ANGLIA RUSKIN UNIVERSITY

FACULTY OF SCIENCE AND ENGINEERING

BODILY SELF-CONSCIOUSNESS IN AUTISM SPECTRUM DISORDER: INVESTIGATING THE RELATIONSHIP BETWEEN INTEROCEPTION, SELF-REPRESENTATION AND EMPATHY

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ABSTRACT

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BODILY SELF-CONSCIOUSNESS IN AUTISM SPECTRUM DISORDER: INVESTIGATING THE RELATIONSHIP BETWEEN INTEROCEPTION, SELF-REPRESENTATION AND EMPATHY

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Recent theories of the self propose that interoception - the conscious and unconscious processing of signals originating from within the body – has an essential role in bodily self-consciousness, the basic sense of self that is rooted in the body. Furthermore, the processing of signals from within the body is thought to affect emotion, behaviour, cognition and social cognition. The aim of this thesis was to investigate if individuals with autism, a developmental condition historically described as a disorder of self, show differences in interoceptive processing and an altered bodily self, and investigated if these are related to deficits in the understanding of self and others. Experiment one investigated interoceptive processing on three dimensions, and found that participants with autism had lower interoceptive sensibility, lower interoceptive accuracy and a less pronounced heartbeat evoked potential. Experiments two and three investigated the relationship of interoceptive processing with alexithymia and empathy, and differences in automatic mimicry. These experiments found that autistic traits, interoceptive sensibility, alexithymia and empathy were associated, and that alexithymia played a mediating role in the relationship between interoception and empathy. This could explain why participants with autism and alexithymia had lower empathy than participants without autism, and lower than autistic participants without alexithymia. Experiment four investigated bodily self-consciousness with two multisensory paradigms – the full body illusion and an audio-tactile peripersonal space task. This experiment found that in contrast to neurotypical participants, participants with autism were not susceptible to the full body illusion, and that their peripersonal space was smaller with a sharper boundary. In conclusion, these results show that participants with autism show reduced interoceptive processing and altered bodily self-consciousness. There was additional evidence that bodily self-consciousness underlies deficits in the understanding of own emotions and the emotions of others. How this furthers our understanding of core characteristics of autism at a theoretical level is discussed.

Key words: Autism Spectrum Disorder, bodily self-consciousness, interoception, empathy, alexithymia, full body illusion, peripersonal space, heartbeat evoked potential, multisensory integration

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# Chapter 1

Introduction

Autism Spectrum Disorder (ASD) is a developmental disorder characterised by several impairments, which encompass restricted and repetitive behaviours or interests, hyper- or hyposensitivity to sensory input, and difficulties in social communication and social interaction (American Psychiatric Association, 2013). ASD is a spectrum disorder, and a wide range of behaviours are included in the description of the disorder. The severity and frequency of the behavioural symptoms is heterogenous; they vary greatly amongst individuals with ASD (Jones & Klin, 2009; Wing, 1997). The heterogeneity includes IQ, from intellectually disabled to highly intelligent, and language function; individuals with ASD may be verbal, non-verbal, or have a developmental language delay or language impairment (Fombonne, 2009; Tager-Flusberg, 2000). Currently diagnosis of ASD in the United Kingdom is based on the characteristics described in the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5 – APA, 2013). A diagnosis requires evidence of difficulties with communication, social interaction, and restricted, stereotyped and repetitive behaviours, interests or activities. These difficulties must have been present from early childhood. There is now a single category ASD diagnosis, which replaces earlier diagnosis of the subdivisions of Autism disorder, Asperger’s disorder, and Pervasive Developmental disorder - not otherwise specified (PDD-NOS). There is also a separate category of Social Communication disorder, which has similar criteria for social communication to ASD, but doesn’t include the behavioural criteria for repetitive and restricted behaviours (APA, 2013).

The social communication deficits of ASD may be shown by a lack of eye contacts, limited facial expressions, and limited understanding of other people’s point of view or emotions: a lack of understanding and use of verbal and nonverbal communication, especially indirect forms of communication where meaning must be inferred, such as sarcasm. There is a lack of reciprocal communication and difficulty adjusting social behaviour to the context. Often a limited interest in social interaction is seen, as well as monotonous or idiosyncratic speech patterns, and in young children, a lack of imaginative play and joint attention (Charman, 2008; Johnson & Myers, 2007; Lord, Rutter, & Le Couteur, 1994; Wing, 1997).

The restrictive and repetitive behaviours may be shown by repetitive body movements, such as rocking, tapping, hand flapping; repetitive play such as lining up cars, repetitively manipulating (e.g. opening and closing, or flipping) moving parts of objects. There may be echolalia. There is a need to adhere to routines, an insistence on sameness and an inability to adjust to (small changes) or difficulty with transitions; Many people with ASD have restricted interests that are abnormal in their intensity or subject matter, or show perseverative behaviours and rigid thinking. Additionally, there may be hyper or hyporeactivity to sensory input or an unusual interest in specific sensory stimulations (Charman, 2008; Constantino & Charman, 2016; Johnson & Myers, 2007; Lord, Rutter, & Le Couteur, 1994; Volkmar, Chawarska, & Klin, 2005; Wing, 1997).

The heterogeneity of ASD poses difficulties for correct and early diagnosis, which is compounded by high co-occurrence of other psychiatric conditions in individuals with ASD (Georgiades, Szatman, & Boyle, 2013; Matson & Williams, 2013). For example, many children with ASD also meet criteria for Attention Deficit Hyperactivity Disorder (Gadow, De Vincent, Pomeroy, & Azizian, 2005; Gargaro, Rinehart, Bradshaw, Tonge, & Sheppard, 2011), anxiety disorders (Simonoff et al., 2008; Matson & Williams, 2013), intellectual disability (Fombonne, 2009) or specific language impairment (Bishop, 2010; Kjelgaard & Tager-Flusberg, 2001). Moreover, it is now recognised that some defining features of ASD are continuously – not categorically – distributed in the general population (Constantino & Charman, 2016). These factors contribute to delays in early diagnosis for children, but also to late diagnosis, particularly in verbally and cognitively able children, and adults (Crane et al., 2018; Rogers, Goddard, Hill, Henry & Crane, 2016). A clinical observational interview is used for diagnosis (e.g. Autism Diagnostic Observation Schedule (ADOS – Lord et al., 2000; Autism Diagnostic Interview – Revised (ADI-R, Rutter, Le Couteur & Lord, 2003)), although current National Institute for Health and Care Excellence (NICE) standards recommend that multi-agency observations and assessments (from e.g. GP, educational psychologist, clinical psychologist, occupational therapist, paediatrician) are also taken into account, in order to build a comprehensive picture of the developmental and medical history of the individual (National Screening Committee, 2011).

