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Discrepancies between dimensions of interoception in Autism: Implications for emotion and anxiety

Running head: ALTERED INTEROCEPTION IN AUTISM

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Highlights

-   Emotional processes are influenced by signals from the body

-   Autism is associated with heightened anxiety and deficits in emotion processing

-   Autism group had poorer interoceptive accuracy and higher interoceptive sensibility

-   The discrepancy between these measures forms a trait prediction error (TPE)

-   TPE predicts both heightened anxiety and emotion deficits

Abstract

Emotions and affective feelings are influenced by one's internal state of bodily arousal via *interoception.* Autism Spectrum Conditions (ASC) are associated with difficulties in recognising others' emotions, and in regulating own emotions. We tested the hypothesis that, in people with ASC, such affective differences may arise from abnormalities in interoceptive processing. We demonstrated that individuals with ASC have reduced interoceptive accuracy (quantified using heartbeat detection tests) and exaggerated interoceptive sensibility (subjective sensitivity to internal sensations on self-report questionnaires), reflecting an impaired ability to objectively detect bodily signals alongside an over-inflated subjective perception of bodily sensations. The divergence of these two interoceptive axes can be computed as a trait prediction error. This error correlated with deficits in emotion sensitivity and occurrence of anxiety symptoms. Our results indicate an origin of emotion deficits and affective symptoms in ASC at the interface between body and mind, specifically in expectancy-driven interpretation of interoceptive information.

Emotions represent shifts in mental and physiological state and are associated with an acute motivational reorientation. Within the human brain, emotions are supported by a matrix of cortical and subcortical structures, including ventral prefrontal, anterior cingulate and insular cortices, amygdala, ventral striatum and dorsal brainstem (Phan, Wager, Taylor, & Liberzon, 2002). Interestingly, activity within most of these regions resonates with changes in bodily physiology including heart rate (Critchley et al., 2005), blood pressure (Critchley, Corfield, Chandler, Mathias, & Dolan, 2000) and temperature (Nummenmaa, Glerean, Hari, & Hietanen, 2014). However, shared physiological architecture in brain and body is proposed to mediate the embodiment of emotion, in accord with 'peripheral' theories of emotion that propose a basis for emotional feelings in the central representation and perception of changes in bodily arousal (Lange & James, 1967). In this view, emotional experience is governed by our ability to detect and perceive fluctuations in internal physiological state and the function of visceral organs (Cameron, 2001; Seth, 2013; Sherrington, 1948), a process known as interoception. Correspondingly, people with higher interoceptive accuracy on heartbeat detection tasks report a greater intensity of emotional experience (Pollatos, Traut-Mattausch, Schroeder, & Schandry, 2007; Wiens, Mezzacappa, & Katkin, 2000). Moreover, individual differences in interoception influence vulnerability to both physical and psychological symptoms (Dunn et al., 2010; Schaefer, Egloff, Gerlach, & Witthoft, 2014; Scheuren, Sutterlin, & Anton, 2014). Together, these findings support the proposal that detection of bodily sensations can shape emotional and affective experience.

Autism Spectrum Conditions (ASC) are pervasive neurodevelopmental conditions characterized by lifelong difficulties in social and emotional functioning alongside other traits including restricted and stereotyped patterns of behaviour, interests and activities (Frith, 2014). The emotion processing difficulties observed in ASC have been linked theoretically to impaired mechanisms for identifying and distinguishing emotions in self and others. Even when marked behavioural deficits are not overt, adults with ASC manifest characteristic altered patterns of brain activity and neural connectivity during the processing of emotional information, particularly regarding impaired activation (Duerden et al., 2013; Hadjikhani et

al., 2009; Watanabe et al., 2012) and impoverished functional connectivity (Ebisch et al., 2011) of the insula. The insula maps both bodily and emotional processes in a way accessible to consciousness (Terasawa, Shibata, Moriguchi, & Umeda, 2013; Zaki, Davis, & Ochsner, 2012). This region is therefore considered central to the representation of bodily signals in a manner that informs emotional feelings and behaviours (Craig, 2015).

Consequently, we hypothesized that emotional deficits expressed by individuals with ASC may originate in impaired interoceptive processing. People with ASC differ from typical controls in evoked autonomic indices of stimulus salience, and in basal measures of sympathovagal balance that probably reflect raised anxiety levels and rumination (Palkovitz & Wiesenfeld, 1980; S. W. Porges, 1976; Zahn, Rumsey, & Van Kammen, 1987). However, a demonstration of altered interoceptive ability in ASC would provide more direct evidence for an aberrant primary viscerosensory representation within this population.

Objective measures of interoceptive ability centre on behavioural tests to assess how well people perceive their own internal bodily sensations. The focus is most commonly the accuracy with which an individual can detect her/his own heartbeats at rest. This is largely pragmatic: heartbeats are distinct, frequent, internal events that can be easily measured and quantified. Consequently, heartbeat detection tasks have emerged as the dominant method to assess objective interoceptive accuracy (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; Dunn, et al., 2010; Katkin, Reed, & Deroo, 1983; Pollatos, et al., 2007; Schandry, 1981; Whitehead, Drescher, Heiman, & Blackwell, 1977), typically either via silent counting of heartbeats perceived within specified time-frames (Schandry, 1981), or by judging whether an external stimulus (e.g. tone) is presented synchronously or asynchronously to one's own heartbeat (Katkin, et al., 1983; Whitehead, et al., 1977). These tests represent one means to explore whether deficits in interoceptive accuracy relate to emotion processing deficits in ASC.

