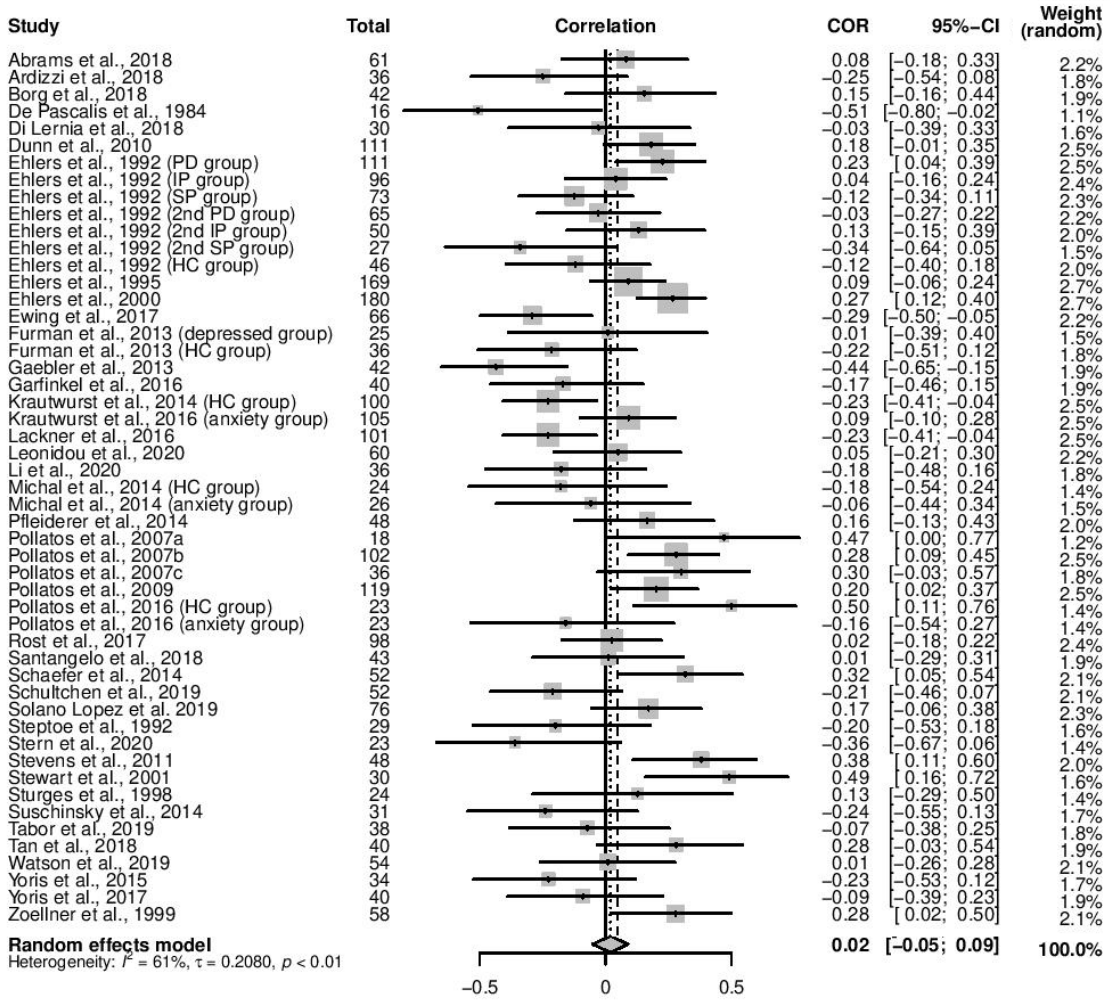
3. Results

3.1 HCT and variants with trait anxiety

In this category we included studies using any questionnaire measure of anxiety that was not state dependent (i.e., participants reported their anxiety levels over an extended period of time), in addition to studies that adopted between group designs comparing anxious and non-anxious individuals. All diagnoses and questionnaire measures (general, health anxiety and social phobia) were accepted. For these, the lowest level of heart rate perturbation (baseline) was taken if there were multiple conditions. This resulted in 51 effect sizes for this analysis.