## **Autism as a disorder of self**

Autism has long been described as a disorder of self, especially when referring to the deficits in reciprocal interactions with others. Kanner (1943) described autistic children’s extreme self-focus as a characteristic that set these children apart from typical children, describing their behaviour as self-sufficient, self-absorbed, self-satisfied and as living within themselves. In 1944, Asperger reported similar observations: ‘the autist is only himself’ (Asperger, 1991). The word autism itself, coined by Bleuler in 1911 to describe severely withdrawn patients with schizophrenia, was derived from the Greek work ‘autos’, meaning ‘self’ (Lyons & Fitzgerald, 2007). Since then, many studies have shown altered self-processing beyond atypical interactions with others, for example, weaker auto-biographical memory (Crane & Goddard, 2008; Crane, Pring, Jukes, & Goddard, 2012) and self-referenced memory (Henderson et al., 2009; Lind & Bowler, 2009), deficits in emotional self-awareness (Griffin, Lombardo, & Auyeung, 2015; Hill, Berthoz, & Frith, 2004; Shalom et al., 2006; Silani et al., 2008), lower recognition of ‘self-conscious’ emotions such as shame, embarrassment and guilt (Heerey, Keltner, & Capps, 2003), atypical use of pronouns (i.e. talking about themselves in the second or third person) (Lee, Hobson, & Chiat, 1994), and differences in other aspects of self-referential cognition (Burrows, Usher, Mundy, & Henderson, 2017; Gillespie‐Smith, Ballantyne, Branigan, Turk, & Cunningham, 2017; Lombardo, Barnes, Wheelwright, & Baron-Cohen, 2007; Lombardo, Chakrabarti, Lai, & Baron-Cohen, 2012; Mundy, Gwaltney, & Henderson, 2010).

Arguably the most basic manifestation and definition of self is that the self is the subject of conscious experience. I am the entity that has experiences (sees, feels, hears, tastes, smells, thinks and does things) and that I, the subject, am localised in a body that I feel ownership for (Gallagher, 2000). The experiences of being a subject and of owning and being located in a body, which is the spatial origin of the first person perspective, are aspects of this fundamental and foundational level of self: bodily self-consciousness (Blanke & Metzinger, 2009; Blanke, Slater, & Serino, 2015). Despite the differences in self-processing previously found in ASD, such as those mentioned in the paragraph above, bodily self-consciousness in ASD has barely been studied. The investigation of bodily self consciousness in ASD, and relations between bodily self-representation and the understanding of one’s own emotions and those of others, is the focus of this thesis.

To date, research into bodily self consciousness has been conducted from two main approaches. The first approach is based on the understanding that bodily self-consciousness is based on the neural representations in the brain of signals originating within the body, such as those from the heart and the gut (Craig, 2009; Damasio, 2000; Seth, Suzuki, & Critchley, 2012; Seth, 2013). Interoception, the processing of afferent sensory signals arising from within the body (Craig, 2002), is regarded by some authors as the basis for subjective experience, which comprises the sense of an experiencing self, conscious perception and emotional feelings (Park & Tallon-Baudry, 2014). Interoceptive processes can affect cognition and behaviour both with and without conscious awareness (Cameron, 2001) and much of recent research has concentrated on investigating interoception and its effects on a wide range of cognitive processes and behaviours (e.g. see Azzalini, Rebollo, & Tallon-Baudry, 2019; Ceunen, Vlaeyen, & Van Diest, 2016; Khalsa et al., 2018), which include emotion processing (Craig, 2008; Murphy, Catmur, & Bird, 2018; Schachter & Singer, 1962; Shah, Hall, Catmur, & Bird, 2016; Wiens, Mezzacappa, & Katkin, 2000; Zaki, Davis, & Ochsner, 2012; Zamariola, Frost, Van Oost, Corneille, & Luminet, 2019) and empathy (Ainley, Maister, & Tsakiris, 2015; Ernst, Northoff, Böker, Seifritz, & Grimm, 2012; Fukushima, Terasawa, & Umeda, 2011; Singer, Tania, Critchley, & Preuschoff, 2009; Terasawa, Moriguchi, Tochizawa, & Umeda, 2014).

The second approach to studying bodily self is based on investigating the contribution of multi-sensory integration of sensory signals to bodily self-consciousness (Aspell, Lenggenhager, & Blanke, 2009; Blanke, 2012). When multisensory integration is disturbed, the sense of self is affected (Blanke & Mohr, 2005; Blanke, 2012). This manifests in changes in key aspects of bodily self-consciousness; the identification with one’s body (self-identification or body-ownership), the experience of where “I” am located in space (body-location) and the experience of perceiving the world from where “I” am (first-person perspective) (Blanke, 2012). Neurological disturbances of bodily self-consciousness may occur as a result of brain damage to multisensory brain areas as the temporo-parietal junction and can manifest in autoscopic phenomena: illusory visual experiences of one’s own ‘double’ (Blanke & Mohr, 2005). For example, in the out-of-body experience, a person feels as if they’re outside their own body, and looks at their own body from an elevated, disembodied perspective. This appears to be caused by a dysfunction of visual, tactile, proprioceptive, kinaesthetic, and vestibular integration processes (Blanke & Mohr, 2005). Similar illusory changes in body ownership, first person perspective and self-location can be experimentally induced by introducing multisensory conflicts, notably visual-tactile conflicts (Blanke & Metzinger, 2009; Ehrsson, 2007; Lenggenhager, Tadi, Metzinger, & Blanke, 2007). Recently, it has been shown that conflicts of multisensory interoceptive and exteroceptive signals can also induce these body illusions (Aspell, et al., 2013; Heydrich et al., 2018; Suzuki, Garfinkel, Critchley, & Seth, 2013). These studies provide support for theoretical proposals that the sense of self is ultimately founded in multisensory neural representations of the body (Craig, 2009; Damasio, 2012; Park & Tallon-Baudry, 2014b; Park & Blanke, 2019; Seth, et al., 2012; Seth & Tsakiris, 2018).

This thesis addresses the gap in the literature regarding the study of bodily self-consciousness in ASD. It will report on studies that investigated bodily self-consciousness with the multisensory approach and the interoceptive approach. It will show present data that demonstrates altered multisensory bodily self-consciousness and altered interoceptive processing in ASD, and these relate to differences in the understanding of one’s own emotions and empathy for the emotions of others. Empathy is often considered a hallmark of the social functioning deficits in people with ASD, and a relationship between bodily self-consciousness and empathy in ASD supports a recent consideration of whether ASD should be reframed as a disorder of self (Tordjman, Celume, Denis, Motillon, & Keromnes, 2019).

## **1.2. Interoception**

Interoception, defined as the sense of the physiological condition of the body (Craig, 2002), is a set of processes involved in the detection of signals from the internal milieu of the body sent to the brain by internal organs, the vascular system, and the glandular system. Through interoception, vital internal processes such as breathing, digestion, body temperature, blood pressure and blood composition, are monitored and regulated via the autonomic nervous system (Cameron, 2001; Vaitl, 1996). These processes are life sustaining, as they enable regulation of the body’s internal milieu which has to stay within strict parameters. Blood pressure, body temperature, heartbeat etc cannot increase or decrease without limit, without endangering the survival of the body. Originally, interoception was defined as the perception of stimuli from the internal organs only (Sherrington, 1966) (see for the origin and evolution of the concept of interoception: Ceunen et al., 2016), but since then it has been argued that the perception of pain, temperature, itch and sensual touch share the same homeostatic pathways as the internal organs, and on this basis these should also be classed as interoceptive, as well as somatosensory (Craig, 2008; Craig, 2003).