Importantly, the hypothesis that *impaired* interoceptive ability may form the basis for emotion processing difficulties in ASC, does not at first glance, accord with clinical observations that individuals with ASC tend to report a *heightened* sensitivity to internal

bodily sensations. However, as we have recently reported, a finer grained analysis of interoceptive processes may help resolve this apparent discrepancy (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015). For example, interoceptive processing is not a unitary construct, but is instead comprised of discrete dimensions that can be distinguished by qualitative differences in conscious access (Ceunen, Van Diest, & Vlaeyen, 2013; Garfinkel & Critchley, 2013; Garfinkel, et al., 2015). Specifically, *interoceptive accuracy* is defined by accurate performance on behavioural tests (e.g. correctly identifying when your heart is beating using a heartbeat detection test). This objective performance measure is dissociable from *interoceptive sensibility,* a subjective self-report measure based on how good at interoceptive processing people *believe* themselves to be (e.g. as assessed using questionnaires, or average confidence ratings). Similarly, *interoceptive awareness*, defined as metacognitive insight into one's own interoceptive performance (i.e. knowing you are good when you are good, or knowing you are bad when you are bad), also does not always correspond directly to interoceptive performance (interoceptive accuracy) or subjective self-perceptions (interoceptive sensibility) which may be swayed by response bias (Garfinkel, et al., 2015). Previously we demonstrated that these measures are dissociable in a large sample (N=80), and tend only to be aligned in those individuals with greatest interoceptive accuracy (Garfinkel, et al., 2015). On this basis, our first hypothesis was that ASC individuals will display *impaired* interoceptive accuracy while at the same time showing *heightened belief* in their interoceptive ability (i.e. enhanced interoceptive sensibility) (Figure 1).

Anxiety is the most common co-morbidity experienced by people with ASC (Simonoff et al., 2008), and it is therefore noteworthy that interoceptive ability has important implications for anxiety. A number of studies indicate that anxiety is associated with enhanced interoceptive sensibility, as reflected by an enhanced tendency for people with anxiety to *believe* that they are interoceptively proficient as indexed via self-report (Ehlers & Breuer, 1992; Naring & Vanderstaak, 1995). Moreover, enhanced interoceptive accuracy on heartbeat detection tasks is also commonly reported to be over expressed among anxiety

patients (Dunn, et al., 2010; Pollatos, et al., 2007). However, a straightforward relationship between interoception and anxiety is challenged by a number of empirical studies which either do not show a relationship between anxiety and interoceptive accuracy (Antony et al., 1995; Barsky, Cleary, Sarnie, & Ruskin, 1994; Ehlers, Margraf, Roth, Taylor, & Birbaumer, 1988), or which reveal a reverse relationship, with reduced interoceptive accuracy related to heightened anxiety (Depascalis, Alberti, & Pandolfo, 1984). In a more sophisticated approach, Paulus and Stein proposed that anxiety may result from an altered interoceptive prediction signal, manifest as a heightened discrepancy between observed and expected bodily states (Paulus & Stein, 2006, 2010). One potential approach to operationalize this discrepancy is to define it as the difference between interoceptive sensibility and interoceptive accuracy, which we call 'interoceptive trait prediction error' (ITPE). Applying this measure in the setting of anxiety allows us to examine whether *relationships* between interoceptive dimensions are a critical predictor for anxiety symptoms. In addition, formulation of this variable and characterizing its relationship to anxiety may also address inconsistencies in the previous literature when interoceptive accuracy and interoceptive sensibility have been assessed in isolation.

We therefore systematically investigated interoceptive processing in ASC, to explore the relationship between interoceptive deficits and corresponding impairments in emotional processing and affective (anxiety) symptoms. Our specific hypotheses were that 1) ASC status will be associated with impaired *interoceptive accuracy* (i.e. reduced performance on a behavioural test of interoception). 2) Individuals with ASC will display enhanced *interoceptive sensibility* reflecting elevated subjective perception about their interoceptive aptitude. 3) Interoceptive dimensions will be related to deficits in emotion sensitivity and, 4) the discrepancy between *interoceptive accuracy* and *interoceptive sensibility* (i.e. actual versus presumed interoceptive ability, operationalized via ITPE) will predict anxiety symptoms.

Methods and Materials

Participants

Twenty patients with ASC (18 male) were recruited from a specialist service for diagnosis and evaluation of adults with suspected ASC (the Neurobehavioural Clinic, Sussex Partnership NHS Foundation Trust). All patients had received a formal (DSM-IVR/ ICD10) diagnosis of an Autism Spectrum Disorder (Asperger Syndrome or High Functioning Autism) by a psychiatrist following a corroborated multidisciplinary assessment. Twenty healthy control participants (18 male) were also recruited to match the ASC patients. Procedures were approved by a Brighton and Sussex committee of the National Research Ethics Service (NRES) and the local Brighton and Sussex Medical School Research Governance Ethics Committee. All participants provided informed consent.

Stimuli and Procedure

Interoceptive accuracy was gauged by the participants' ability to detect their own heartbeats using a heartbeat tracking task (Schandry, 1981) and a heartbeat discrimination task (Katkin, et al., 1983; Whitehead, et al., 1977). For the heartbeat tracking task, participants' heartbeats were monitored via a pulse oximeter with the sensor mounting attached to their index finger. Participants were required to count their heartbeats during six randomized time windows of varying length (25, 30, 35, 40, 45 and 50 sec) and, at the end of the trial, to report the number of heartbeats detected to the experimenter. For the heartbeat discrimination task, each trial consisted of ten tones presented at 440 Hz and having 100ms duration which were triggered by the heartbeat. Under the asynchronous condition, a delay of 300 ms was inserted, adjusting for the average delay (~250ms) between the R-wave and the arrival of the pressure wave at the finger (Payne, Symeonides, Webb, & Maxwell, 2006). Tones were thus presented at 250 ms or 550 ms after the R-wave, which correspond to maximum and minimum synchronicity judgements respectively (Wiens & Palmer, 2001). At the end of each trial, participants signalled to the experimenter whether they believed the tones to be synchronous or asynchronous with their heartbeats. On each

interoceptive trial, participants completed a visual analogue scale (VAS) to signal confidence in their interoceptive decision.

Interoceptive sensibility was determined using the awareness section of the Porges Body Perception Questionnaire (Garfinkel & Critchley, 2013; S. Porges, 1993). This subscale incorporates 45 bodily sensations (e.g. stomach and gut pains) and participants indicated their awareness of each sensation using a five-point scale ranging from 'never' to 'always'. This subjective measure of interoceptive sensibility denotes the participants' belief in their own interoceptive aptitude, irrespective of actual (objectively determined) interoceptive accuracy. One participant with ASC did not complete the BPQ and thus was excluded form analyses.

Interoceptive awareness was calculated for the heartbeat discrimination task using the trial-by-trial correspondence between accuracy (correct synchronous / asynchronous decisions) and confidence assessed via score on the trial-by-trial VAS.

