TITLE: Interoceptive impairments do not lie at the heart of Autism or Alexithymia

SHORT TITLE: Unimpaired interoception in Autism and Alexithymia

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Abstract

Background: Quattrocki and Friston (2012) argued that abnormalities in interoception–the process of representing one's internal physiological states–could lie at the heart of autism, because of the critical role interoception plays in the ontogeny of social-affective processes. This proposal drew criticism from proponents of the *alexithymia hypothesis*, who argue that social-affective and underlying interoceptive impairments are not a feature of autism per se, but of alexithymia (a condition characterised by difficulties describing and identifying one's own emotions), which commonly co-occurs with autism. Despite the importance of this debate for our understanding of ASD, and of the role of interoceptive impairments in psychopathology more generally, direct empirical evidence is scarce and inconsistent.

Methods: Experiment 1 examined in a sample of 137 neurotypical individuals the association among autistic traits, alexithymia, and interoceptive accuracy on a standard heartbeat tracking measure of interoceptive accuracy. In Experiment 2, interoceptive accuracy was assessed in 46 adults with ASD (27 of whom had clinically-significant alexithymia) and 48 neurotypical adults.

Results: Experiment 1 confirmed strong associations between autistic traits and alexithymia, but yielded no evidence to suggest that either was associated with interoceptive difficulties. Similarly, Experiment 2 provided no evidence for interoceptive impairments in autistic adults, irrespective of any co-occurring alexithymia. Bayesian analyses consistently supported the null hypothesis.

Conclusions: The observations pose a significant challenge to notions that interoceptive impairments constitute a core feature of either ASD or alexithymia, at least as far as the direct perception of interoceptive signals is concerned.

General scientific summary: This article suggests that impairments in interoception–the process of representing one's internal physiological states–do not lie at the heart of either autism or alexithymia.

Introduction

Interoception refers to the representation of one's internal physiological states, such as breathing, hunger, thirst, and heart rate (Craig, 2003). Recently, studies have linked interoceptive accuracy (i.e., the extent to which one can detect interoceptive signals accurately) to a number of important psychological functions, such as emotion-processing (Barrett, Quigley, Bliss-Moreau, & Aronson, 2004; Shah, Catmur, & Bird, 2016; Zaki, Davis & Ochsner, 2012), empathy (Fukushima, Terasawa, & Umeda, 2011), theory of mind (Demers & Koven, 2015; Shah, Catmur, & Bird, 2017), and self-awareness (Seth, 2013). These associations support theories that suggest cognition is "embodied" (Gallese & Sinigaglia, 2011; Glenberg, 2010; Goldman & de Vignemont, 2009), and imply that interoception impairments might play a critical role in psychological disorders. Indeed, impairments in interoception have been implicated recently in increasingly prominent theories of one developmental disorder, in particular, namely autism spectrum disorder (ASD; Quattrocki & Friston, 2014).

ASD is a neurodevelopmental disorder diagnosed on the basis of behavioural impairments in social-communication and behavioural flexibility (American Psychiatric Association (APA); 2013). At the cognitive level, difficulties with theory of mind (Yirmiya, Erel, Shaked, & Solomonica-Levi, 1998), emotion-processing (Gaigg, 2012), and psychological aspects of self-awareness (Williams, 2010) are well-established among people with ASD. Moreover, approximately 50% of autistic individuals have clinically significant levels of alexithymia (Berthoz & Hill, 2005; Hill, Berthoz, & Frith, 2004; Joukamaa et al., 2007; Milosavljevic et al., 2016) - a condition characterised by difficulties with representing, understanding, and describing one's own emotional states (Taylor, 1984). This collection of impairments led Quattrocki and Friston (2014) to suggest that impairments in interoception, due to a dysfunctional oxytocin system, may be the root cause of autism. Oxytocin is a hormone and neurotransmitter that plays a significant role in regulating social-affiliative behaviours. Quattrocki and Friston (2014) argue that a dysfunctional oxytocin system could lead to abnormalities in the production and modulation of interoceptive signals, and their integration with exteroceptive information about the environment. As a result, autistic children develop impoverished internal models of emotional states (i.e., alexithymia) and the self, more generally, whilst external social-emotional signals hold less salience and therefore lead to the specifically characteristic social-affective impairments of the disorder. A crucial prediction that follows from this view is that interoceptive accuracy should be associated with the number of ASD traits manifested by a person and also be reliably impaired among people with a diagnosis of ASD (Hypothesis 1).

In contrast, others have argued that self-awareness difficulties in ASD should be restricted to awareness of one's own cognitive and emotional states (i.e., the *psychological* Self), leaving basic *detection* of one's own physiological states (i.e., the *physical* Self) essentially unimpaired (Lind, 2010; Uddin, 2011; Williams, 2010). This view is derived from observations of a preserved sense of agency (Schauder, Mash, Bryant, & Cascio, 2015; Cascio, et al., 2012; Paton, Hohwy, & Enticott, 2012) and preserved self-recognition (Dawson & McKissick, 1984; Ferrari & Matthews, 1983; Lind & Bowler, 2009) in ASD. This account, therefore, leads to the prediction that interoceptive accuracy should not be associated with ASD traits or impaired in people with a full diagnosis of ASD (Hypothesis 2).

Distinct from the two views above is the more recent idea that many of the social-affective difficulties experienced by people with ASD are, in fact, the result of co-occurring alexithymia, rather than the result of ASD itself (Bird & Cook, 2013; Cook, Brewer, Shah, & Bird, 2013; Bird et al., 2010; Oakley, Brewer, Bird & Catmur, 2016). According to this '*alexithymia hypothesis*', difficulties with emotion-processing and empathy are only apparent in people with ASD who also have high levels of alexithymia (or comorbid alexithymia).