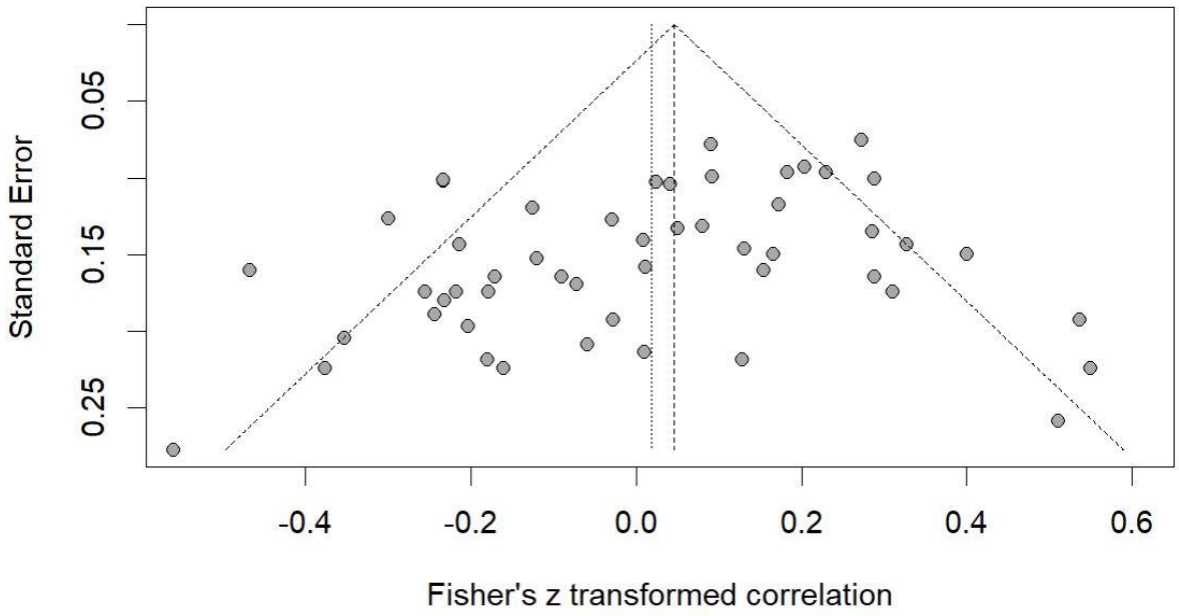
No significant association was observed between anxiety and HCT variants, with a pooled effect size of .02 (p=.609, see Fig 2). There did appear to be evidence of slight publication bias, whereby negative correlations were favoured, as indicated by a significant Egger's test (p=.043), although the funnel plot was mainly symmetrical (Fig. 3). In terms of heterogeneity, a significant Q statistic (Q=129.68, p<.001) and an I^2 value of 61% both indicated moderate-high heterogeneity in the total sample. 10 studies were identified as outliers that significantly deviated from the 95% confidence interval of the pooled effect size (De Pascalis et al., 1984; Ehlers et al., 2000; Ewing et al., 2017; Krautwurst et al., 2014; Lackner et al., 2016; Pollatos et al., 2007b; Pollatos et al., 2016 (non-anxious group); Stevens et al., 2011; Steward et al., 2001). However, the removal of these papers did not meaningfully change the pattern of results observed (r=.02, p=.508). In the total sample, influence analysis indicated effect sizes ranged from 0.01 to 0.03, all of which were non-significant, suggesting little influence of individual studies on the pooled effect size.

Figure 2:



Note: PD = panic disorder; IP = infrequent panic; SP = simple phobia; HC = healthy control

Figure 3:



Further analyses suggested that the pooled effect size was similar when examining studies reporting correlations with questionnaire measures and those using group designs (Q=.02, p=.887), with no significant relationship observed for studies using group (k=20, r=.02, p=.712) or correlational designs (k=31, r=.01, p=.761). The effect size was also relatively unchanged when excluding questionnaire measures that did not assess general 'trait' anxiety, restricting inclusion to studies assessing anxiety using the ASI, ASI-3, BAI, STAI-T (excluding those that created composite scores with the STAI-S), SPRAS, PROMIS, MASQ-S, IPAT or DASS (k=32, r=.04, p=.327). Similarly, restricting analyses to the most commonly used measure – the STAI-T – revealed no significant association (k=18, r=.07, p=.267).