Anxiety was assessed using the Spielberger State / Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). This questionnaire is divided into two 20-question sections, one which assesses state anxiety, with questions such as "*I am tense*" and "*I am presently worrying over possible misfortunes"* and a response scale which runs from "*Not at all*", to "*Very much so*", to capture current state. The other section includes questions such as "*I lack self-confidence"* and "*I have disturbing thoughts*", but with a response scale which runs from "*Almost never"* to "*Almost always"* in order to capture a more stable dispositional tendency for (trait) anxiety.

Autism-spectrum severity was gauged using the Cambridge Autism-Spectrum Quotient (AQ) http://www.enterprise.cam.ac.uk/industry/licensing-opportunities/autism-spectrum-quotient/ and was administered to all ASC participants and controls. This fifty-item test provided an AQ score indicative of ASC severity and included questions such as "*I find it difficult to imagine what it would be like to be someone else"* and "*I notice patterns in things*

all the time". One participant with ASC did not complete the AQ and thus were excluded from all analyses that incorporated this variable.

Emotion sensitivity was gauged using the Cambridge Empathy Quotient (EQ) http://www.enterprise.cam.ac.uk/industry/licensing-opportunities/empathysystemizing-quotient-eq-sq/ and was administered to all ASC participants and controls. The EQ was originally conceived to be a measure of empathy (Baron-Cohen & Wheelwright, 2004; Lawrence, Shaw, Baker, Baron-Cohen, & David, 2004). However, empathy is a multidimensional construct (Bernhardt & Singer, 2012; Singer & Lamm, 2009) which incorporates autonomic/embodied reactions in addition to psychological/cognitive/metacognitive processes. Indeed, mirrored autonomic reactions to the emotions/pain of others may underscore empathic responses (Chauhan, Mathias, & Critchley, 2008), and these appear to be intact in ASC (Gu et al., 2015). As such autonomic responses cannot be assessed with a questionnaire measure, the EQ serves as a proxy for subjectively assessed emotion sensitivity. This forty-item test included items such as "*I can tell if someone is masking their true emotion"* and *"I am quick to spot when someone in a group is feeling awkward or uncomfortable".* Two participants with ASC did not complete the EQ and thus were excluded from all analyses pertaining to this variable.

Experimental procedure: Following informed consent, all participants performed the cardiac perception (interoceptive tasks). To prevent the temporal-timing of tones priming participants towards their own heartrate, the heartbeat discrimination task was always presented after the heartbeat tracking task. Just prior to starting, participants were asked to sit quietly and told to focus internally, in order to try to feel their own heart beating. For the heartbeat tracking task, participants were given the following instructions: "'*Without manually checking, can you silently count each heartbeat you feel in your body from the time you hear "start" to when you hear "stop"'.* This was repeated a total of 6 times using a variety of randomized trial lengths (25, 30, 35, 40, 45 and 50 sec). Following each trial, participants were asked to score their confidence on a VAS ranging from *Total guess (No heartbeat awareness)* to *Complete confidence (Full perception of heartbeat).* Once this task was

completed, participants then performed the heartbeat discrimination task. Here, each

participant was provided with the following instructions: '*You will hear ten tones. Please can*

you tell me if the tones are in or out of sync with your heartbeat'. This was repeated for a

total of 15 times, and after each trial participants again completed the confidence VAS.

Questionnaires (STAI, awareness section of BPQ, AQ and EQ) were completed by all

participants. No time limit was imposed.

Data analysis

   Interoceptive accuracy. To derive measures for interoceptive accuracy, heartbeat

tracking scores were calculated on a trial-by-trial basis based upon the ratio of perceived to

actual heartbeats $1 - \dfrac{\left| nbeats_{real} - nbeats_{reported} \right|}{(nbeats_{real} + nbeats_{reported})/2}$ (Garfinkel, et al., 2015; Hart, McGowan,

Minati, & Critchley, 2013) and these were averaged to form a mean heartbeat tracking score.

This measure calculates interoceptive accuracy independent of the amount of heartbeats in

the trial by normalising the absolute error in perceived heartbeats as a function of the overall

number of heartbeats. This interoceptive accuracy score was also used to analyse

performance across trial lengths (i.e. to explore whether accuracy changed in trials of

different length). In addition, to highlight biases in reporting, interoceptive accuracy across

trial length was also probed using the heartbeat (HB) error score (HB actual – HB reported).

   Interoceptive accuracy for the heartbeat discrimination task was assessed as a ratio

of correct to incorrect synchronicity judgments.

   Interoceptive sensibility. To assess interoceptive sensibility, total score on the

awareness section of Porge's Body Perception Questionnaire (BPQ) was calculated for each

participant (Garfinkel, et al., 2015).

   Interoceptive awareness. A receiver operating characteristic (ROC) analysis (Green

& Swets, 1966) was performed to determine the diagnostic significance of confidence for

accuracy on a trial-by-trial basis during heartbeat discrimination (Garfinkel, et al., 2015).

Correct identification of whether the tones were synchronous or asynchronous with heart served as the state variable and confidence served as the test variable. Area under the ROC curve denoted the degree to which confidence is predictive of accuracy (Garfinkel, et al., 2015)

Interoceptive trait prediction error (ITPE). The ITPE was defined operationally as the difference between objective interoceptive accuracy and subjective interoceptive sensibility. For each interoceptive accuracy and sensibility variable (heartbeat tracking score, heartbeat detection score, and awareness sub-section of the BPQ), scores were converted to standardized Z-values. On a within-participants' basis, ITPE values were calculated as the difference between interoceptive sensibility and interoceptive accuracy. ITPEs were calculated separately using accuracy scores from each task (heartbeat tracking $ITPE_T$ and heartbeat discrimination $ITPE_D$), using in each case a sensibility score provided by the awareness section of the BPQ. Positive values of ITPE indicate a propensity for individuals to *over-estimate* their interoceptive ability, while negative scores reflected a propensity for individuals to *under-estimate* their own interoceptive ability.