Most important, unlike Quattrocki and Friston (2014) who view interoceptive abnormalities as central to the aetiology of ASD, the *alexithymia hypothesis* considers interoceptive abnormalities central to the aetiology of alexithymia (Shah, Hall, Catmur, & Bird, 2016; Hatfield, Brown, Giummarra & Leggenhager, 2017; Herbert, Herbert, & Pollatos, 2011; Brewer, Happé, Cook, & Bird, 2015). This leads to the prediction that interoceptive accuracy should be associated with the level of alexithymia, rather than the number of ASD traits, manifested by a person and that it should be significantly impaired only among people with ASD who manifest clinically significant levels of alexithymia (Hypothesis 3).

Although distinguishing the three competing predictions above is of central importance to our understanding of the defining features of ASD, only four studies have assessed interoceptive accuracy in this population and the results are highly inconclusive. In line with Hypothesis 1, Garfinkel and colleagues (Garfinkel et al., 2016) found *reduced* accuracy among 20 adults with ASD on a classic heartbeat tracking task that required participants to keep count of their heartbeats without physically taking their own pulse. Likewise, Palser et al. (2018) found reduced interoceptive accuracy on the heartbeat tracking task in 30 autistic children. In contrast, Schauder et al. (2015) observed no impairments on the same heartbeat tracking task in a group of 21 autistic children. In keeping with Hypothesis 2, this study furthermore found that heart beat tracking accuracy was correlated with a test of bodily awareness on which children with autism were also unimpaired, thus confirming a putative link between preserved interoception and a preserved awareness of the *physical* self in ASD. Finally, Gaigg, Cornell, and Bird (2016), using a physiological arousal tracking paradigm, and Shah et al., (2016), using the traditional heartbeat tracking task, obtained partial evidence for Hypothesis 3 by showing that interoceptive accuracy was unimpaired in adults with ASD who were matched to a comparison group on self-reported levels of alexithymia. This group matching ensured that levels of alexithymia were experimentally controlled when examining interoceptive accuracy, leading the authors to suggest that interoceptive impairments *would* have been observed in ASD if groups had *not* been matched on alexithymia and that differences in findings across other studies (e.g., Garfinkel et al., 2016; Schauder et al., 2015) likely reflect differences across ASD samples in the prevalence of alexithymia.

The evidence concerning interoception in ASD is not only difficult to interpret because of the inconsistencies across studies, but also because three of the five studies essentially argue for the null hypothesis (i.e., no difference between ASD and comparison groups) on the basis of very small samples. Moreover, in the studies of Gaigg et al. (2016) and Shah et al. (2016), the group matching strategy meant that the majority of individuals scored in the sub-clinical range for alexithymia, rendering the ASD groups non-representative of the wider autism spectrum where an estimated 50% of individuals manifest alexithymia (Berthoz & Hill, 2005). In other words, the central claim of the alexithymia hypothesis–that interoceptive impairments *would* be observed in individuals with ASD who have clinically significant levels of alexithymia– remains untested. To test this prediction and contrast it effectively with the alternative predictions outlined above, it is necessary to compare interoceptive accuracy among individuals with ASD who report clinically significant alexithymia (ASD-high alexithymia) with interoceptive accuracy among matched individuals with ASD who report sub-clinical levels of alexithymia (ASD-low alexithymia). If Hypothesis 1 is correct, regardless of alexithymia level, individuals with ASD should show impaired interoception relative to an NT comparison group. In contrast, if Hypothesis 2 is correct, individuals with ASD should show unimpaired interoception, regardless of alexithymia level. Finally, if Hypothesis 3 is correct, then only ASD-high alexithymia individuals should manifest diminished interoceptive accuracy, with the ASD-low alexithymia individuals demonstrating equivalent interoceptive accuracy to the NT group. In

Experiment 2, we tested these predictions among 46 individuals with ASD and 48 NT participants. First, however, Experiment 1, examined the associations predicted by Hypothesis 1 and 3 among interoceptive accuracy, alexithymia, ASD traits, and theory of mind in 137 NT individuals.

Experiment 1: Method

Participants

One hundred and thirty-seven students (114 female) from the University of Kent took part in Experiment 1. The average age of participants was 19.73 years (*SD* = 2.98; range = 18-23 years). No participant had a history of ASD, according to self-report. All participants gave informed consent and received course credit in partial fulfilment of their degree, for taking part in the study. The experiment was approved by the School of Psychology Research Ethics Committee, University of Kent (Ethics ID: 201714870662234338).

Materials and procedures

Interoception was measured using a standard heartbeat tracking task (Schandry, 1981). In a quiet room, participants were asked to close their eyes and, without taking their pulse, silently count their heartbeat during four different time intervals (25, 35, 45 and 100 sec), which were presented in a randomised order. An auditory tone signalled the beginning and end of each time interval. A pulse oximeter (Contec Systems CMS-50D+; Qinhuangdao, China) attached to participants' index finger measured their actual heart rate. Interoceptive Accuracy (IA) was calculated as: 1 – (│recorded number of heartbeats – counted number of heartbeats│)/((recorded heartbeats + counted number of heartbeats)/2), (Garfinkel et al., 2015). This provided a value between -1 and 1 for each time interval, with more positive values indicating better IA[1]. It should be noted that the heartbeat tracking task has come under recent scrutiny, with some claiming that the task is not always/necessarily a valid measure of interoception (see Brener & Ring, 2016 for a review). We consider this concern further in the Discussion section, below. Here, we note only that the heartbeat tracking task is (for better or worse) by far the most widely used measure of interoception in the literature, in part because of ease of administration and in part because monitoring one's own heartbeat is fundamental to emotional experience. The task has good test-retest reliability (Mussgay, Klinkenberg & Rüddel (1999), is sensitive to individual differences (Christensen, Gaigg & Calvo-Merino, 2018; Dunn et al., 2010; Garfinkel et al., 2015) and is mediated by brain regions that are involved in awareness of one's physiological states (Critchley et al., 2004; Pollatos et al., 2007). Nevertheless, to address some of the concerns that exist in relation to this task, we also present some additional analyses in Supplement 1 (see point 4 of the supplementary material, in particular).