 Interoception is often treated as a single phenomenon, but this is at odds with the physiology (Vaitl, 1996). A diverse array of interoceptive signals reach the brain via the cranial and spinal nerves and through blood circulation. In the body, local changes in chemical composition, pressure, dilation, contraction or temperature are picked up by afferent neurons that convert these changes into electrical signals that project into the nucleus of the solitary tract in the medulla oblongata, from which they will project further into the brainstem, the amygdala, the thalamus and hypothalamus and into the cortex (Cameron, 2001; Craig, 2002; Critchley & Harrison, 2013; Palma & Benarroch, 2014; Quadt, Critchley, & Garfinkel, 2018). The insular cortex integrates the information with the topographic representation of the body and enables motivated behavioural changes and conscious awareness of signals from the body through connections with the somatosensory cortex, ventral striatum, anterior cingulate cortex (ACC), and orbitofrontal cortex (Craig, 2009; Critchley, 2005).

Several studies support the notion that the insula functions as an interoceptive hub involved in the mapping and representation of visceral signals into a representation of the body’s, and integrates signals from all modalities from the external environment (Bandy, Chen, Craig, & Reiman, 2000; Craig, 2008; Craig, 2009; Simmons et al., 2012). The ACC is involved in the integration of visceral signals with cognitive processes such as anticipation and appraisal, and, in co-activation with the anterior insula, generates autonomic responses such as changes in arousal (Craig, 2008; Craig, 2009; Critchley et al., 2003; Medford & Critchley, 2010). In a model of insula functioning it has been suggested that the posterior insula may be seen as the primary cortex for interoception (Craig, 2009; Critchley, 2005). Here interoceptive signals are mapped somatotopically: the topography of the body can be recognised in the topography of the posterior insula; i.e. different parts of the posterior insula process signals from different parts of the body (Brooks, Zambreanu, Godinez, Craig, & Tracey, 2005; Craig, 2009). Representations from mid-to-anterior insula integrate homeostatic motor functions, environmental conditions, hedonic conditions, and eventually, motivational, social and cognitive conditions (Craig, 2009; Harrison, Gray, Gianaros, & Critchley, 2010). It has been suggested that the representation occurs repeatedly, progressively integrating and re-representing the physiological state of the body with various sources of information, starting in the dorsal posterior and moving sequentially and progressively towards the anterior insula. In the middle insula sensory input from other modalities and input from the amygdala and hypothalamus is integrated, while in the anterior insula there are connections with the ACC, orbitofrontal cortex and dorsolateral prefrontal cortex (Craig, 2009). A meta-analysis of 811 neuro-imaging studies differentiated between functions within the insula and confirms this view (Kurth, Zilles, Fox, Laird, & Eickhoff, 2010).

From the culmination of representations of the physiological state of the body in the anterior insula, the subjective awareness of all feelings emerges, not just those associated with bodily functions such as hunger, thirst, “air hunger”, fullness of the stomach, intestines and bladder, pain, heartbeat, etc (Craig, 2009; Damasio, 2012). Neuroimaging studies have shown that activity in the right anterior insula correlates with the self-reported intensity of emotions (Critchley & Harrison, 2013; Gu, Hof, Friston, & Fan, 2013; Nguyen, Breakspear, Hu, & Guo, 2016; Zaki et al., 2012), anxiety (Paulus & Stein, 2010), depression (Avery et al., 2014; Paulus & Stein, 2010), disgust (Jabbi, Bastiaansen, & Keysers, 2008; Wicker et al., 2003), and social emotions and empathy (Immordino-Yang, Yang, & Damasio, 2014; Lamm, Claus & Singer, 2010; Singer et al., 2009). It has been proposed that the representation of the physiological state of the body provides the neural basis for the self as an experiencing subject, which also generates the distinction between self and non-self (Craig, 2009; Park & Tallon-Baudry, 2014). Supporting this, the insula has been shown to be involved in the attention switching from internal stimuli to external stimuli (Menon & Uddin, 2010; Sridharan, Levitin, & Menon, 2008).

Interoceptive sensitivity is thought to be a trait-like ability which varies between individuals (Cameron, 2001). There are different ways to measure interoceptive processing in humans, with various self-report and psychophysiological tasks. Following a proposal that the terminology regarding interoceptive processing should clarify the different dimensions of interoception that these measurements reflect (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015), in this thesis, the subjective experience of bodily sensations measured via questionnaires will be referred to as *interoceptive sensibility*, and the objectively measured accuracy of the perception of bodily sensations during psychophysiological tasks such as heartbeat perception tasks will be called *interoceptive accuracy.* Garfinkel and colleagues (2015) propose to reserve the term *interoceptive awareness* for metacognition of interoceptive accuracy, i.e. the ability of someone to know whether they are accurately perceiving their bodily sensations, which may for example be measured with confidence ratings following trials of accuracy tasks. The three dimensions reflect different processes which don’t always correlate with each other (Garfinkel, et al., 2015), reflecting that the subjective awareness of interoceptive information involves not only sensory detection but also interpretation, and as such is subject to influences of cognitive, affective and motivational processes (Cameron, 2001).

A participant’s day-to-day level of conscious awareness of bodily feelings may be quantified with self-report questionnaires which contain statements like “When I am tense, I notice where the tension is located in my body” (from the Multi-dimensional Assessment of Interoceptive Awareness Questionnaire – MAIA – (Mehling et al., 2012)) or “During most situations, I am aware of muscle tension in my arms and legs” (from the Body Perception Questionnaire – BPQ – (Porges, 1993)), to which participants indicate their level of agreement on a Likert scale. Questionnaires provide an assessment of perceived interoceptive sensibility and are subjective measures that are likely influenced by biases and beliefs about body awareness (Cameron, 2001). These beliefs may or may not be an accurate assessment, as illustrated by a study that compared subjective and objective measures of interoceptive awareness of experienced meditators and non-meditators (Khalsa et al., 2008). It was found that although meditators scored higher in interoceptive sensibility on a self-report measure, this was not translated into a more accurate perception compared to non-meditators, as assessed with a psychophysiological heartbeat detection task. Since then, many studies have reported an absence of a correlation between interoceptive sensibility and interoceptive accuracy (e.g. (Calì, Ambrosini, Picconi, Mehling, & Committeri, 2015; Ceunen, Van Diest, & Vlaeyen, 2013; Garfinkel, et al., 2015; Weineck, Messner, Hauke, & Pollatos, 2019)