Statistical analyses. Group differences in axes of interoception (accuracy, sensibility), anxiety, AQ and EQ were determined using independent t-tests. In the case of state, trait anxiety, heartrate variability and BPQ, Levene's Test for Equality of Variances was significant, and thus equal variances were not assumed; df, t and significance values were adjusted accordingly. Pearson's r assessed the relationships between anxiety (state and trait) / emotional sensitivity (EQ score) and interoceptive sensitivity measures (interoceptive accuracy and ITPE).

The regression analysis was performed using a multiple linear regression model with trait anxiety as the dependent variable. All variables were initially included in the model (interoceptive accuracy, interoceptive sensibility, ITPE, Autism severity and Group). Heartbeat tracking served as the measure for interoceptive accuracy and $ITPE_D$ was calculated as described above. When accuracy on heartbeat detection and $ITPE_T$ were instead entered into the regression model, the significant contribution of interoceptive

accuracy and the interoceptive error to anxiety was maintained. In addition, the inclusion of demographics (age and gender) did not significantly affect results obtained. Regression analyses incorporated N=38 participants (two ASC individuals were excluded as they did not have values for both AQ and EQ)

Effect sizes. Cohen's *d* was used as an effect size measure for all pair-wise comparisons. Cohen's *d* can be interpreted as: *d* = 0.20 (small effect); *d* = 0.50 (medium effect) and *d* = 0.80 (large effect) (Cohen, 1992). Partial eta squared ($\eta^2 p$) was used as an effect size measure in all analyses of variance (ANOVA) can be interpreted as: $\eta^2 p$ = 0.01 (small effect); $\eta^2 p$ = 0.06 (medium effect) and $\eta 2 p$ = 0.14 (large effect) (Cohen, 1988).

Results

Participant demographics and baseline measures

Controls and ASC individuals were matched for key demographics with no significant group differences for sex and age. In addition, heart rate and heart rate variability (HRV, as indicated by standard deviation of interbeat interval) were also equivalent across the groups [t(38)=0.38, *p*=0.71; d = 0.12; t(28.62)=-0.51, *p*=0.61; d = -0.16] (Table 1).

The ASC group had significantly greater AQ scores [t(37) = -8.78 *p*<0.001; d = -2.79] and significantly reduced EQ scores [t(37) = 5.69, *p*<0.001; d = 1.85]. In addition, both state [t(34.35)=-4.81, *p*<0.001; d = -1.52] and trait [t(34.2)=-5.00, *p*<0.001; d = 1.57] anxiety scores were significantly elevated in ASC individuals (Table 1).

Interoceptive accuracy

ASC individuals were objectively impaired in interoceptive accuracy, as reflected by a significantly reduced performance in the heartbeat tracking test [t(38)=3.51, *p*=0.001; d = 1.10] (see Figure 2a). While performance of the ASC group was also impaired during the heartbeat discrimination task (proportion correct 0.55, SEM .046) relative to controls

(proportion correct 0.62, SEM 0.041), this difference did not meet threshold significance [t(38)=1.11, p=0.28; d = 0.35] (Figure 2b).

Interoceptive sensibility

In contrast to results about interoceptive accuracy, ASC individuals scored significantly higher on the awareness subscale of the Porges Body Perception Questionnaire (BPQ). This indicates enhanced subjective interoceptive sensibility, manifesting as an increased belief in interoceptive aptitude relative to control participants [t(26.43)=-6.34, p<0.001; d = -2.02] (Figure 2a).

Interoceptive performance as a function of trial duration.

Interoceptive accuracy on the heartbeat tracking task significantly varied with trial duration [F(5, 185)=2.42, p=0.037; η^2p = 0.061], but there was no interaction between trial duration and group [F(5, 185)=1.19, p=0.31; η^2p = 0.031] signalling that the change in interoceptive accuracy score as a function of trial duration did not vary with group status. However, a main effect of group [F(1, 37)=6.65, p=0.014; η^2p = 0.15] demonstrated individuals with ASC tended to perform more poorly than control participants, again reflecting the previous finding of reduced interoceptive accuracy in ASC individuals (Figure 3a).

A parallel analysis was performed using heartbeat error score (observed – reported heartbeats) within the tracking task (i.e. unlike interoceptive accuracy, this measure was not normalized for the total amount of heartbeats recorded on a given trial). As expected, heartbeat error score increased with trial duration [F(5, 185) = 11.54, p< 0.001; η^2p = 0.24]. Paralleling the previous finding in heartbeat accuracy, heartbeat error score did not interact with group [F(5, 185) = 1.14, p= 0.34; η^2p = 0.03]. Moreover, the heartbeat error score did not reveal a main effect of group [F(1, 37) =1.19, p=0.28; η^2p = 0.03]. Together, these findings signal that this error score did not significantly differ in individuals with ASC, either as a function of trial duration or in terms of absolute levels (Figure 3b).

Across the entire sample, the two objective measures of interoceptive accuracy were significantly correlated [r=0.36, *p*=0.021]. However, interoceptive sensibility and interoceptive accuracy (as determined using heartbeat tracking and heartbeat discrimination) did not correlate [r=-0.18, *p*=0.28; r=-0.17, *p*=0.31, respectively], suggesting that subjectively reported interoceptive aptitude did not predict objectively assessed interoceptive accuracy. This is in line with our previously reported findings in a non-clinical population (Garfinkel, et al., 2015).

Interoceptive awareness

There was no difference in interoceptive awareness between the ASC and control groups [t(36) = -0.57, *p*=0.57; d = -0.19].

Interoceptive trait prediction error

The ITPE, defined as the difference between subjective sensibility and objective accuracy for the heartbeat tracking task ($ITPE_T$) and the heartbeat discrimination task ($ITPE_D$), tended to be positive for the ASC group [mean (SEM): 0.97 (0.22); 0.84 (0.33)]. Together these ITPE scores signal that ASC participants were likely to score higher on subjective sensibility relative to the two objective tests of interoceptive accuracy. In contrast, the reverse trend was displayed by control participants, who tended to display greater accuracy values for both the tracking and discrimination tasks relative to subjective sensibility, resulting in negative scores for both $ITPE_T$ [-1.19 (0.17)] and $ITPE_D$ [-0.87 (0.24)]. Moreover, the values for $ITPE_T$ and $ITPE_D$ both significantly differed between the two groups [t(38)=-7.80, *p*<0.001; d = -2.49; t(38)=-4.17, *p*<0.001; d = -1.33, respectively].