The 50-item Autism-spectrum Quotient (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) was administered as a self-report measure of autistic traits, and the 20-item Toronto Alexithymia Scale (TAS-20; Bagby, Parker, & Taylor, 1994) as a self-report measure of alexithymia. Each questionnaire requires participants to indicate to what extent a series of statements applies to them (e.g., AQ: "I find social situations easy"; TAS-20: "I have feelings that I can't quite identify"), with scores on the AQ ranging from 0-50 (scores > 26 are suggestive of a possible diagnosis of autism) and scores on the TAS-20 ranging from 20-100 (scores > 60 indicate clinically significant alexithymia). In addition, participants completed the Reading the Mind in the Eyes (RMIE) task (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). This widely recognised measure of emotional theory of mind requires participants to decide which of four mental state terms (mostly emotional in nature) best describes the feelings conveyed by the eye-region of faces as portrayed in 36 unique photographs. Scores range from 0-36, with higher scores indicating better emotional theory of mind. We included the RMIE task specifically because it differentiates groups of ASD participants from groups of neurotypical participants and because it taps those emotional aspects of ToM that are thought to be related to alexithymia (see Oakley et al, 2016). Given that recent studies have shown an association between interoceptive accuracy and emotional, but not non-emotional, aspects of mindreading (Shah et al., 2017), we included the RMIE to investigate the relation between emotional ToM and interoception.

Statistical power and analysis

An *a priori* power calculation using G*Power3 (Faul, Erdfelder, Buchner, & Lang, 2009) revealed that, to detect an association between interoceptive accuracy and TAS score of r = -.37 (as found by Herbert et al., 2011, and Shah et al., 2016) on 80% of occasions using two-tailed tests, 55 participants are required. A larger sample was recruited here to allow for the cross validation of the findings, by randomly splitting the total sample into two subsamples (*n* = 68 and 69, respectively), each with sufficient power (>.90) to detect a reliable association between TAS-20 score and interoceptive accuracy. Bayesian analyses were also conducted (using JASP 0.8.1; JASP Team, 2016) to provide a more graded interpretation of the data than is possible using *p* values or effect sizes alone (e.g., Dienes, 2014; Rouder et al., 2009). Bayes factors (BF_{10}) > 3 provide firm evidence for the alternative hypothesis (with values > 10, > 30, and >100 providing strong/very strong/decisive evidence) and values under 1 provide evidence for the null (with values < 0.33 providing firm evidence; see Jeffreys, 1961).

Experiment 1: Results

Among the entire sample, the 137 participants scored a mean of 25.82 (SD = 3.97) on the RMIE task, 16.99 (SD = 6.66) on the AQ, and 50.82 (SD = 10.29) on the TAS. The mean interoceptive accuracy score on the heartbeat detection task was .50 (SD = .27). Crucially, there was no significant association between interoceptive accuracy and TAS total score, r = .008, p = .92, BF_{10} = 0.11, or between interoceptive accuracy and any of the other variables: (AQ total score: r = -.11, p = .22, BF_{10} = 0.22; RMIE: r = .03, p = .73, BF_{10} = 0.11). TAS total score was, however, associated significantly with both AQ total score, r = .42, p <.001, BF_{10} > 100, and RMIE, r = -.24, p = .005, BF_{10} = 5.16, whereas AQ total score and RMIE were not significantly associated in the current sample, r = .11, p = .21, BF_{10} = 0.24 (and note that the association between TAS and RMIE remained significant after controlling for AQ, r_p = -.21, p = .01).[2] Finally, Fisher's Z tests revealed that the interoceptive accuracy × TAS correlation was significantly different from that reported by Herbert et al., (2011), Z = 3.35, p < .001, and Shah et al., (2016), Z = 2.03, p = .04. For ease of reference, this pattern of correlations is set out in Table 1 along with those for experiment 2.

(INSERT TABLE 1 ABOUT HERE)

Although interoceptive accuracy and TAS were not significantly associated, it may be that interoceptive accuracy would nonetheless be significantly impaired among individuals with significant levels of alexithymia. To investigate this, the current sample was divided according to scores on the TAS. Those with scores above the cut-off were assigned to a "high alexithymia" group (n = 30) and those with scores below the cut-off to a "low alexithymia" group (n = 107). The average interoceptive accuracy score was .49 (SD = .28) among the low alexithymia group and .55 (SD = .26) among the high alexithymia group, a difference that was small and statistically non-significant, t(135) = 1.04, p = .30, d = 0.22, BF_{10} = 0.35. The mean interoceptive accuracy score for each time interval on the heartbeat detection task among each alexithymia group is presented in Table 2. A 2 (Group: high alexithymia/low alexithymia) × 4 (Time interval: 25s/35s/45s/100s) ANOVA was conducted on this data. Results revealed non-significant main effects of time interval, $F(3, 405) = 1.13$, $p = .34$, $\eta_p^2 = .008$, and group, $F(1, 135) = 1.08$, $p = .30$, $\eta_p^2 = .008$. Moreover, the Group × Time interval interaction effect was also non-significant, $F(3, 405) = 1.65$, $p = .18$, $\eta_p^2 = .01$. Thus, there were no significant differences between the high and low alexithymia groups in terms of either overall level or patterns of interoceptive accuracy on the heartbeat tracking task.