Psychophysiological tasks measure objective accuracy of the perception of interoceptive signals and include the widely used heartbeat perception tasks. Perception of one’s heartbeat is mediated by several afferent signals which are processed in parallel, including those arising from receptors detecting the contracting of muscular tissues of the heart, the accompanying blood pressure changes, as well as increase and decrease of pressure on the surrounding muscle tissue in the chest wall and skin tissue of the chest (Cameron, 2001; Khalsa, Rudrauf, Feinstein, & Tranel, 2009; Park & Tallon-Baudry, 2014). Different kind of receptors (e.g. baroreceptors, mechanoreceptors) are involved. In heartbeat perception tasks, participants are asked to count their own heartbeat (heartbeat ‘tracking’ tasks) without having a finger on their pulse (Schandry, 1981), or to judge whether an external stimulus (e.g. sound or a visual stimulus) is presented in synchrony with their heartbeat or not (heartbeat ‘discrimination’ tasks) (Whitehead, Drescher, Heiman, & Blackwell, 1977b). The heartbeat perception measurements may be seen as a more accurate measure of sensitivity to visceral (cardiac) sensations than subjective responses to questionnaires. Activity in the right insula during a heartbeat discrimination task predicted accuracy scores in the heartbeat discrimination task (Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004). Additionally, there are tasks that measure gastrointestinal sensitivity, in which participants are requested to drink small amounts of water until they feel full (the ‘water load test’(Hölzl, Erasmus, & Möltner, 1996; Koch, Hong, & Xu, 2000) and respiratory resistance detection tasks, in which participants have to judge whether an added load of air pressure is present or absent when breathing through a breathing device (Dahme, Richter, & Mass, 1996; Harver, Katkin, & Bloch, 1993). The latter task, which is used in medical research with patients with respiratory conditions, does not reliably correlate with the heartbeat detection task (Garfinkel, Sarah N. et al., 2016), whereas the gastric interoception task has been shown to correlate moderately (Herbert, Muth, Pollatos, & Herbert, 2012).

In psychological studies, the heartbeat tasks have been most used as they are simple, non-invasive methods, and possible extraneous factors influencing measurements, such as gender, body weight, or body position, have been extensively studied (Jones, 1994; Jones, Jones, Rouse, Scott, & Caldwell, 1987; Rouse, Jones, & Jones, 1988). In the heartbeat tracking task (Schandry, 1981) participants are asked to silently count their own heartbeats, without feeling their pulse, during brief intervals, and report the number of heartbeats they have counted. Comparing this response with electrocardiogram recordings of the actual heartbeats in those intervals provides a measure of cardiac interoceptive accuracy. Good heartbeat perceivers may be distinguished from poor heartbeat perceivers by a median split (Tsakiris, Tajadura-Jimenez, & Costantini, 2011), or more often, by reaching a certain threshold in accuracy (e.g. accuracy above 0.85 (Herbert, Pollatos, & Schandry, 2007; Pollatos, Herbert, Matthias, & Schandry, 2007; Werner, Jung, Duschek, & Schandry, 2009). In the heartbeat discrimination task (Whitehead et al., 1977) participants are asked to judge whether a series of auditory notes, triggered by the participant’s heartbeat, is presented in synchrony or asynchrony with their heartbeats. Here, good heartbeat perceivers are identified as those who have a score above chance (Eshkevari, Rieger, Musiat, & Treasure, 2014; Harver et al., 1993; Wiens, 2005).

Both heartbeat perception tasks have weaknesses. Cardiovascular variables may affect performance in both tasks. For example, people with high blood pressure perform better (Koroboki et al., 2010) and people with a larger stroke volume do too (Schandry, Bestler, & Montoya, 1993). The heartbeat tracking task may be confounded by prior knowledge about heartrate (Knapp-Kline & Kline, 2005; Murphy, Brewer, Hobson, Catmur, & Bird, 2018; Phillips, G. C., Jones, Rieger, & Snell, 1999; Ring & Brener, 1996; Ring, Brener, Knapp, & Mailloux, 2015; Ring & Brener, 2018). Performance on the task is also characterised by under-reporting of heartbeats (Desmedt, Luminet, & Corneille, 2018; Zamariola, Maurage, Luminet, & Corneille, 2018). These confounds have led to attempts to control for this, for example by controlling for time-estimation ability (e.g. (Shah, Catmur, & Bird, 2016). The heartbeat discrimination task is less affected by this knowledge, but instead has the problem of a floor effect; healthy participants find this task hard and most will perform at chance or slightly above chance level, making the distinction between poor and good perceivers unreliable (Ehlers & Breuer, 1996; Knapp-Kline & Kline, 2005; Phillips, G. C. et al., 1999). Additionally, the heartbeat discrimination task requires participants to associate stimuli in two different modalities (auditory tone and interoceptive heartbeat) with each other, which may divide attention and may hamper the detection of the less obvious stimulus (heartbeat). Furthermore, instead of mere detection of their heartbeat, participants are asked to make a judgement about their heartbeat. The heartbeat discrimination task and the heartbeat tracking task may therefore not necessarily measure the same ability (Phillips, G. C. et al., 1999); indeed, the two heartbeat tasks do not always correlate (Phillips, G. C. et al., 1999; Schulz, Lass-Hennemann, Sütterlin, Schächinger, & Vögele, 2013)

A third commonly used measure of interoceptive processing is the heartbeat evoked potential (HEP). Measured by electroencephalogram (EEG), the HEP is the event-related potential (ERP) elicited by the heartbeat. ERPs are postsynaptic graded potentials time-locked to an event, usually the onset of a stimulus, and in case of the HEP, the heartbeat. Graded potentials are small fluctuations in the amplitude of the resting potential and can’t be observed in the raw EEG recording. To isolate the HEP from ongoing brain activity, neural responses to the heartbeat are extracted by averaging recordings of brain activity that are time-locked to recording periods (epochs) around the heartbeat. Other spontaneous activity that is unrelated to the heartbeat is thus averaged out, and an ERP wave will become evident, which reflects only the activity that is consistently associated with the heartbeat. To facilitate the time-locking of the EEG recording to the occurrence of heartbeats, the heartbeat needs to be recorded simultaneously, by an electrocardiogram (ECG).

The amplitude of the HEP is most pronounced in fronto-central regions of the cortex, but can also be observed in the parietal regions (Gray et al., 2007; Schandry & Montoya, 1996). While the amplitude of the HEP has been found to be positively correlated to accuracy in heartbeat perception tasks, a HEP is nevertheless also detectable in poor heartbeat perceivers (Fukushima et al., 2011; Pollatos & Schandry, 2004). Interoceptive activity in the insula, the ACC and the somatosensory cortex have been shown to contribute to the HEP (Kern, M., Aertsen, Schulze-Bonhage, & Ball, 2013; Park et al., 2017; Pollatos, Kirsch, & Schandry, 2005).

##  **1.3 Interoception and emotion**

Changes in the physiological state of the body have long been acknowledged as intrinsically linked to the experience of emotions, not just to sensations related to bodily processes (Cannon, 1927; Damasio, 2000; Gendron & Barrett, 2009; James, 1894; Schachter & Singer, 1962). Nowadays it is generally accepted that emotions are psychological states comprising of behavioural, experiential and visceral changes (Gendron & Barrett, 2009; Seth, 2013). The emotional experience involves sensing physical changes in the body and their affective value, the appraisal of those changes and the appraisal of the environment, although the exact role of bodily sensations in emotion experience in relation to appraisal of events external and internal to the body is still a subject of debate. In this respect, Damasio (2000) proposes that there are two ways in which emotions may be generated: The “body-loop” and the “as-if body loop”. The body loop is the process of an actual altered body state that is registered in the representation of the physiological state of the body, the instinctive and automatic bodily responses to stimuli. The “as-if body loop” bypasses the body itself but generates representations of a changed body landscape; it is an instance of cognitively induced emotions by, for example, imagination or memory. Both types of representation will continue to feed forward to and receive feedback from other brain regions and the body in a continuous interactive process which constitutes the emotional feeling. There is now a growing understanding that cognitive expectations and feed-back loops are part of how the brain operates; the active inference and predictive coding account of perception and action is based on feed forward and feed backward loops (Barrett, 2017; Friston, 2005; Seth & Critchley, 2013; Seth & Friston, 2016)

The previous discussion suggests that research that investigates interoceptive processes and emotions may make a valuable distinction between physiological states of the body, the sensing of these states and one’s conscious appraisal of these states (Damasio, 2000; Lambie & Marcel, 2002). Individuals differ in the way actual physiology changes, interoceptive accuracy (in perceiving these changes) and interoceptive sensibility (appraising these changes) are associated. For example, interoceptive sensibility of arousal may be enhanced when a person has a strong cognitive bias to focus on sensations of arousal, which may not reflect actual levels of arousal measured by skin conductance (Barrett, Quigley, Bliss-Moreau, & Aronson, 2004; Dunn et al., 2010; Herbert et al., 2007). Measuring different dimensions of interoception is therefore a valuable approach, in particular when assessing the relationship of interoception with symptoms or characteristics of clinical samples.