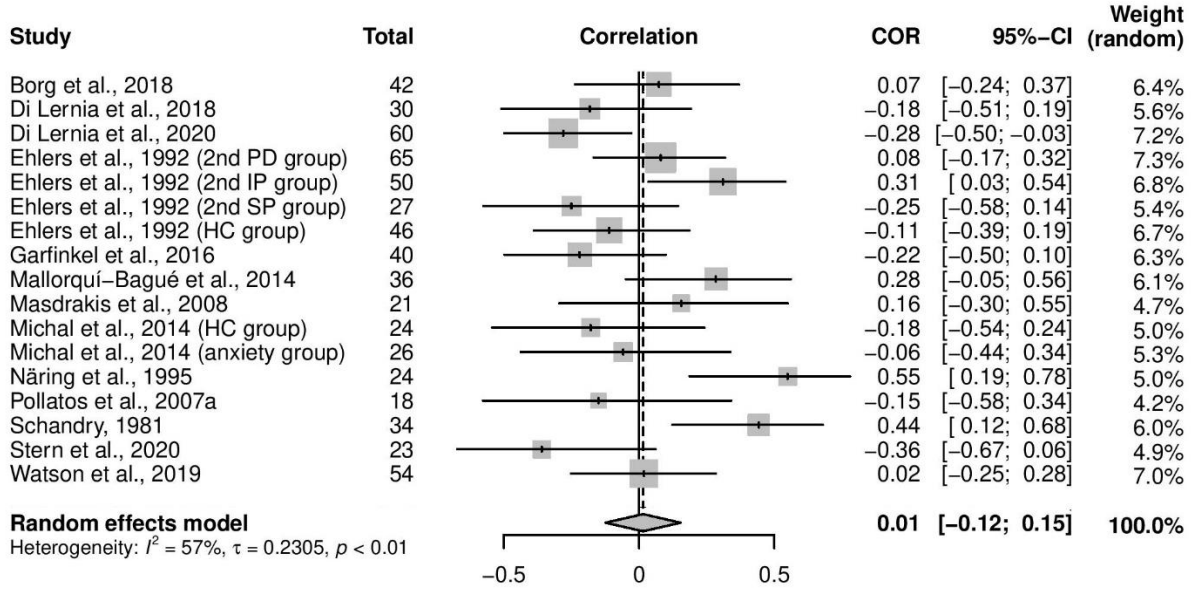
3.2 HCT and variants with state anxiety

In this category we included studies using any questionnaire measure of state anxiety (uniformly assessed by the STAI-S), in addition to one study that examined HCT performance

in individuals who suffered a panic attack following a caffeine challenge (Masdrakis et al., 2008).

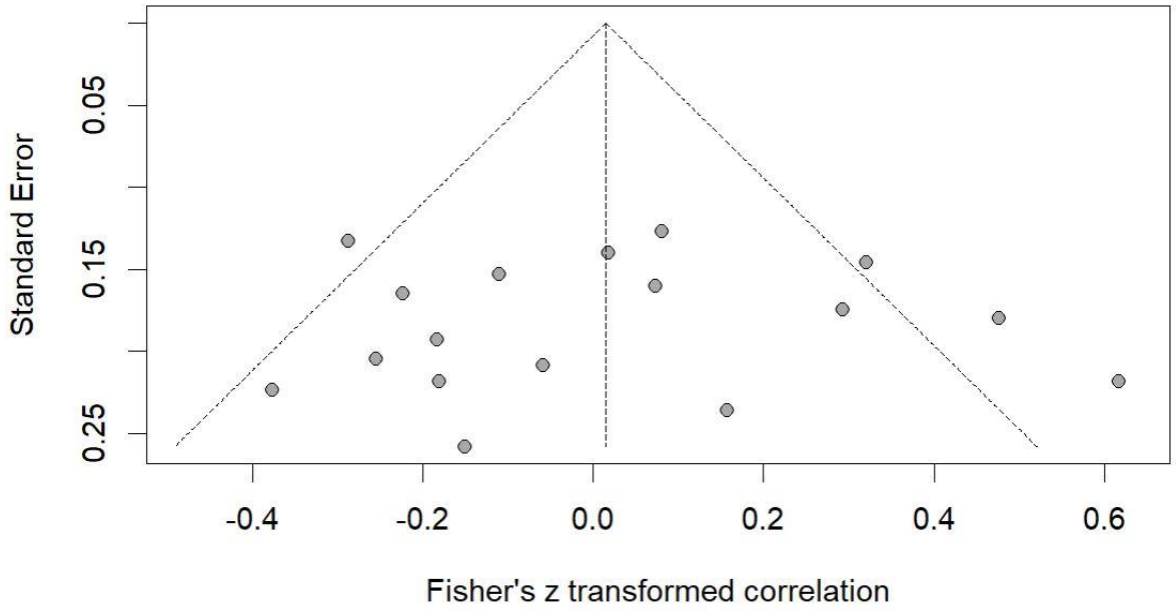
No significant association was observed between state anxiety and HCT variants, with a pooled effect size of .02 (p =.835, see Forest plot Fig 4). There did not appear to be evidence of publication bias, as indicated by the symmetry of the funnel plot (Fig. 5) and a non-significant Egger's test (p=.971). A significant Q statistic (Q=37.12, p<.005) and an I^2 value of 56.9% both indicated moderate-high heterogeneity in the total sample. In terms of outliers, 2 studies significantly deviated from the 95% confidence interval of the pooled effect size (Naring et al., 1995; Schandry, 1981), but the removal of these papers did not alter the overall results obtained (r=-.05, p=.454). Effect sizes ranged from -0.02 to 0.04 in the influence analysis, all of which were non-significant. Results remained non-significant when considering only studies that used the most common measure of state anxiety (the STAI-S; k=13, r=.05, p=.562).