Cross-validation of results.

We assessed the reliability of the current findings by randomly splitting our sample into two groups of *n* = 68 and 69 participants respectively and re-analysing the data in each sub-sample. The results are presented in full in Supplement 1. In summary, results were identical in each sub-sample and replicated the results observed in the full sample of 137.

(INSERT TABLE 2 ABOUT HERE)

Experiment 2: Method

Participants

Forty-six adults with ASD and 48 neurotypical comparison adults aged between 20 and 64 years were recruited and tested either at City, University of London, or the University of Kent. Verbal, performance, and full-scale IQ scores were gained for all participants using either the Wechsler Abbreviated Scale for Intelligence-II (Wechsler, 1999) (*n* = 38), or the Wechsler Adult Scales of Intelligence (Wechsler, 2008) (*n* = 56). Participants in the ASD group had received verified diagnoses, according to conventional criteria (American Psychiatric Association, 2000; World Health Organisation, 1993). In addition, participants with ASD completed the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000), a detailed observational assessment of ASD features. Participant groups were closely matched for age, sex, VIQ, PIQ and FSIQ, but differed significantly in AQ, TAS, and RMIE scores (see Table 3). All participants in the ASD group scored above the ASD cut-off score of 7 on the ADOS and/or 26 on the AQ. Ten of the 46 participants with ASD scored above the ASD cut-off on the AQ only (with ADOS scores of 6, 6, 6, 6, 5, 5, 5, 4, 3, 3, respectively). Importantly, none of the results reported in Experiment 2 changed substantively when these 10 participants with ASD were excluded from analyses (see supplemental material).

(INSERT TABLE 3 ABOUT HERE)

Materials and procedures

Participants from each group completed a version of the heartbeat tracking task used in Experiment 1. Thirty-eight (17 ASD, 21 NT) completed the heartbeat tracking task at location 1 (University of Kent), using identical materials and procedures as in Experiment 1. The remaining 56 participants completed the heartbeat tracking task at location 2 (City, University of London), using almost identical materials and procedures as in Experiment 1. The only difference was that, rather than sitting with their eyes closed and an auditory tone signalling the start and stop of each interval, participants saw a start/stop signal on a screen (a heart appeared along with the word ‘Go’ at the start, then the heart disappeared at the end and was replaced by ‘Stop’) followed by a screen that asked participants to enter their count using the keyboard. In addition, the hardware used to record heart beats was different and consisted of an ADInstruments© PowerLab unit (ML845) with a bioelectrical signal amplifier (ML408) that recorded the ECG signal through three shielded snap-connect electrodes placed on the participants chest and elbow (the reference electrode). LabChart 7 software was used to record the raw ECG signal at 1kHz and the data were processed offline to extract the heart beat frequencies. A ‘Stop’ and ‘Go’ signal was superimposed on the ECG trace through a hardware link with the stimulus presentation computer. Importantly, there were no systematic differences in results across the two locations.

Statistical power and analysis

Given ambiguities in the methods and results of previous studies, we based our sample size on that required to detect a small-to-moderate overall group difference in interoceptive accuracy, given that it is arguable that any effect smaller than this is unlikely to be clinically significant (even if it is statistically significant). A sample of 94 participants provides sufficient power to detect a between-group difference of 0.50 if it exists. Crucially, Bayesian analyses were used to supplement null hypothesis significance testing.

Experiment 2: Results

The average *interoceptive accuracy* score was .57 (SD = .27) among the ASD group and .61 (SD = .32) among the NT group, a difference that was statistically small and non-significant, $t(92) = 0.63$, $p = .53$, $d = 0.13$, $BF_{10} = 0.26$. The mean interoceptive accuracy score for each time interval on the heartbeat detection task in each diagnostic group is shown in Figure 1. A 2 (Group: ASD/NT) × 4 (Time interval: 25s/35s/45s/100s) ANOVA was conducted on this data. Neither the main effect of group, $F(1, 92) = 0.39$, $p = .53$, $\eta_p^2 = .004$, nor the Group × Time interval interaction effect, $F(3, 405) = 1.65$, $p = .18$, $\eta_p^2 = .01$, was significant. Thus, there were no significant differences between the ASD and comparison groups in terms of either overall level of interoceptive accuracy or patterns of interoceptive accuracy across the four time intervals.

Out of 46 participants with ASD, 27 (58.7%) scored over the TAS cut-off for alexithymia, compared to only three of 48 (6.3%) of NT participants, $\chi^2 = 29.73$, p < .001, φ = .56, which is comparable to the prevalence estimates of clinically significant alexithymia in ASD as estimated in the sample of (e.g., Hill et al., 2004). Although the analyses above indicated that the ASD group *as a whole* did not manifest a deficit in interoception, it is possible that (in accordance with the alexithymia hypothesis) interoceptive accuracy *would* be diminished among those participants with ASD who self-report clinically significant levels of alexithymia on the TAS. In order to investigate this, the ASD sample was divided according to TAS score. Those with scores above the cut-off were assigned to a "high alexithymia" ASD group and those with scores below the cut-off to a "low alexithymia" ASD group. These sub-samples were matched in terms of age, VIQ, PIQ, FSIQ, sex, ADOS total score, and RMIE total score, all *p*s >.40, all *d*s <0.27.