In the general population, experimental research shows that interoceptive accuracy and interoceptive sensibility are linked to how emotions are experienced, e.g. good heartbeat perceivers report experiencing a higher intensity of emotions (Herbert et al., 2007; Terasawa et al., 2014; Wiens et al., 2000), and stronger feelings of arousal (Barrett et al., 2004; Pollatos et al., 2005). Individuals with good heartbeat perception also have a better memory for emotional words (Werner, Peres, Duschek, & Schandry, 2010). Another study found an association between interoceptive accuracy and emotional recognition thresholds to emotional faces (Terasawa et al., 2014). Individuals who have higher levels of alexithymia, a condition characterised by a lack in ability to recognise, describe and understand one’s own emotions, tend to have lower interoceptive accuracy (Herbert, Herbert, & Pollatos, 2011; Murphy et al., 2018). These studies all suggest that individuals who are more aware of interoceptive sensations are also more strongly aware of their emotions.

Neuroimaging studies provide further evidence of the involvement of interoception in emotion processing. Critchley et al. (2004) showed that activity in the insula, the ACC and somatomotor cortex increases during the heartbeat detection task, and that the volume of and the activity in the right anterior insula was predictive of the accuracy in the task as well as participants’ reported awareness of bodily feelings. Similarly, Zaki and collegues showed that activity in the right anterior insula is correlated with the reported intensity of emotions (Zaki et al., 2012). Activation of the insula whilst reflecting on one’s own emotional state is negatively correlated with levels of alexithymia (Bird et al., 2010), and damage to the insula is associated with alexithymia (Hogeveen, Bird, Chau, Krueger, & Grafman, 2016). Increased insula activity has been reported during a wide range of tasks involving subjective awareness of particular emotions, including those of disgust (Jabbi et al., 2008; Phillips et al., 1998; Wicker et al., 2003), empathy (Ernst et al., 2012; Fukushima et al., 2011; Immordino-Yang et al., 2014; Singer, Tania et al., 2009), pain (Botvinick et al., 2005; Craig, 2003; Lamm, Claus, Decety, & Singer, 2011; Moriguchi et al., 2007; Ochsner et al., 2008; Singer et al., 2004) and fear (Critchley, Mathias, & Dolan, 2002; Phillips. et al., 1998)..

It has also been shown that deviant interoceptive processing is associated with emotion disorders. In anxiety disorders typically heightened interoceptive awareness is accompanied by maladaptive thought processes, such as negatively evaluating, catastrophizing and ruminating about bodily feelings (Domschke, Stevens, Pfleiderer, & Gerlach, 2010; Dunn et al., 2010; Ehlers, 1993; Paulus & Stein, 2010; Pollatos, Traut-Mattausch, Schroeder, & Schandry, 2007). High interoceptive sensibility and strong negative self-referential beliefs and predictions may contribute to the cause and maintenance of anxiety disorders (Paulus & Stein, 2010). In depression the opposite is commonly found: depression is associated with decreased interoceptive accuracy and sensibility (Domschke et al., 2010; Dunn, Dalgleish, Ogilvie, & Lawrence, 2007; Dunn et al., 2010; Lackner & Fresco, 2016; Paulus & Stein, 2010).

In autism, research into emotions processing has been dominated by studies assessing the processing of the emotions of others, e.g. emotion recognition and empathy, but results have been mixed. Several studies have shown reduced recognition of emotional facial expressions (Ashwin, Chapman, Colle, & Baron-Cohen, 2006; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), of emotions in verbal and nonverbal signals (Gebauer, Skewes, Hørlyck, & Vuust, 2014; Lindner & Rosén, 2006; Philip et al., 2010; Stewart, McAdam, Ota, Peppé, & Cleland, 2013), and of emotion in body movements (Atkinson, 2009; Philip et al., 2010). Others have reported no differences (Loveland et al., 1997; Ozonoff, Pennington, & Rogers, 1990; Tracy, Robins, Schriber, & Solomon, 2011). Meta-analyses revealed only a small reduction in emotion recognition (Uljarevic & Hamilton, 2013) or a more nuanced picture (Nuske, Vivanti, & Dissanayake, 2013). However, when it comes to experiencing one’s own emotions, it is clear that on average people with ASD have greater difficulty understanding, describing and distinguishing between emotions than the typical population (Berthoz & Hill, 2005; Hill et al., 2004; Samson, Huber, & Gross, 2012; Shalom et al., 2006; Tani et al., 2004), as evidenced by the high incidence (> ~50%) of alexithymia in the ASD population (Hill et al., 2004).

When this PhD was designed, there were no published studies that investigated the relationship between emotion processing and interoception in ASD. Since then, several studies have shown that the high incidence of clinical levels of alexithymia in the autistic population might be related to emotion processing and explain the mixed results in autism emotion studies (Bird & Cook, 2013; Brewer, Happé, Cook, & Bird, 2015; Cook, Brewer, Shah, & Bird, 2013; Heaton et al., 2012; Shah et al., 2016; Shah et al., 2016a). A relationship between interoception and alexithymia has also been proposed (Brewer et al., 2015; Quattrocki & Friston, 2014). Just a few studies have combined interoceptive measures, emotional measures and alexithymia measures in studies with autistic participants (Shah et al., 2016; Shah et al., 2016b). These studies have shown a relationship between interoceptive accuracy, alexithymia and the emotion task (an emotional decision task and an emotion recognition task), but found that these relationships were independent from levels of autistic traits. This PhD research, which includes an investigation of the contribution of interoception on the understanding of one’s own emotions and those of others in ASD participants, will therefore elaborate on and supply much needed evidence for these relationships.

## **1.4 Interoception and empathy**

The discussion above shows the association of emotional processing and interoception. Empathy, recently defined as “an affective state that involves being sensitive to and experiencing the emotions of others, which is supported by or may arise from the cognitive understanding of the emotions of others” (Reniers, Corcoran, Drake, Shryane, & Völlm, 2011), includes affective facets as well as cognitive ones. Empathy is a multifaceted construct that comprises an element of Theory of Mind (ToM), i.e. being able to see things from another’s perspective and make inferences about somebody else’s emotional state (cognitive empathy); an affective element of having an emotional response to another’s emotional state (affective empathy); and a monitoring element that identifies the origin of the affective response (self or other) (Bird & Viding, 2014; Lamm, Claus, Batson, & Decety, 2007; Reniers et al., 2011). The affective element of empathy is sometimes described as sharing an emotion observed in another (Decety & Jackson, 2006; Grynberg & Pollatos, 2015), which suggests emotion processing that might be related to interoceptive processing.