Figure 4:



Note: PD = panic disorder; IP = infrequent panic; SP = simple phobia; HC = healthy control

Figure 5:



3.3 HDT and variants with trait anxiety

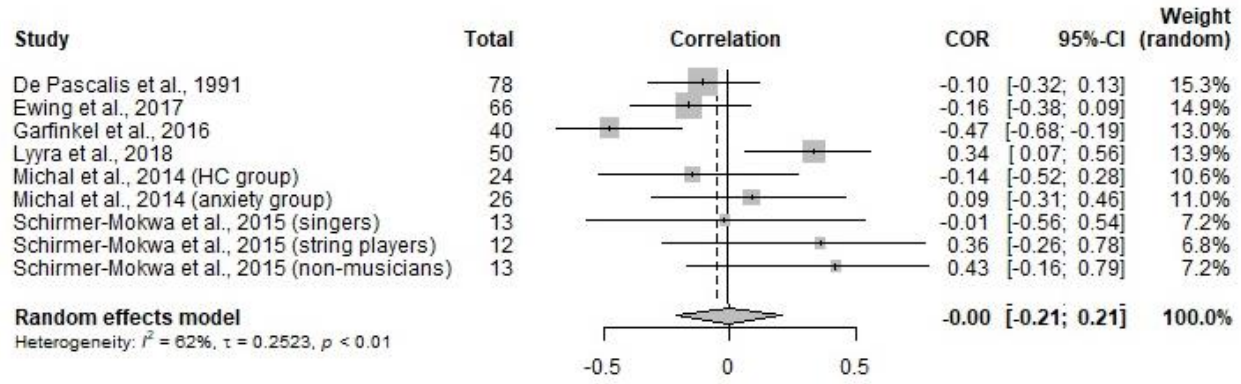
In this category we included studies using any questionnaire measure of trait anxiety as assessed by questionnaires, in additional to studies that adopted between group designs comparing anxious and non-anxious individuals.

Again, no significant association was observed between anxiety and HDT variants, with a pooled effect size of -.00 (p=.977, see Forest plot Fig 6). There did not appear to be evidence of publication bias, as indicated by the symmetry of the funnel plot (Fig. 7) and a non-significant Egger's test (p=.383). In terms of heterogeneity, a significant Q statistic (Q=21.30, p<.01) and an I^2 value of 62.4% both indicated moderate heterogeneity in the total sample. One study was identified as an outlier that significantly deviated from the 95% confidence interval of the pooled effect size (Garfinkel et al., 2016). When this paper was removed, there was not a notable change in the pooled effect size (r=.06, p=.528). Effect sizes from the influence

analysis were again all non-significant, ranging from -0.06 to 0.06, demonstrating that individual studies had little effect on the pooled effect size.

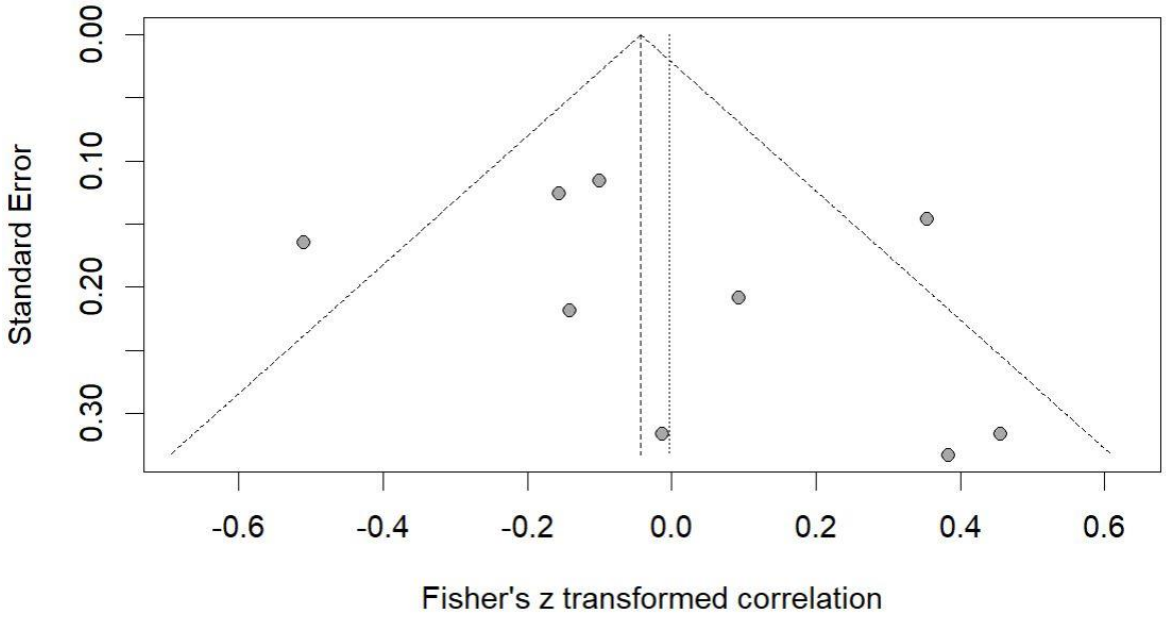
Further analysis indicated that results were still non-significant when only including studies that used the most commonly used measure, the STAI-T (k=7, r=-0.04, p=.758).