Relationship to emotion

EQ was not related to either interoceptive accuracy, whether assessed using the heartbeat tracking task (r=0.26, *p*=1.00) or the heartbeat discrimination task (r=0.22, *p*=1.00). However, the ITPE, defined as the difference between objective accuracy and

subjective sensibility, displayed a significant relationship with EQ, for both the tracking task (r=-0.62, *p*<0.001) and the discrimination task (r=-0.48, *p*=0.03) (see Figure 4).

Relationship to anxiety

Across the entire sample, state anxiety was positively related to BPQ (r=0.48, *p*=0.02), but was not associated with either performance accuracy on the heartbeat tracking (r=-.22, *p*=1.00) or heartbeat discrimination tasks (r=-0.35, *p*=0.26). Similarly trait anxiety was positively related to BPQ (r=0.58, *p*<0.001), and negatively related to heartbeat discrimination accuracy (r=-0.47, *p*=0.02). No significant relationship emerged between trait anxiety and heartbeat tracking (r=-0.17, *p*=1.00).

Addressing our central hypothesis, we tested for a correlation between anxiety (state and trait scores) and ITPE. This was examined separately for heartbeat discrimination and heartbeat tracking task accuracy. Throughout, a positive relationship emerged: the subjective overestimation of interoceptive perception relative to accuracy on the heartbeat discrimination task predicted both state (r=0.54, *p*=0.004) and trait (r=0.69, *p*<0.001) anxiety scores (see Figure 5). Similarly, the corresponding subjective overestimation of interoceptive perception relative to objective interoceptive accuracy, as assessed using the heartbeat tracking task, positively predicted trait (r=0.51, *p*=0.01) anxiety although state anxiety fell just short of significance after stringent Bonferroni correction (r=0.40, *p*=0.11) anxiety.

In order to dissect the relative contribution of interoceptive accuracy, interoceptive sensibility, ITPE and ASC severity and group membership to anxiety, all variables were entered into a multiple-regression analysis (Table 2).

Replicating previous research, 'autism severity', as reflected in AQ score, was positively related to anxiety (MacNeil, Lopes, & Minnes, 2009; Simonoff, et al., 2008; White, Oswald, Ollendick, & Scahill, 2009). In addition, and again replicating previous research,

interoceptive accuracy made an independent contribution to anxiety symptoms (Dunn, et al., 2010; Ludwickrosenthal & Neufeld, 1985; Schandry, 1981). Of particular note however, was that ITPE also strongly and independently predicted anxiety.

Conclusions

Interoceptive accuracy was significantly impaired for participants on the Autistic Spectrum (ASC), as marked by diminished objective performance on a heartbeat-tracking task. In contrast, ASC displayed an increased self-reported perception of their interoceptive aptitude (i.e. enhanced *interoceptive sensibility*). This dissociation between objectively and subjectively quantified interoceptive indices is consistent with a dimensional model of interoception (Garfinkel & Critchley, 2013), wherein the dissociation between interoceptive facets is greatest in those individuals low on interoceptive accuracy (Garfinkel, et al., 2015). This finding thus reinforces the perspective that behavioural performance for interoceptive accuracy does not necessarily accord with self-perceived judgment of interoceptive aptitude. The ASC group formed the extremes of these dimensions, with diminished interoceptive accuracy and raised interoceptive sensibility.

Detection of bodily signals can contribute to emotional feeling states (Wiens, et al., 2000). Enhanced coherence between subjective and cardiac signatures of emotion are observed in populations with specialized training in body awareness, such as Vipassana meditators and dancers (Sze, Gyurak, Yuan, & Levenson, 2010). ASC is associated with disrupted emotional processing, where difficulties identifying and describing feelings in self and other are considered integral characteristics of Autistic Spectrum Conditions (Hadjikhani, et al., 2009; Hill, Berthoz, & Frith, 2004). Given that we observed reduced interoceptive accuracy in ASC, deficits in emotional processing in these individuals could potentially arise in part through a compromised interoceptive channel: diminished accuracy with which internal bodily sensations are detected could impede this information from informing emotion judgments. Thus, the objective difficulty displayed by ASC individuals in

accessing internal signals may disrupt subsequent performance in emotion, as supported by previous research linking ASC to alexithymia (Bird et al., 2010) and alexithymia with impoverished interoceptive accuracy (Ernst et al., 2014).

Emotions draw on central representations of bodily arousal and share common neural substrates: in particular, the anterior insula subserves both interoceptive accuracy (Critchley, et al., 2004), and underscore deficits in emotion processing (Berthoz et al., 2002; Frewen, Dozois, Neufeld, & Lanius, 2008; Karlsson, Naatanen, & Stenman, 2008), thus lending credence to the proposal that integrative processing within this region permits the detection of bodily state to inform emotional experience (Terasawa, et al., 2013). Aberrant activation of the insula during emotional processing is noted as a feature of ASC (Duerden, et al., 2013; Hadjikhani, et al., 2009; Watanabe, et al., 2012). Moreover, the functional connectivity of the insula is impaired in ASC, including the observation that there is less efficient cross-talk between anterior insula and somatosensory cortices (Ebisch, et al., 2011). Together, these results suggest that the capacity of anterior insula to integrate emotional and motivational state with sensory information concerning the physical state of the body may underscore core symptoms and emotion processing deficits in ASC.

To assesses interoceptive accuracy, two tests were administered: heartbeat tracking (Schandry, 1981) and heartbeat discrimination (Katkin, et al., 1983; Whitehead, et al., 1977). The ASC group had diminished interoceptive accuracy when assessed using heartbeat tracking, and while they revealed lower mean scores for interoceptive accuracy derived using heartbeat discrimination, this difference did not reach significance. Prior interoceptive research demonstrates a relationship between objective performance on these two heartbeat tests (e.g. Garfinkel, et al., 2015; Hart, et al., 2013; Knoll & Hodapp, 1992), however this relationship is not always observed, especially in smaller samples (e.g. Phillips, Jones, Rieger, & Snell, 1999; Schulz, Lass-Hennemann, Sutterlin, Schachinger, & Vogele, 2013). Moreover, different factors can differentially impact performance on these two heartbeat perception tasks, such as stress (Schulz, et al., 2013). Heartbeat tracking may be considered a "purer" test of interoception, as performance depends on internal monitoring of

bodily state, while tests of heartbeat discrimination typically also involves an external stimulus (e.g. tone or light) and success thus depends on simultaneous multimodal internal-external integration in order to make successful judgments of synchronicity (Kootz, Marinelli, & Cohen, 1982). Given that we did not observe differences in heartbeat discrimination performance between the two groups, our results suggest that this integrative process remains relatively intact in ASC individuals.