 Affective empathy and cognitive empathy can be measured separately and are dissociable (Blair, 2005), and are likely reciprocally reinforcing processes (Bird & Viding, 2014). Simulation theory proposes that the understanding of others’ emotions is partly achieved through vicariously experiencing these emotions through mirroring mechanisms, consciously or unconsciously (Decety & Jackson, 2006; Keysers & Gazzola, 2009; Lockwood, 2016). Supporting this idea, neuroimaging studies have shown that certain brain areas that are activated when someone observes for example pain or disgust being experienced by another person match the brain areas that are activated when someone experiences pain or disgust themselves (Lamm, Bukowski, & Silani, 2016; Lamm et al., 2007; Lamm,et al., 2011; Singer et al., 2004). This process may be attributed to the existence of mirror neurons, which activate during observation of an action as well as during the execution of an action, and which are thought to facilitate imitation, learning, and social cognition (Rizzolatti & Craighero, 2004).

Behaviourally, mirroring is shown in the process of automatic mimicry where an observed emotional facial or postural expression is automatically and unconsciously mimicked by the observer (Dimberg, Thunberg, & Elmehed, 2000; Dimberg,1982; Dimberg, Andréasson, & Thunberg, 2011). The automatically activated matching neural/body representation of an observed emotion may generate the same emotion in the observer, which contributes to the recognition and understanding of the emotion in others (Decety & Jackson, 2006; Keysers & Gazzola, 2009; Preston & De Waal, 2002). It has been shown that when one is prevented from using mimicry, recognition of others’ emotions is reduced (Oberman, Winkielman, & Ramachandran, 2007). This suggests that individuals who are more sensitive to the bodily sensations induced by mimicry and who experience these emotions more intensely (Barrett et al., 2004; Wiens, 2005) may be more sensitive to the emotions of others and feel more empathy for others.

A small number of studies have investigated the relationship between interoceptive sensitivity and empathy. Grynberg and Pollatos (2015) found that individuals who are better at sensing their own heartbeat tend to give higher estimations of the level of pain when viewing pictures of people in pain. The good heartbeat perceivers also self-reported higher levels of arousal and feelings of compassion in response to the pictures (Grynberg & Pollatos, 2015). A neurological index of interoceptive processing, the HEP amplitude, was related to self-reported empathic concern on an empathy questionnaire (Fukushima et al., 2011), and similarly, neural activity in the insula, which is the primary brain region for processing interoceptive signals, was also associated with self-reported empathy (Singer et al., 2004). Furthermore, comparing the level of activation of brain regions during an empathy task after an interoceptive awareness task showed increased activation of the anterior insula and midline structures, suggesting a role for interoceptive awareness in empathy (Ernst et al., 2012). However, a relationship is not always found. Recently Ainley and colleagues (2015) found no relationship between heartbeat tracking scores and two behavioural tasks of cognitive empathy, nor with self-reported levels of affective and cognitive empathy on two questionnaires (Ainley et al., 2015).

 Social and communication deficits belong to the core characteristics of ASD (American Psychiatric Association, 2013). These include reduced emotional reciprocity and a reduced sharing of affect and emotion, amongst other things. Based on the Theory of Mind explanation of social deficits (Baron-Cohen, Leslie, & Frith, 1985), in psychological research a lack of understanding of other people’s thoughts and feelings is usually considered a hallmark of autism. This has somewhat conflated the concepts of ToM, which is cognitive in nature, and empathy, which is considered multi-faceted. For example, cognitive empathy (inferring other people’s emotions) may be referred to as affective ToM (Lockwood, 2016). Furthermore, empathy has been operationalized by tests that are more cognitive in nature than affective, such as the Mind in the Eyes test (Baron-Cohen et al., 2001), which is a test of emotion recognition from photographs of eyes only, the Yoni task (Shamay-Tsoory et al., 2007) that requires participants to infer emotions and intentions of a cartoon character from a very limited number of facial expressions, and the Director’s task (Dumontheil, Apperly, & Blakemore, 2010) which measures perspective taking ability. The Multifaceted Empathy Test (MET - Dziobek et al., 2008) is a behavioural task specifically designed to measure the cognitive (emotion recognition) and affective (the extent to which viewing an emotional person elicits the same emotion in the viewer) facets of empathy. Similarly, the Questionnaire of Cognitive and Affective empathy (QCAE - Reniers et al., 2011) was specifically designed to distinguish between cognitive and affective empathy. When cognitive and affective empathy are separately assessed, it shows that people with ASD tend to have impaired cognitive empathy, and intact affective empathy (Dziobek et al., 2008; Reniers et al., 2011; Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Rueda, Fernández-Berrocal, & Baron-Cohen, 2014). However, if and how the different facets of empathy are related to interoceptive processing in ASD has not been investigated. This thesis will address this gap in knowledge.

Recently, Bird & Viding (2014) tried to capture the multifaceted character of empathy in their Self To Other Model of Empathy (SOME – see figure in Appendix 1). This model proposes relationships between sensory input, affective input, cognitive input, mirroring input, and the understanding of social situations and conventions, to emotion processing and empathy. The authors propose that impairments in any or multiple input systems of the SOME may explain emotion processing deficits seen in some disorders and conditions, including autism and alexithymia. They suggest that people with autism might have impaired functioning of their cognitive input system in particular, the Theory of Mind System, which is in line with research findings that show impaired cognitive empathy but intact affective empathy in autism (Dziobek et al., 2008; Reniers et al., 2011; Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Rueda, Fernández-Berrocal, & Baron-Cohen, 2014). Additionally, the SOME’s Affective Representation System is proposed to generate understanding of one’s own emotions (using input from all systems, including the sensory system and the mirroring system), and an impairment in this system may be related to alexithymia. Because ASD and alexithymia co-occurs in ~50% of individuals with ASD (Hill et al., 2004; Samson, Huber & Gross, 2012), it will be interesting to see whether this might have implications for the generation of empathy in those individuals, as the model suggests, when input from two systems instead of one is not processed optimally.

## **1.5 Interoception and multisensory bodily self-consciousness in ASD - Hypotheses**

The aims of the PhD research reported in this thesis is to establish (i) if interoceptive processing and multisensory bodily self-consciousness in Autism Spectrum Disorders (ASD) are impaired in people with ASD than in the neurotypical population and (ii) if this is related to impairments in emotion processing of self and others in ASD.

Differences in multisensory bodily self-consciousness may be expected based on the evidence of altered self processing in autism presented at the start of the Introduction, and based on evidence for differences in sensory processing in ASD (Robertson & Baron-Cohen, 2017). Since 2013, sensory sensitivities are included in the diagnostic criteria of ASD, such as an inability to cope with certain sounds, lights, textures of clothing or food, or proximity of people. There may be an apparent insensitivity to temperature or pain, a need to touch, feel, smell or taste things, or a fascination with certain visual qualities of displays such as moving objects or colours (APA 2012).