Figure 6:



Note: HC = healthy control

Figure 7:



3.4 Moderation analysis

Whilst we examined potential moderators, many of these moderation analyses were under-powered (K<10). As such, the overall findings are reported here for completeness, with full results detailed in the supplement.

None of the pre-registered moderators (whether no guessing instructions were used for the HCT, and whether anxiety questionnaires captured depression) significantly impacted the pooled effect size. None of the exploratory moderators (whether any participants had a diagnosis of any anxiety disorder, panic disorder, depression or any other clinical condition, the ratio of female to male participants, or whether or not participants' heart rates were manipulated to make them more detectable) significantly impacted the pooled effect size (see supplement for details). Only one significant relationship emerged; for the HCT and state anxiety, the pooled effect size from studies using group designs were significantly larger than studies that employed correlational designs. However, these results should be interpreted with caution as only three studies were included in the group design category.

4. Discussion

The aim of this pre-registered systematic review and meta-analysis was to establish the presence or absence of a relationship between cardiac interoceptive accuracy and anxiety. Overall, we found no evidence for an association. Neither trait nor state anxiety related to performance in the HCT task, and trait anxiety did not relate to performance on the HDT task. Our analyses indicated moderate to high levels of heterogeneity across categories assessed, that did not seem to be accounted for by the examined moderators. Such findings are inconsistent with theoretical proposals that implicate interoception in the aetiology of anxiety (Domschke et al., 2010; Ehlers, 1993; Paulus & Stein, 2010; Garfinkel et al., 2016).

One explanation is that there is simply no association between anxiety and cardiac interoceptive accuracy. Indeed, whilst it is possible that methodological limitations of both the HCT and the HDT may underlie the results obtained (see Desmedt et al., 2018; Ring et al., 2015; Murphy et al., 2018; Brener et al., 1993), it is notable that studies using novel tasks or analytic approaches that overcome these limitations have also produced mixed results with some studies reporting relationships between anxiety and cardiac interoceptive accuracy (Smith et al., 2021) and others not (Plans et al., 2020). Whilst task differences or differences in the anxiety measures employed may account for these discrepant results, such discrepancies are in line with the mixed results noted throughout this meta-analysis. As such, the results of this meta-analysis are not consistent with the proposal that anxiety relates to cardiac interoceptive accuracy and recent work remains inconclusive.

Although a number of different factors have been proposed to moderate this association, including participants' clinical diagnoses and the instructions given for the HCT task (Domschke et al., 2010; Ehlers et al., 1995; Smith et al., 2021), we found no evidence that these moderators significantly impacted the association between anxiety and interoception. Whilst some of these moderator analyses may have been insufficiently powered, for the six comparisons where sufficient power was present, we found no evidence of a moderating effect. Such results suggest that discrepant results for the HCT and anxiety are not explained by the use of correlational vs group designs, depression influencing anxiety scores on questionnaires, the inclusion of individuals with an anxiety diagnosis, above threshold symptom reporting, a panic diagnosis, or indeed any of the other diagnoses explored in this meta-analysis (see Tables 2 and 3).

The results from this meta-analysis are difficult to interpret considering recent evidence that cardiac interoceptive training reduces anxiety, as measured by the STAI-T, in autistic samples (Quadt et al., 2021). However, one possibility is that anxiety relates to other facets of

interoception, but not interoceptive accuracy. Interoception has been shown to be separable into various dimensions; one can dissociate between the accuracy of an individual's perception of their internal states, and how much attention they pay to internal signals, and both of these can be measured in terms of objective performance, or subjective beliefs (Murphy et al., 2019). Interoception also encompasses evaluations of interoceptive signals, and whether or not they are interpreted negatively (Suksasilp & Garfinkel, 2022). Whilst we focused on cardiac interoceptive accuracy given theories suggesting such a link (Ehlers, 1993; Garfinkel et al., 2016; Paulus & Stein, 2010), there is evidence that anxiety may relate to other aspects of interoception; for example, anxiety seems to relate to greater self-reported interoceptive attention (Anderson & Hope; 2009; Palser et al., 2018), more negative interpretations of interoceptive states (e.g., Paulus, 2013; Taylor et al., 1991) and greater physiological reactivity and perceived intensity of interoceptive states (Teed and colleagues 2022). It is plausible that it is these facets specifically, or the interaction between these facets and interoceptive accuracy, that are anxiogenic (e.g., Garfinkel et al., 2016; Palser et al., 2018). This may explain why intervention studies have found that interoceptive training reduces anxiety (Quadt et al., 2021). Training may result in downstream effects on other facets of interoception, thus reducing anxiety through those mechanisms. Alternatively, as training protocols often include psychoeducation aimed at attention to, and interpretations of, interoceptive signals (e.g., Quadt et al., 2021), it may be that the benefits of interoceptive training on anxiety are via those mechanisms, and not interoceptive accuracy. Further studies comparing interoceptive training protocols are required to isolate the mechanism by which anxiety relates to interoception.