Heartbeat tracking scores can be influenced by beliefs about heart rate (Ring, Brener, Knapp, & Mailloux, 2015), it is thus possible that differences between the groups could be influenced, in part, by altered beliefs/knowledge about heart-rate in ASC individuals. While explicit knowledge about heart rate was not probed in the current experiment, it should be noted that such altered beliefs relative to actual heart rate can also be conceptualized as an error in trait prediction. Work in children with ASC (aged 8 to 17 years) suggests that, for longer intervals only, children with Autism are actually superior at tracking their heartbeats. This effect was attributed to a heightened ability to sustain attention in children with ASC (Schauder, Mash, Bryant, & Cascio, 2014).

Importantly, we showed using a regression analysis that the discrepancy (prediction error) between interoceptive accuracy and interoceptive sensibility predicted anxiety symptomatology beyond the effect of ASC severity. It has been proposed that noisy interoceptive input in combination with noisily amplified self-referential interoceptive predictive belief states is fundamental to the pathogenesis of anxiety (Paulus & Stein, 2010). By demonstrating that the interoceptive trait prediction error (ITPE) predicts anxiety symptoms, our results are consistent with this model and suggest that interoceptive structure may be a vulnerability factor for anxiety.

The relationship between interoception and emotion can be conceived in the context of *predictive processing* (Clark, 2013), whereby emotional content emerges through predictive inference on the causes of interoceptive signals (Seth, 2013). Within this framework of 'interoceptive inference' ASC has been proposed to emerge from a failure to adequately assimilate the contribution of interoceptive sensory signals in the formation of

self-models during early childhood (Quattrocki & Friston, 2014). This in turn rests on dysfunctional weighting of interoceptive prediction error signals, perhaps mediated by failures of neuromodulatory control. Importantly, prediction errors in this setting refer to synchronic (i.e., moment-to-moment) discrepancies between expected and actual interoceptive signals, rather than trait-based differences between objective and subjective performance (as indexed by ITPE). Nonetheless these two forms of interoceptive prediction error could be related within ASC, since mismatches between objective and subjective performance (ITPE) could rest on a failure to optimally incorporate 'bottom-up' interoceptive (error) signals when updating 'top-down' interoceptive predictions that inform (hierarchically higher) subjective judgments of sensibility. A failure to connect hierarchically high levels of interoceptive inference (underlying sensibility) with low levels (underlying accuracy) could also relate to alexithymia and disruptions in autonomic regulation and homeostatic control which are also characteristic of ASC (Quattrocki & Friston, 2014).

For the heartbeat detection task, two intervals were used based on the empirical recommendations of Wiens and Palmer (Wiens & Palmer, 2001) (which also accord with the preference distributions identified by (Brener & Kluvitse, 1988)). The approach acknowledges that there may be heterogeneity across participants as to when in the cardiac cycle they best report detection of heartbeats (Brener & Kluvitse, 1988; Brener, Liu, & Ring, 1993; Ring & Brener, 1992). Such variability would make it harder to detect group differences in measures task accuracy (or symptom correlations). It is thus possible this may have masked potential group differences in the present study. Future research may usefully employ a range of tone-delays to explore such effects (e.g. using methodology of Weins and Palmer 2001) to test if there may be systematic differences in people with autism. Increasing the number of trials in the heartbeat discrimination task may also enhance the sensitivity of the current paradigm to detect population-level group differences (Kleckner, Wormwood, Simmons, Barrett, & Quigley, 2015). Moreover, performance on the heartbeat tracking task (Schandry, 1981) can be influenced by beliefs and/or knowledge about one's

own heartrate (Ring & Brener, 1996; Ring, et al., 2015). Our experimental procedures sought to minimise such potential effects. We observed that both controls and ASC individuals have a tendency to underreport heartbeats. We show this this tendency is exaggerated in individuals with ASC. It is thus theoretically possible that group differences in interoceptive accuracy using this measure could have been driven by systematic differences in beliefs or knowledge about heart rate in the ASC group relative to controls. Future studies are needed to probe knowledge and beliefs about heart rate and their relation to interoceptive experience in ASC individuals. Finally, in light of recent findings which indicate that interoceptive accuracy is actually superior in children with Autism at longer trial durations (e.g. 100sec), future studies could employ longer trial durations. Enhanced capacity for sustained attention in repetitive tasks is reported for ASC (there are also reports of impaired capacity for sustained attention (Chien et al., 2014)). Thus a goal of future research is to disentangle any potential confounding attentional affects which might drive apparent group differences in interoceptive aptitude. These methodological considerations may be informed by other techniques such as heartbeat evoked potentials (HEP) and fMRI, to delineate better the interplay between neural, psychological, and perceptual factors that contribute to apparent interoceptive deficits in ASC. However, despite these methodological considerations, the measures of interoception obtained in the present study display high predictive validity, differentiating the two groups (with potential implications for patient screening), and predicting emotion and anxiety symptomatology in a manner consistent with the theory- driven hypothesis of underlying interoceptive perturbation.

Future research should further delineate the relationship between different constructs of emotion and affective (e.g. anxiety) symptoms in relation to dimensions of interoception. In the present study, only a questionnaire measures was used to assess emotional sensitivity, and thus future studies could investigate how interoception deficits in ASC may be associated with other measures of emotion, such as behavioural tests of emotion identification and autonomic indexes of emotion such as blood pressure, galvanic skin

response and heartrate variability. Such work could also better inform understanding of how bodily changes and interoception contribute to emotional experience in ASC. It should be noted that the precise contribution of bodily state to emotional experience is not universally demonstrated. For example, patients with high spinal cord transection in whom afferent information from the lower body is partially interrupted by the lesioning of spinal sensorimotor and viscerosensory pathways, may show no deficits in subjective indices of emotion (Cobos, Sanchez, Garcia, Vera, & Vila, 2002) or even exaggerated affective responses (Nicotra, Critchley, Mathias, & Dolan, 2006). It is possible that the degree to which changes in bodily state map onto emotion experience may be further disrupted in ASC as mediated by impaired interoceptive accuracy.