The average interoceptive accuracy score on the heartbeat detection task was .51 (SD = .24) among the low alexithymia sub-sample and .61 (SD = .29) among the high alexithymia sub-sample, a difference that was small and statistically non-significant, $t = 1.30$, $p = .20$, $d = 0.39$, $BF_{10} = 0.58$. The mean interoceptive accuracy score for each time interval on the heartbeat detection task among each sub-sample of ASD participants is shown in Figure 1. A 2 (Subsample: high alexithymia/low alexithymia) × 4 (Time interval: 25s/35s/45s/100s) ANOVA was conducted on this data. Neither the main effect of subsample, $F(1, 44) = 1.69$, $p = .20$, $\eta_p^2 = .04$, nor the Subsample × Time interval interaction effect, $F(3, 132) = 0.57$, $p = .64$, $\eta_p^2 = .01$, was significant. Thus, there were no significant differences between the high and low alexithymia sub-samples of ASD participants in terms of either overall level or patterns of interoceptive accuracy.

In terms of associations, interoceptive accuracy was non-significantly associated with TAS total score among both participants with ASD, $r = .08$, $p = .59$, $BF_{10} = 0.21$, and NT participants, $r = .21$, $p = .16$, $BF_{10} = 0.47$. Likewise, interoceptive accuracy was non-significantly associated with AQ total score among both participants with ASD, $r = .03$, $p = .83$, $BF_{10} = 0.19$, and NT participants, $r = .21$, $p = .16$, $BF_{10} = 0.47$. Fisher's Z tests revealed that the interoceptive accuracy × TAS total score correlation was significantly smaller in magnitude than those reported by Herbert et al. (2011) and Shah et al. (2011) among both participants with ASD (all *Z*s > 2.00, all *p*s < .04) and NT participants (all *Z*s > 2.00, all *p*s < .001)[3].

General Discussion

The current findings appear to provide a significant challenge to recent theories of the mechanisms underlying the ASD phenotype in general, as well to theories of self-awareness in this disorder. In terms of theories of the phenotype, within a predictive coding framework, it has been suggested that interoceptive inference might be impaired in ASD due to a developmental pathophysiology related to oxytocin (Quattrocki & Friston, 2014). Yet, in our experiments, we found no evidence that interoception was associated with autistic traits or that it was impaired in adults with ASD, despite the fact that the ASD adults in Experiment 2 displayed the characteristic impairments in attributing mental/emotional states to others (on the RMIE task) that are argued to be one of the consequences of interoceptive impairments (see Table 3). The significant between-group difference in performance on the RMIE task was large and associated with a Bayes factor that strongly suggested the ASD group had a mindreading impairment. In contrast, the group difference in accuracy on the heartbeat tracking task was non-significant, and associated with only a negligible effect size and a Bayes factor that supported the null hypothesis. Moreover, there was no significant association between RMIE and interoceptive accuracy in any of the samples we tested in either experiment, which again counter-indicates the claim of predictive coding theories that interoception contributes significantly to social-*cognitive* abilities (in addition to underpinning the *behavioural* impairments diagnostic of ASD).

One point to note here is that we did not collect any index of participants' body mass index (BMI), or levels of mental health difficulties. High BMI values can result in attenuated interoceptive accuracy (e.g., Herbert et al., 2014), as can high levels of depression and anxiety (Garfinkel et al., 2016; but see Palser et al., 2018). The literature on BMI in adults with ASD is not entirely consistent, but shows a clear trend for adults with this condition to be overweight/obese, on average (Eaves & Ho, 2008; Jones et al., 2016; Tyler et al., 2011; Ogden et al., 2014). If our sample was representative, we might assume that there was a greater proportion of overweight individuals with ASD than overweight neurotypical individuals. In that case, the participants with ASD would have been at a disadvantage on the heartbeat detection task. Likewise, rates of depression and anxiety are significantly higher among people with ASD (~ 44%; Simonoff et al., 2008) than among people in the general population (~9%; McManus et al., 2016), so participants with ASD might have been at a disadvantage on the heartbeat tracking task. It seems highly unlikely that both the ASD and control samples were so unrepresentative that rates of depression and anxiety were greater in control participants than in ASD participants. If this was the case (and if controls had elevated rates of undiagnosed depression and anxiety), then several other results should have been apparent, but they were not. For example, there is evidence that mindreading, particularly for emotional states like those involved in the RMIE task, is diminished in people with depression/anxiety (e.g., Ferguson & Cane, 2017; Wolkenstein et al., 2011; Bourke et al., 2010; Wang, et al., 2008). Likewise, depressive symptoms are associated with elevated rates of alexithymia (e.g., Herbert et al., 2014; Lyvers et al., 2017). If the controls in our Experiment 2 had unusually high rates of mood disorder and if this explained the failure to find group differences in interoceptive accuracy, then we should also have failed to observe between-group differences in performance on the RMIE task (cf. Lee et al., 2005) or TAS. Yet, we observed significant (and large) between-group differences in each of these measures, as predicted and would be expected on the basis of the extensive literature on these abilities in ASD. These findings provide reassurance that we have not committed a type II error in concluding that interoceptive accuracy is undiminished in ASD. Moreover, the sample size in our Experiment 2 (n = 94) was nearly 2.5 times that of the sample size in any other study of interoceptive accuracy in ASD. Thus, confidence in the reliability of the current findings should be relatively high. In the context of an interoceptive inference account of ASD, our findings would suggest that any potential dysregulation of the interoceptive system lies not at the level of perception, but rather interpretation and integration, and is unlikely to be specific to interoception alone.