It is also worth acknowledging that whilst our results suggest no relationship with cardiac interoceptive accuracy, a relationship between anxiety and interoceptive accuracy may be observable in other domains of interoception (e.g., respiratory, gastric) given evidence that interoceptive accuracy dissociates across interoceptive domains (Pollatos et al., 2016;

Garfinkel et al., 2016; Ferentzi et al., 2018). Like cardiac interoceptive accuracy, there are good theoretical reasons to expect a relationship between anxiety and respiratory interoceptive accuracy (Paulus, 2013) and there is initial evidence of such an association (Tiller et al., 1987; Harrison et al., 2021; Teed et al., 2022). As evidence suggests respiratory and cardiac interoceptive accuracy dissociate (Garfinkel et al., 2016), it remains a possibility that associations between anxiety and interoception may be observed in the respiratory domain and indeed other domains of interoception.

Alternatively, the measurement of anxiety may contribute towards the mixed results observed; for example, the STAI (used by most studies) shows poor agreement with other measures of anxiety, such as the BAI and DASS-A (Desmedt et al., 2020; Kohn et al., 2008; Grös et al., 2007), and may index depression symptoms (Julian, 2011; Kennedy et al., 2001). Whilst our meta-analysis was unable to examine specific aspects of anxiety (e.g., anxiety sensitivity) due to the small number of studies identified, we cannot rule out that specific aspects of anxiety may relate to differences in cardiac interoceptive accuracy. Future research employing fine grained assessment of anxiety symptoms is required to examine this further.

Despite the importance of these results for understanding the relationship between anxiety and cardiac interoceptive accuracy, it is important to acknowledge limitations. First, many of our moderator analyses were underpowered (K<10; Schwarzer et al., 2015). As such, we cannot conclusively say that these moderators do not impact the relationship between anxiety and cardiac interoceptive accuracy. Second, due to small numbers it was not possible to explore the moderating effect of certain factors for the HDT and HCT with state anxiety. Third, due to the variety of clinical conditions included in the papers, we were unable to explore the moderating effects of specific conditions other than anxiety, and only considered the effects of including participants with *any* clinical diagnosis. Finally, PubMed was the only database

searched due to the large number of records identified. Whilst we checked for additional papers using citation searches, it is possible that a small number of studies may have been missed.

Despite these limitations, this pre-registered meta-analysis triangulated findings from numerous studies to provide a unifying overview of the relationship between anxiety and cardiac interoceptive accuracy. Our findings suggest no relationship between anxiety and cardiac interoceptive accuracy, though more work is required to investigate whether certain factors moderate this relationship and whether relationships between interoception and anxiety are observed for other domains and dimensions of interoception. Such work is important for understanding discrepancies between theoretical and empirical work, and for understanding the mechanism by which interoceptive training improves anxiety.

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Pre-registered moderators

Given previous suggestions that a number of factors may moderate the relationship between cardiac interoception and anxiety, a number of further analyses were conducted. As outliers, and the specific measures of anxiety and cardiac interoceptive accuracy employed, had little influence on results for primary analyses these were retained in subgroup analyses. It is important to note that in a number of these comparisons, $k<10$, meaning they were underpowered to detect significant effects.

Supplement 1:

Analysis	Category	Group	*Q*	*p*	*k*	PES	*p*
		Pre-registered					
HCT instructions	HCT + trait		0.34	.560			
		No guessing instructions *			2	0.12	.484
		No no guessing instructions			48	0.02	.634
Influence of depression	HCT + trait		0.21	.646			
		Anxiety measure captured depression			18	0.07	.267
		Anxiety measure captured anxiety			18	0.03	.690
		Exploratory					
Inclusion of P's with AD	HCT + trait		2.55	.110			
		AD included			22	-0.03	.563
		AD not included			22	0.09	.109
	HCT + state		0.03	.866			
		AD included *			5	0.07	.516
		AD not included *			7	0.04	.715
	HDT + trait		2.11	.147			
		AD included *			2	-0.08	.574
		AD not included *			5	0.20	.140
Inclusion of P's with AD OR above threshold	HCT + trait		0.67	.412			
		High anxiety included			26	0.00	.978
		High anxiety not included			18	0.07	.300
	HCT + state		1.31	.252			
		High anxiety included *			6	0.14	.254
		High anxiety not included *			6	-0.03	.707
Inclusion of P's with PD	HCT + trait		0.01	.939			
		PD included			11	0.02	.758
		PD not included			34	0.03	.504
	HCT + state		1.41	.235			
		PD included *			3	0.18	.066
		PD not included *			8	0.01	.948