Sensory difficulties in individuals with ASD are not restricted to one modality, and both hyper- and hyposensitivity to stimuli can occur within one person (Crane, Goddard, & Pring, 2009; Elwin, Ek, Kjellin, & Schröder, 2013; Fiene & Brownlow, 2015; Leekam, Nieto, Libby, Wing, & Gould, 2007; Robertson & Baron-Cohen, 2017). Severity of abnormal sensitivity correlates across different modalities, suggesting that individuals with ASD have a global deficit in sensory processing (Kern et al., 2007), which may include processing of interoceptive signals. Qualitative research that mainly focuses on exteroceptive sensory difficulties report indifference or hyposensitivity to interoceptive signals like pain, temperature, hunger, and thirst in both adults and children with ASD (Elwin, Ek, Schröder, & Kjellin, 2012; Elwin et al., 2013), although indications of increased sensitivity to pain have also been reported (Fan, Chen, Chen, Decety, & Cheng, 2014). Importantly for multisensory bodily self-consciousness, differences in multisensory integration have also been found (Foss-Feig et al., 2010; Iarocci & McDonald, 2006; Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2011; Stevenson et al., 2014). Bodily self-consciousness which relies on multisensory integration of signals, originating from the inside and outside of the body (Park & Blanke, 2017), may therefore be affected in ASD. Early indications that bodily self-consciousness is affected in ASD has been provided by body illusions that use a multisensory conflict to elicit changes in body part ownership and body part self-location: individuals with ASD tend to be less susceptible to the rubber hand illusion (Cascio, Foss-Feig, Burnette, Heacock, & Cosby, 2012; Paton, Hohwy, & Enticott, 2012; Schauder, Mash, Bryant, & Cascio, 2014).

Indications that interoception may be altered in people with ASD, and that this may have be associated with emotion processing, is provided by neuroimaging studies of the brain areas involved in interoception and self processing. In individuals with ASD, the right insula appears not only to have decreased activity in a resting state (Paakki et al., 2010), and reduced functional connectivity (Ebisch et al., 2011; Guo et al., 2019; Uddin & Menon, 2009). Furthermore, a meta-analysis of 24 functional neuroimaging studies shows that the ACC and the anterior insula are the two brain regions consistently hypoactive during a variety of tasks that require emotion processing (Di Martino et al., 2009).

 At the start of this PhD research, no studies focusing on interoception in ASD had been published. Since then a handful of studies have looked at interoceptive processing in ASD, with mixed results. Garfinkel and colleagues (2016) have reported higher interoceptive sensibility measured by self-report (Garfinkel, Tiley, O'Keeffe, Harrison, Seth, & Critchley, 2016), but lower interoceptive sensibility has been found by another study (Fiene & Brownlow, 2015), and a third study reported no differences in interoceptive sensibility in children with ASD compared to typical children (Palser, Fotopoulou, Pellicano, & Kilner, 2018). Interoceptive accuracy was unaffected in one sample of children with ASD (Schauder et al., 2014), but reduced in another sample (Palser et al., 2018), while others found that their accuracy may deteriorate with age as they get older (Mash, Schauder, Cochran, Park, & Cascio, 2017). In adults with ASD, reduced interoceptive accuracy has been found in two studies (Garfinkel, S. N., Tiley, C., O'Keeffe, S., Harrison, N. A., Seth, A. K., & Critchley, H. D., 2016; Shah, Catmur, & Bird, 2016), although in one of them this was a trend that became non-significant after correction for multiple comparisons (Shah et al., 2016a). The heartbeat evoked potential as an index of interoceptive processing has never been studied in ASD.

 Given the gaps in our understanding outlined above, this thesis will address the following three questions:

1. Is interoception, the sense of the state of the internal body, impaired in ASD?
2. Is multisensory bodily self-consciousness impaired in ASD?
3. Are any impairments in interoception and multisensory bodily self-consciousness related to impairments in emotion understanding of self and other in ASD?

Based on existing impairments in ASD in sensory processing, emotion processing and empathy, differences in functional connectivity and activity in interoceptive regions in the brain like the insula and the ACC, and theoretical indications of cascading influences of altered interoception on bodily self-consciousness, it is hypothesized that interoception and bodily self-consciousness are impaired in ASD. Furthermore, this is expected to be related to impaired processing of the emotions of self and other.

In the studies reported in this thesis, interoception was measured with the MAIA questionnaire (Mehling et al., 2012), with heartbeat perception tasks (Schandry, 1981; Whitehead, Drescher, Heiman, & Blackwell, 1977) and with the heartbeat evoked potential recorded with EEG (Pollatos & Schandry, 2004). These methods were intended to determine if individuals with ASD process interoceptive signals differently than neurotypical individuals, and to determine on which dimension of interoceptive processing they would differ, if any. The understanding of one’s own emotions was measured with a widely used alexithymia questionnaire TAS-20 (Bagby, Parker, & Taylor, 1994). Understanding of others’ emotions was measured with assessments of cognitive and affective empathy. Empathy was measured by questionnaire (Reniers et al., 2011), and with the Multifaceted Empathy Test ((Dziobek et al., 2008), a behavioural task that measures emotion recognition (cognitive empathy) and the extent in which one shares the emotion of another (affective empathy) when presented with pictures of individuals expressing an emotion. Following proposals that automatic mimicry might be a mechanism by which the vicarious experience of an emotion observed in another is induced (Keysers & Gazzola, 2009), group differences in automatic mimicry were assessed with an experiment measuring muscle activity in two facial muscles in response to viewing pictures of happy and sad faces using EMG (Dimberg, Thunberg, & Elmehed, 2000b; Dimberg, 1982). Finally, multi-sensory bodily self-consciousness was measured via responses to the full body illusion (Lenggenhager et al., 2007), the graphesthesia task (Arnold, Spence, & Auvray, 2017) and a task measuring peripersonal space (Canzoneri, Magosso, & Serino, 2012). These experiments assessed different aspects of bodily self-consciousness; self location, self identification, first-person perspective (Blanke, 2012) and the space of bodily self in interaction with the outside world (Noel, Pfeiffer, Blanke, & Serino, 2015).

Chapter 2 will describe some of the non-experimental methods used in the studies, and give descriptions of the autistic participants used in studies 1, 3 and 4. Chapter 3 and 4 address questions one and three. In Chapter 3, differences between ASD participants and non-ASD participants have been assessed in three levels of interoceptive processing: interoceptive sensibility, interoceptive accuracy, and the HEP. Expanding on this, Chapter 4 reports on two studies investigating of the relationships between interoception and the understanding of one’s own emotions and those of others. Correlation, multiple regression and mediation analyses were used to test the relationships between interoception, bodily self-consciousness, alexithymia and empathy. The results of the automatic mimicry task are also reported in Chapter 4. Chapter 5 addresses question two, by investigating, in ASD, two key aspects of bodily self-consciousness; self identification and self-location (Blanke, 2012), as well as peripersonal space. Chapter 6 provides an overall conclusion and discussion of the findings of this PhD.