Our results have therapeutic implications through indicating a potential pathway to alleviate symptom distress via the training both enhanced interoceptive accuracy, and greater predictive control of internal bodily signals (Schaefer, et al., 2014). Other techniques associated with enhanced body awareness, including meditation, are known to have an anxiolytic effect (Serpa, Taylor, & Tillisch, 2014). Thus, our findings suggest that interoceptive training may represent potentially valuable approach to reduce anxiety and subjective distress in people with Autism Spectrum Conditions.

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Legends for Figures

Figure 1: Interoceptive accuracy, interoceptive sensibility and interoceptive awareness form the three facets of interoception. These three dimensions respectively map onto objective, subjective and metacognitive awareness measures of interoception.

Figure 2: Interoceptive accuracy, as gauged using heartbeat tracking, was elevated in Control individuals while self-assessed interoceptive sensibility was elevated in the ASC group.

Figure 3: A main effect of group signified that the ASC group were significantly poorer at interoceptive accuracy, irrespective of trial duration (**A**). The heartbeat error score (HB actual – HB reported) increased monotonically with trial duration, but this increase was not affected by group (**B**).

Figure 4: A negative interoceptive trait prediction error ($ITPE_T$), reflecting a tendency to be more interoceptively accurate (heartbeat tracking) than self-reported interoceptive sensibility, predicted enhanced emotional sensitivity. In contrast to the control group, ASC was associated with a tendency to over-estimate interoceptive aptitude (as marked a positive $ITPE_T$ reflecting greater interoceptive sensibility scores relative to interoceptive accuracy scores), which was associated with reduced emotional sensitivity (EQ) scores.

Figure 5: A negative $ITPE_D$, reflecting a tendency to be more interoceptively accurate (heartbeat discrimination) relative to self-reported interoceptive sensibility, was associated with reduced anxiety. In contrast to the control group, patients with ASC were characterised by a tendency to over-estimate interoceptive aptitude (as marked by a positive $ITPE_D$ (reflecting greater sensibility scores relative to accuracy scores), which was associated with enhanced anxiety.
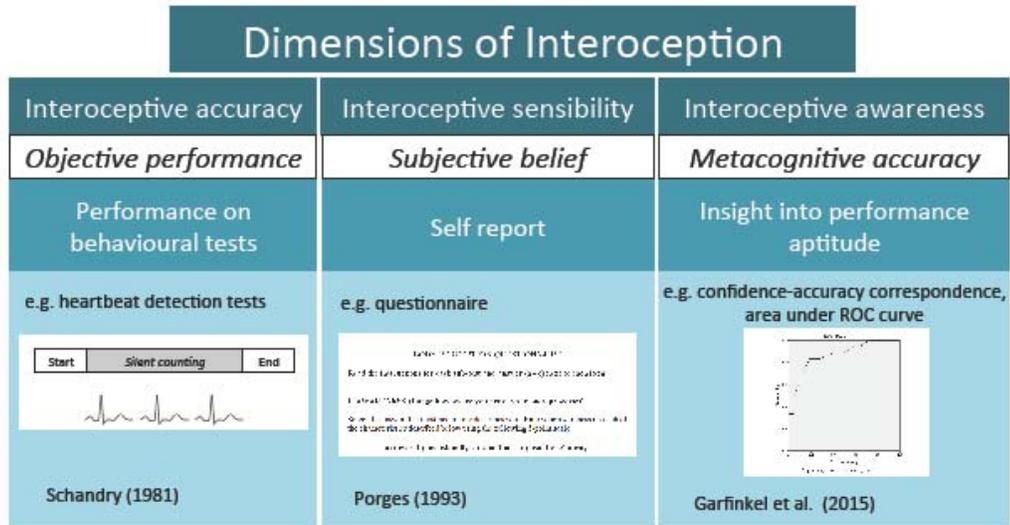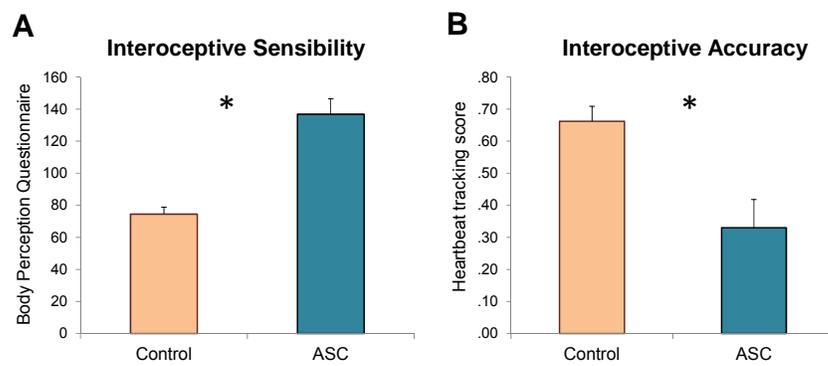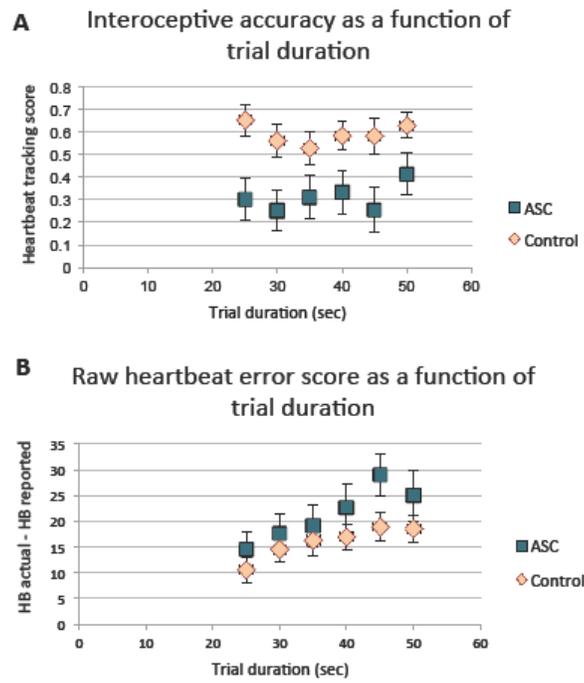
Figure 1