Inclusion of P's with depression diagnosis	HCT + trait		1.38	.240			
		Depression included *			9	-0.06	.452
		Depression not included			20	0.06	.532
Inclusion of P's with other clinical diagnosis	HCT + trait		1.17	.280			
		Other diagnosis included			12	-0.04	.543
		Other diagnosis not included			34	0.05	.298
	HCT + state		0.38	.537			
		Other diagnosis included *			5	-0.05	.639
		Other diagnosis not included			10	0.04	.688
	HDT + trait		1.79	.180			
		Other diagnosis included *			2	-0.22	.436
		Other diagnosis not included *			5	0.20	.140
Age of participants	HCT + trait		0.73	.392			
		Children *			5	0.12	.279
					51	0.02	.608
Female to male ratio	HCT + trait		0.98	.323			
		More females			37	0.05	.165
		More males *			9	-0.05	.594
	HCT + state		0.18	.674			
		More females			10	0.01	.883
		More males *			6	0.08	.590
	HDT + trait		1.56	.212			
		More females *			4	0.08	.578
		More males *			4	-0.18	.225
Heartrate manipulation	HCT + trait		1.05	.304			
		Manipulation *			3	-0.12	.378
		No manipulation			48	0.03	.504

Note: PES = pooled effect size, AD = anxiety disorder (clinical diagnosis), PD = panic disorder (clinical diagnosis), * = k<10, likely underpowered.

Supplementary Materials

Pre-registered moderators

Instructions for HCT

For studies which considered trait anxiety, two conducted the HCT with explicit no guessing instructions provided, whereas 48 studies either did not use no guessing instructions or did not report that they used no guessing instructions. Overall there was no significant difference (Q= 0.34, p=.560) in the pooled effect sizes, and neither the studies that gave no guessing instructions (k=2, r=.12, p=.484) or those that did not (k=48, r=.018, p=.634) showed a significant pooled effect size.

We were unable to run this analysis on the studies looking at state anxiety, as only one study employed no guessing instructions.

Influence of depression

Clinician ratings of the questionnaires used to measure anxiety highlighted that only the STAI-T captured depression in over 50% of the items. Therefore, this analysis compared effect sizes from studies using the STAI-T to all other questionnaire measures of anxiety. For this analysis, we removed any effect sizes that were created using composite measures of the STAI-T and other measures of anxiety. This included those using an average of the STAI-S and STAI-T. Of the studies using the HCT, 18 used the STAI-T and 18 studies used other measures. Results indicated no significant difference in the effect sizes across studies employing the STAI-T and other measures (Q=0.21. p=.646); neither studies using the STAI-T (k=18, r=.07, p=.267) or other measures (k=18, r=.03, p=.690) showed a significant pooled effect size.

We could not run this analysis on studies using the HDT, as there were no studies using anxiety measures that had been confirmed to not capture depression.

Exploratory moderators

Group versus correlational design

This analysis is reported in the main body text for the HCT and trait measures of anxiety.

For the HCT and state measures of anxiety, there did appear to be a significant difference in the effect sizes between studies employing group versus correlational designs (Q=9.01, p=.003), with correlational studies showing a non-significant, negative effect size (k=14, r=.06, p=.374) and group studies showing a significant, positive effect size (k=3, r=.43, p=.004). However, it is important to note that this analysis was extremely under-powered, with only 3 studies employing group studies.

We could not conduct this comparison for studies using the HDT and trait measures of anxiety, as there was only one study employing a group design.

Inclusion of anxiety diagnoses

Given suggestions that relationships may be more likely to be observed where individuals with anxiety are included in samples (Domschke et al., 2010), we also assessed whether such sample characteristics may moderate relationships. For these analyses, we excluded papers where such sample characteristics were not reported. In studies using the HCT and trait measures of anxiety, there was no significant difference between studies including participants who had clinical anxiety diagnoses and those who did not (Q=2.55, p=.110; studies including participants with clinical anxiety: k=22, r=-.03, p=.563; studies not including participants with clinical anxiety: k=22, r=.09, p=.109). There was also no difference between participants who either had clinical anxiety or scores above established thresholds for high anxiety on questionnaire measures and participants who did not (Q=0.67,

p=.412; studies including anxious participants, as measured by diagnosis or questionnaire: *k*=26, *r*=.00, *p*=.978; studies not including anxious participants: *k*=18, *r*=.07, *p*=.300).

For studies using the HCT and state measures of anxiety, there was no difference in studies that included participants with clinical diagnoses of anxiety and those that did not (*Q*=0.03, *p*=.866). Both were non-significant (studies including participants with clinical anxiety: *k*=5, *r*=0.07, *p*=.517; studies not including participants with clinical anxiety: *k*=7, *r*=0.04, *p*=.715). The same was found when including participants who scored over thresholds that indicated high anxiety (*Q*=1.31, *p*=.252; including anxious participants: *k*=6, *r*=.14, *p*=.254; not including anxious participants: *k*=6, *r*=-.03, *p*=.707).