Of course, the current results should be interpreted within the context of the heartbeat tracking task we employed as the measure of interoception. It is possible that different results would be observed with a different measure of interoception, such as reporting changes in heart rate following administration of a beta-adrenergic agonist, which raises heart rate and blood pressure, allowing easier detection of heartbeats (Khalsa et al., 2009), or reporting of respiratory or gastric interoception (Garfinkel et al., 2018; van Dyck et al., 2016). The heartbeat tracking task has recently come under scrutiny over concerns that it may not always/necessarily provide a valid measure of interoception (e.g., Khalsa et al., 2009; see also Brener & Ring, 2016 for a review). While use of alternative, complementary measures will be important in future studies to develop a comprehensive view of the functional integrity of interoception in disorders such as autism and alexithymia, the predictions of the theories tested in the current study were nevertheless derived almost exclusively from studies of the heartbeat tracking task. Almost all existing studies of a) interoception in ASD and b) the relation between interoception and alexithymia have employed this task as an objective (rather than self-report) index of interoceptive accuracy (Garfinkel et al., 2015; Herbert et al., 2014; Shah et al., 2016, 2017; Schauder et al., 2015; but, for exceptions, see Gaigg et al., 2017, Murphy et al, 2017). Therefore, the current findings are highly relevant in that they speak to, and challenge, current thinking about what role interoceptive difficulties might play in the aetiology of autism and alexithymia.

In particular, the current findings challenge previous research showing an association between alexithymia and interoceptive accuracy. Across the two experiments reported here, we failed to find a significant association between heartbeat tracking accuracy and TAS score in any of five analyses in four entirely independent subsamples, each of which had more than sufficient statistical power to detect the predicted association. In every case, Bayesian analyses indicated that the data were in keeping with the null hypothesis. Also, in all but one analysis, Fisher's *Z* tests indicated that the associations observed in the current study were significantly different (smaller/less negative) than those reported previously. Given the well-established "file-drawer" problem and evidence that some results in psychology are difficult to replicate (e.g., Pashler & Wagenmakers, 2012), we suggest the current results are important and should contribute to theory building in this area. For instance, it is interesting to note that a number of studies have recently reported associations between alexithymia and interoception using self-report measures of interoception (Longarzo et al., 2015; Brewer et al., 2016; Betka et al. 2018). As Garfinkel et al., (2015) have recently pointed out, self-report questionnaires and objective measures of interoception such as the heartbeat tracking task, capture dissociable aspects of interoception. Specifically, whereas self-report questionnaires provide insight into people's *interoceptive sensibility* (i.e., the extent to which they tend to be aware of interoceptive signals), heart beat tracking tasks provide insight into their *interoceptive accuracy* (i.e., the extent to which they perceive interoceptive signals accurately), and both dimensions can vary independently. The findings reported in the current paper suggest that *interoceptive accuracy* is neither related to Alexithymia nor impaired in ASD, but do not speak to the role of other facets of interoception in the aetiology of either Alexithymia or ASD.

Another implication of the current findings is that the results appear problematic for the ‘alexithymia hypothesis’ of autism, which argues that some of the cognitive/emotional-processing difficulties which are common in the condition, are due to alexithymia and should not be characterised as central components of the ASD phenotype (Bird & Cook, 2013). The current results test several of the predictions arising from this theory. On the one hand, in Experiment 1, we found that performance on the RMIE task was associated significantly with performance on the TAS, but not the AQ (and that the TAS × RMIE correlation remained significant after controlling for AQ score). This replicates Oakley et al.’s (2016) findings and suggests, in accordance with the alexithymia hypothesis, that emotional aspects of mindreading are related to level of alexithymia rather than number of ASD traits. On the other hand, in Experiment 2, there were no significant differences between ASD participants with and without clinically significant levels of alexithymia in RMIE task performance. Thus, difficulties with emotional aspects of mindreading are still apparent in individuals with ASD who do not have alexithymia, contrary to the alexithymia hypothesis. Regardless, the assessment of the relation between alexithymia and mindreading was a secondary aim of the current study. The primary aim was to assess a different prediction stemming from the alexithymia hypothesis, namely that only individuals with ASD who manifest high levels of alexithymia should display diminished interoception, whereas interoceptive accuracy should be unimpaired in those with ASD who manifest low levels of self-reported alexithymia (see Shah et al., 2016; Gaigg et al., 2016). The current study provided a complete test of this hypothesis *for the first time*. Previous studies aiming to test the alexithymia hypothesis have matched ASD and comparison groups for (sub-clinical) levels of alexithymia, found no between-group differences in interoceptive accuracy, and then claimed that *if* the participant groups had *not* been matched for level of alexithymia then between-group differences in interoceptive accuracy *would* have been found. But to prove such a claim, the interoceptive accuracy of an ASD-high alexithymia group and a matched ASD-low alexithymia group needed to be compared directly. The fact that we observed no significant difference in interoceptive accuracy between these two ASD groups (in fact there was a slight, non-significant trend for the ASD-high alexithymia group to show *superior* accuracy) provides a clear challenge to the alexithymia hypothesis of ASD, at least with regard to predictions about interoceptive accuracy in heart beat detection.