Figure 2

Figure 3

A   Interoceptive accuracy as a function of trial duration

B   Raw heartbeat error score as a function of trial duration
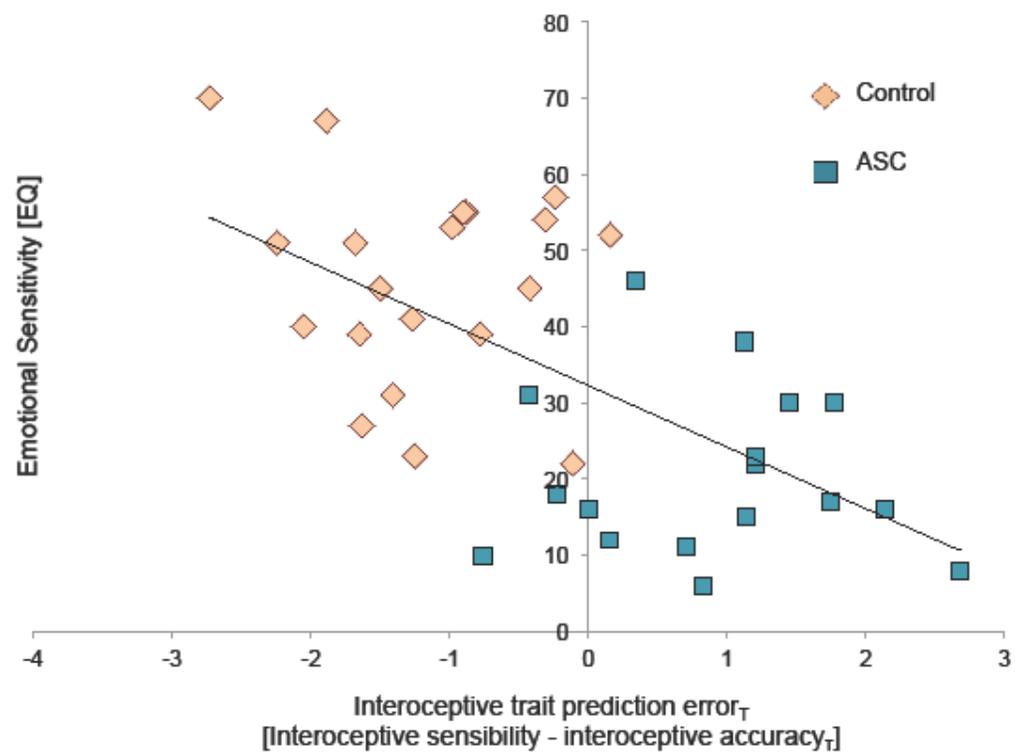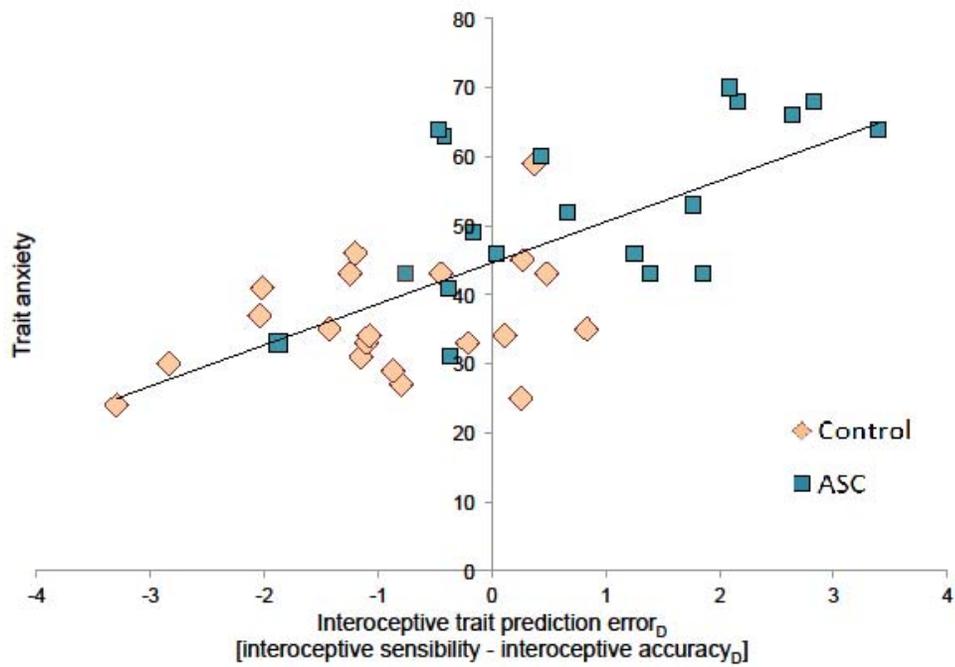
Figure 4

Figure 5

Legends for Tables

Table 1: Demographic and baseline physiological and affective measures. Mean (standard deviation), * Controls and ASC individuals significantly differ.

	Control	ASC
Sex (Males / Females)	18 / 2	18 / 2
Age	27.81 (3.4)	28.06 (8.8)
Heart rate (beats/minute)	76.36 (13.36)	74.87 (11.90)
HRV (beats / minute)	4.77 (1.32)	5.12 (2.83)
AQ *	13.35 (5.8)	34.82 (9.89)
EQ *	45.85 (13.28)	22.94 (12.18)
State anxiety *	30.65 (6.40)	42.94 (8.79)
Trait anxiety *	36.35 (8.47)	53.667 (12.25)

Table 2: Linear regression analysis indicates that in addition to Autism severity (AQ), both interoceptive accuracy and the interoceptive prediction error make an independent contribution to anxiety.

		t	p
AQ *	0.54	3.10	0.005
Interoceptive Accuracy *	0.31	2.58	0.015
Interoceptive Sensibility	-0.35	-1.79	0.083
Interoceptive Prediction Error *	0.66	4.17	<0.00
Group	0.20	0.94	0.354