For studies using the HDT and trait measures of anxiety, there was also no significant difference between studies including participants with a clinical anxiety diagnosis and those without (Q= 2.11, p=.147; studies including participants with a clinical anxiety diagnosis: *k*=2, *r*=-.08, *p*=.574; studies not including participants with a clinical anxiety diagnosis: *k*=5, *r*=-.20, *p*=.140). No additional studies included participants scoring over a threshold for high anxiety.

Inclusion of individuals with panic diagnosis

Given suggestions that relationships may be specific to, or more pronounced in, individuals with panic disorder (Ehlers & Breuer, 1992), we also assessed whether relationships would be more likely to be observed where samples contained individuals with panic disorder. For this, we included data from individuals with infrequent panic. Of the studies using the HCT and trait measures of anxiety, there was no significant difference in the effect sizes obtained from studies including participants with panic disorder and studies that did not (*Q*=0.01, *p*=.939). Neither studies including those with panic disorder (*k*=11, *r*=.02, *p*=.758) or those without panic disorder (*k*=34, *r*=.03, *p*=.504) were significant.

Of the studies using the HCT and state measures of anxiety, there was also no significant difference (Q=1.41, p=.235), with both those including participants with panic disorder (k=3, r=.18, p=.066) and those not including participants with panic disorder (k=8, r=.01, p=.948) not being significant. We could not run analysis on studies using the HDT, as no panic patients were included in any of the studies. ***Inclusion of individuals with a depression diagnosis***

As depression is often reported to show differing relationships with cardiac interoception when compared to anxiety (Dunn et al., 2010; Pollatos et al., 2009), we also examined depression diagnosis as a moderating factor. As before we removed studies that did not report whether or not participants with depression were included or excluded. For the studies employing the HCT and trait measures of anxiety, there was no significant difference between studies with clinically depressed patients versus no clinically depressed patients (Q=1.38, p=.240). Neither group was significant (k=20, r=.06, p=.532 for studies not including participants with depression, k=9, r=-.06, p=.452 for studies including participants with depression). The analysis could not be run on the HCT and state measures studies as no studies reported depressed participants. Similarly, only one study of the studies using the HDT included participants with depression.

Inclusion of any clinical groups

As included papers often employed samples with other clinical diagnoses, we also examined associations removing studies that included samples that had clinical diagnoses that were not anxiety. Within studies using the HCT and trait measures of anxiety, there was no significant difference (Q=1.17, p=.280) between studies that did include participants with clinical diagnoses other than depression and anxiety (k=12, r=-.04, p=.543) and those that did not (k=34, r=.05, p=.298). The same was found within studies using the HCT and state measures

of anxiety (Q= 0.38, p=.537; studies including other clinical participants: k=5, r=-.05, p=.639; studies not including other clinical participants: k=10, r=.04, p=.688) and studies using the HDT and trait measures of anxiety (Q=1.79, p=.180; studies including other clinical participants: k=2, r=-.22, p=.436; studies not including other clinical participants: k=5, r=.14, p=.529).

Age of participants

Given that interoceptive accuracy varies across the developmental timeline (Murphy et al., 2017), we also examined the relationship in child populations, to see if it differed to what was observed in adult populations. This was conducted only for the HCT and trait anxiety given the number of studies conducted in child populations. No significant relationship was observed between trait anxiety and HCT performance in children (k=5, r=.12, p=.279).

Female:Male ratio

Given evidence of sex differences in interoception (Prentice & Murphy, 2021), and suggestions that the relationship between interoceptive accuracy and mental health may vary as a function of sex (Lischke et al., 2020), we also examined if relationships varied according to the proportion of female relative male participants in samples. For this analysis, studies not reporting sample characteristics were excluded and studies with equal numbers of male and female participants were excluded. One study only reported demographics prior to exclusions (Ardizzi et al., 2018), so this ratio was used. When considering studies that examined HCT performance and trait anxiety, there was no significant difference in the effect sizes between studies employing designs with a female versus male majority (Q=0.98, p=.323). No significant pooled effect size was observed for studies with a female (k=37, r=.05, p=.165) or male majority (k=9, r=-.05, p=.594). The same was found for studies using the HCT and state

measured of anxiety (Q=.178, p=.674; studies with a female majority: k=10, r=.01, p=.883; studies with a male majority: k=6, r=.08, p=.590) and the HDT and trait measures of anxiety (Q= 1.56, p=.212; studies with a female majority: k=4, r=.08, p=.578; studies with a male majority: k=4, r=-.18, p=.225).

Manipulation to increase HR

Heartrate manipulation appeared to have no significant effect on the relationships observed in studies using the HCT and trait measures of anxiety (Q=1.05, p=.304). Neither studies with (k=3, r=-.12, p=.378) or without manipulation (k=48, r=.03, p=.504) were significant. We could not assess the effect of heartrate manipulation in studies using the HCT and state measures of anxiety or the HDT and trait measures of anxiety.