Instead, the results are in keeping with theories of self-awareness in ASD that draw a distinction between psychological and physical aspects of self. In the literature on the typical development of self-awareness, a distinction between physical and psychological aspects of self is frequently drawn (Gillihan & Farrah, 2005). Several researchers have applied this framework to ASD and suggested that people with this disorder tend to have a diminished awareness of the psychological self (one’s own mental states, personality traits, autobiographical memories etc.), leaving awareness of the physical self (e.g., awareness of one’s physical appearance, physiological states, motor routines etc.) relatively undiminished (e.g., Lind, 2010; Uddin, 2011; Williams, 2010). It is important to note that these theories do not predict that people with ASD necessarily *interpret* their physiological states accurately, but merely that they can detect them accurately. Interpreting physiological states arguably requires the kind of metacognitive monitoring ability that is known to be impaired in people with this disorder (e.g., (Williams, Lind, & Happé, 2009; Grainger, Williams, & Lind, 2014; Williams, Bergström, & Grainger, 2016), whereas mere detection should not (Carruthers, 2009). At the very least, the finding of unimpaired interoceptive accuracy among individuals with ASD in the current study provides support for this prediction that basic representation of bodily states is undiminished in ASD.

Footnotes

1. Shah and colleagues (2016) used a slightly different calculation to measure interoceptive accuracy on the heartbeat detection task: (1 – (│recorded number of heartbeats – counted number of heartbeats│/recorded heartbeats)) x 100. This calculation, which produces significantly higher mean levels of interoceptive accuracy to the calculation employed by Garfinkel et al. (2015), has the limitation of being open to potential positive accuracy biases in interoceptive accuracy when participants display high variance in their responses, especially in cases where participants overestimate the number of heartbeats in a given time interval. However, for completeness we also analysed data from experiments 1 and 2 using the Shah calculation. Results were substantively identical using both methods. The correlation between interoceptive accuracy calculated using the Shandry equation and interoceptive accuracy calculated using the Garfinkel equation is almost perfect in our experiments 1 and 2 (rs ≥ .98, ps < .001). All significant findings using the Garfinkel et al (2016) scoring were significant using the Shah et al. scoring, and all non-significant findings using the Garfinkel et al scoring were non-significant using the Shah et al. scoring.

2. To confirm that there were no systematic differences between males and females in terms of interoceptive accuracy on the heartbeat detection task, a 2 (Sex: Male/female) × 4 (Time interval: 25s/35s/45s/100s) was conducted on this data. Results revealed a non-significant main effect of group, F(1, 135) = 0.22, p = .64, η_p^2 = .002, as well as a nonsignificant Sex× Time interval interaction, F(3, 405) = 0.63, p = .60, η_p^2 = .005. Thus, there were no significant differences between males and females in terms of either overall level of interoceptive accuracy or patterns of accuracy across time intervals. Likewise, when correlation analyses were conducted among males and females separately, exactly the same pattern held in both sexes: Interoceptive accuracy was non-significantly associated with any other variables in either sex, all rs < .13, all ps > .25. Likewise, AQ and RMIE were non-significantly

associated among both males and females, all rs < .15, all ps > .22. TAS total score was associated with both AQ total score and RMIE total among both males and females, all rs > .19, all ps < .04.

3. To confirm that there were no systematic differences in results across locations, an extra Location variable was included in a second ANOVA. Hence, a 2 (Location: Kent/City) × 2 (Group: ASD/NT) × 4 (Time interval: 25s/35s/45s/100s) was conducted on interoceptive accuracy data. Main effects and interactions involving Group and Time interval were the same as in the original ANOVA and, most important, none of the main effects (all ps > .18, all $\eta_p^2 < .02$) or interaction effects (all ps > .28, all $\eta_p^2 < .02$) involving Location were significant or greater than small in magnitude. Mean interoceptive accuracy among participants at Kent was .66 (SD = .22) and was .69 (SD = .17) among participants at City, a difference that is small and non-significant, t = 0.83, p = .41, d = 0.15. Likewise, when correlation analyses were conducted among participants from each location separately, exactly the same pattern held in both: Interoceptive accuracy was non-significantly associated with any other variables in either location 1 or location 2, all rs < .12, all ps > .47. TAS total score was associated significantly with AQ total score at both locations, all rs > .68, all ps <.001.

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Table 1: Correlations between Interoceptive Accuracy (IAcc), Alexithymia (TAS20), Autistic traits (AQ) and Theory of Mind (RMIE) for Experiment 1 and the ASD and TD participant groups in Experiment 2. Shown are the Pearson's r coefficients, with significant associations highlighted with asterisks.

	Exp. 1 (n = 137)			Exp. 2 ASD (n = 46)			Exp. 2 TD (n = 48)		
	IAcc	TAS20	AQ	IAcc	TAS20	AQ	IAcc	TAS20	AQ
TAS20	.008			.08			.21		
AQ	-.011	.42**		-.03	.61**		.21	.42**	
RMIE	.03	-.24*	0.11	.34	-.10	-.13	.09	-.29	-.20

**p<.01; *p<.05*

Table 2: Interoceptive accuracy in Experiments 1 as a function of the interval duration over which participants tracked their heartbeat. Descriptive statistics are shown for overall group means as well as high and low alexithymia sub-groups where relevant.

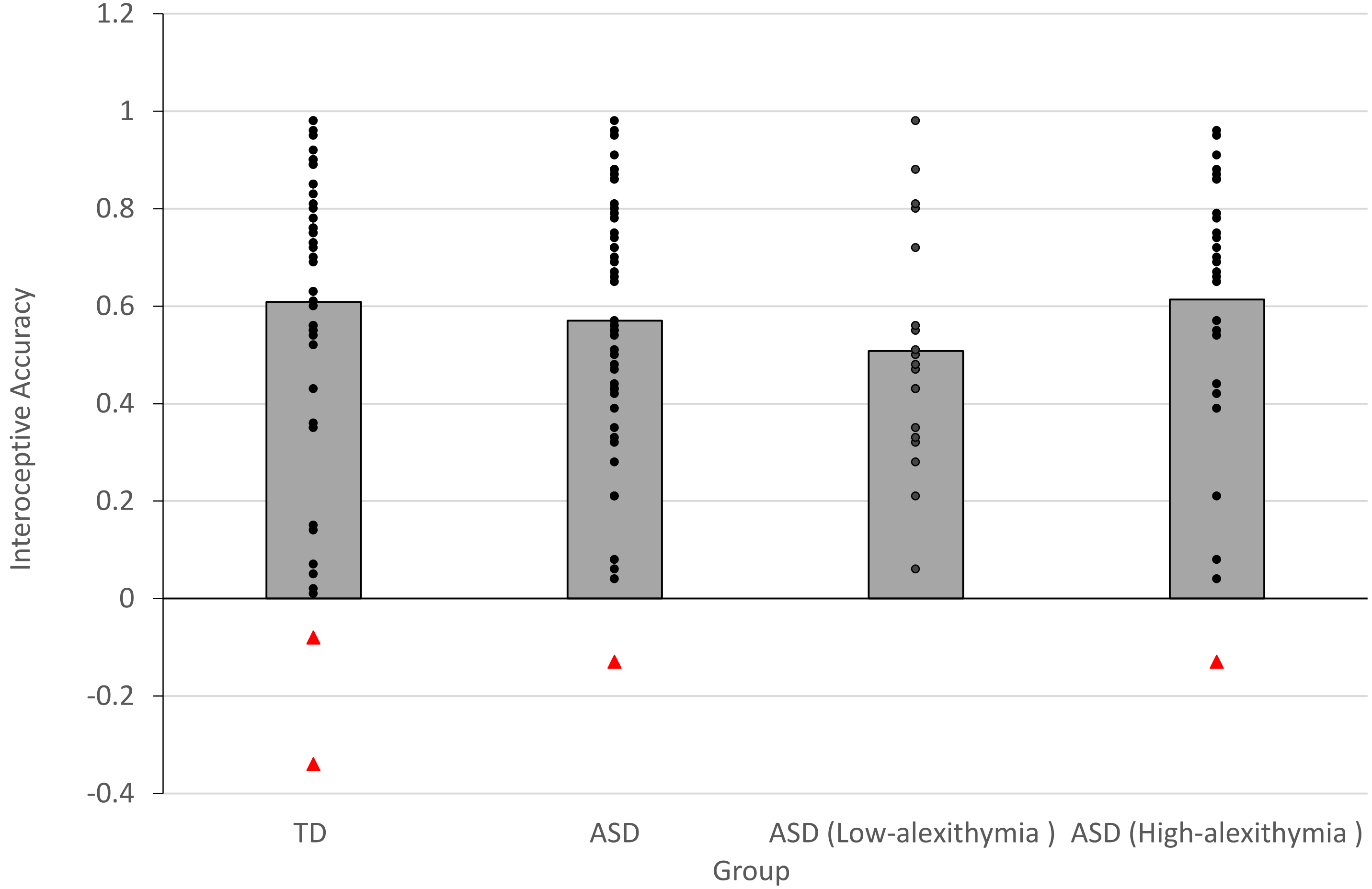
	25 sec		35 sec		45 sec		100 sec		Overall	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Experiment 1										
High Alex (n = 30)	0.55	0.32	0.54	0.32	0.58	0.25	0.52	0.27	0.55	0.26
Low Alex (n = 107)	0.47	0.32	0.54	0.32	0.47	0.31	0.48	0.33	0.49	0.28
Overall (n =137)	0.49	0.32	0.54	0.31	0.5	0.3	0.49	0.32	0.50	0.27
Experiment 2										
NT (n = 48)	0.61	0.36	0.62	0.33	0.58	0.32	0.61	0.32	0.61	0.32
ASD (n = 46)	0.61	0.25	0.58	0.32	0.56	0.30	0.52	0.34	0.57	0.27
High Alex ASD (n = 27)	0.63	0.29	0.64	0.34	0.61	0.32	0.57	0.34	0.61	0.29
Low Alex ASD (n = 19)	0.58	0.19	0.51	0.27	0.50	0.27	0.45	0.34	0.51	0.24

Table 3: Experiment 2 participant characteristics and matching statistics

	ASD (*n* = 46)	Comparison (*n* = 48)	*t*	*p*	*d*	BF_{10}
Age	40.16 (11.72)	41.19 (12.57)	0.41	.68	0.09	0.23
VIQ	109.98 (16.94)	111.17 (13.51)	0.38	.71	0.08	0.23
PIQ	105.52 (17.46)	105.90 (12.67)	0.11	.91	0.03	0.22
FSIQ	108.17 (16.91)	109.10 (12.18)	0.31	.76	0.06	0.23
TAS	59.33 (14.17)	44.88 (9.79)	5.77	<.001	1.19	>100
AQ[a]	32.56 (7.79)	16.91 (5.64)	10.99	<.001	2.31	>100
ADOS[b]	9.40 (4.16)	-	-	-	-	-
RMIE[c]	23.33 (6.17)	26.87 (3.75)	3.28	.001	0.70	21.35

[a] AQ data is missing for one ASD and one comparison participant; [b] ADOS was completed by 40/46 participants with ASD (six participants refused to complete the task or were unable to complete it during the study); [c] RMIE was completed by 42/46 participants with ASD and 46/48 NT participants

Figure 1: Mean interoceptive accuracy across all time intervals, among the ASD group (n= 46), TD group (n= 48), ASD group with low-alexithymia (n=19), and ASD group with high-alexithymia n= (27), reported in Experiment 2. Individual data points have been indicated using black markers and outliers (defined as interoceptive accuracy scores +/- 2SD above/below the group mean) are indicated using red markers.



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