Autism was once framed as a disorder of self and affective contact (Kanner, 1943). This thesis offers a small reapplication of this framing, adding new evidence to the growing literature of self-consciousness research and emotion research. Additionally, the investigation of the two approaches (interoceptive and multisensory processing) offers a holistic method for investigating bodily self-consciousness that recognizes the importance of sensations from within and without the body. And lastly, this thesis acknowledges the contribution of (altered) sensory processing both as an important characteristic of autism, and as a neurobiological mechanism from which self-consciousness may arise.

# Chapter 2

Methods

This chapter will describe the questionnaires that were used in all of the studies conducted and give a description of the three samples of autistic participants used in study 1, 3 and 4. Comparisons with results of their non-autistic control participant counterparts will be reported in the respective chapters describing the studies. In the studies, all participants (ASD and non-ASD) completed four well established, validated questionnaires, which are described below. An online version of the questionnaires was created with Qualtrics software (Qualtrics, Provo, UT, USA), which was also used to collect demographic data (age, diagnosis status, gender) and consent. Participants were given a link to the questionnaires, and they had a week after starting to complete it before the link transpired. This was to offer participants the possibility to complete the questionnaires at their convenience at home, and to reduce the time required to attend at Anglia Ruskin University. Participants were invited to the experimental part of the studies at Anglia Ruskin university. Informed written consent was sought from the participants again before the experimental part of each study.

## **2.1. Questionnaires**

### **2.1.1. The Autism Quotient (AQ)**

The Autism Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin & Chubley, 2001) (Baron-Cohen et al., 2001) is used as a screening tool for autism under the general population, and measures extent of autistic traits. It consists of 50 statements such as “I prefer to do things with others rather than on my own”, in response to which participants indicate their level of agreement on a 4-point scale. A score of over 32 (out of 50) is considered a threshold for clinically significant levels of autistic traits (Baron-Cohen et al., 2001) and has a sensitivity of 95% and a specificity of 52% (Woodbury-Smith, Robinson, Wheelwright, & Baron-Cohen, 2005), although the authors suggest that a threshold score of 26 is useful for screening referrals for ASD assessments in order to correctly identify the greatest number of individuals who might receive a diagnosis of ASD (Woodbury-Smith et al., 2005). The AQ has 5 subscales: social skills, attention switching, attention to detail, communication, and imagination. The subscales were found to have moderate internal consistency (α’s = .63-.77) (Baron-Cohen et al., 2001).

### **2.1.2. The Toronto Alexithymia Scale (TAS-20)**

### The Toronto Alexithymia Scale (TAS-20 - Bagby et al., 1994) assesses alexithymia with statements like “It is difficult for me to find the right words for my feelings”, and participants indicate their level of agreement on a 5-point scale. The TAS-20 has 3 subscales: difficulty describing feelings, difficulty identifying feelings, and externally-oriented thinking. The TAS-20 demonstrates good internal consistency (Cronbach’s alpha = .81) and test-retest reliability (.77, p<.01).  The TAS-20 uses cut off scoring: a score equal to or greater than 61 is considered to indicate alexithymia.

### **2.1.3. The Questionnaire of Cognitive and Affective Empathy (QCAE)**

The Questionnaire of Cognitive and Affective Empathy (QCAE) (Reniers et al., 2011) is a questionnaire that has collated 31 statements from commonly used and validated empathy questionnaires. It has two subscales measuring affective empathy and cognitive empathy and can be summated. Cognitive empathy is defined as “the ability to construct a working model of the emotional states of others”, and affective empathy is defined as “the ability to be sensitive to and vicariously experience the feelings of others” (Reniers et al., 2011). The statements on the QCAE originate from the Hogan Empathy Scale (Hogan, 1969), the Interpersonal Reactivity Index (Davis, 1983), the Impulsiveness-Venturesomeness Empathy Inventory (Eysenck & Eysenck, 1978), and the Empathy Quotient (Baron-Cohen & Wheelwright, 2004). Participants indicate on a 4-point scale how strongly they agree or disagree with statements like “I often get deeply affected with the feelings of a character in a film, play or novel”.

### **2.1.4. The Multi-dimensional Assessment of Interoceptive Awareness (MAIA)**

The Multi-dimensional Assessment of Interoceptive Awareness (MAIA) (Mehling et al., 2012) was used to measure the level of sensibility to bodily sensations with statement like “When I am tense, I notice where the tension is located in my body” and participants indicate how often they experience this on a 6 point scale. The MAIA assesses sensibility to bodily sensations as a multi-dimensional construct, including elements of regulation and appraisal (Cameron, 2001). The MAIA recognises that certain aspects of interoceptive awareness may be maladaptive; excessive focus on, worrying about or avoidance of bodily sensations are related to higher levels of anxiety, catastrophizing, and more difficulties with emotion regulation (Mehling et al., 2012). Therefore, items measuring worrying, avoidance and excessive focus have been reverse scored so that higher scores reflect mentally healthier (beneficial) levels of interoceptive sensibility, rather than more maladaptive awareness. The MAIA has eight subscales that reflect different dimensions of body awareness: Noticing, Distracting, Worrying, Attention Regulation, Emotional Awareness, Self-Regulation, Body Listening, and Trusting. The MAIA scores of the sub-scales provide a profile of conscious interoceptive processing and are intended to inform clinical practice about which aspects of interoceptive sensibility are compromised in individuals or certain clinical populations so that targeted treatment or therapy may be offered/developed. Due to moderate internal consistency on some scales and a poor one factor fit, the subscales are not intended to be summated (Mehling et al., 2012).

## **2.2. Description of autistic participants**

Participants with ASD were recruited via advertising at the two local universities and their disability support services, autism charities, and at local support and social groups for people with ASD and Asperger’s Syndrome. This meant that the ASD sample mostly consisted of individuals with average to above average IQ. As such, the sample may be biased to represent only the high functioning section of the clinical autism spectrum. However, as the control groups were also mostly recruited amongst staff and students at Anglia Ruskin University, there were no differences on IQ between groups (see experimental chapters). Participants received a financial compensation for their time, or received course credit for participation. A previous formal diagnosis of autism or Asperger’s Syndrome was accepted for inclusion in the ASD group. In total 47 participants with an ASD diagnosis were recruited. The previous diagnosis was confirmed by participants attending an ADOS-2 diagnostic interview (module 4) with Dr Steven Stagg, the second supervisor of this PhD. All but one of the participants reached the threshold point for autism spectrum diagnosis or autism. The data from the participant who didn’t reach the threshold was excluded from the study they participated in (Study 1). Thirteen participants took part in two studies, and four participants took part in all three studies. Three participants did not attend the diagnostic interview with Dr Stagg, due to him being their lecturer or supervisor. These participants scored over the 32 threshold on the AQ, which was regarded as an alternative confirmation of their diagnosis. Table 2.1. shows the ADOS-2 scores of the remaining 43 participants. The ADOS-2 assesses communication, social interaction, stereotyped behaviours and restricted interests, and imagination. For a diagnosis of autism spectrum disorder, a cut off point of a summated score of 7 for communication and social interaction must be obtained. A cut off score of 10 for social interaction and communication indicates a diagnosis of autism (Lord et al., 2000). The mean total score of ASD participants on the ADOS was 14.4 (SD: 3.6), the mean score for communication was 5.4 (SD: 2.5) and the mean score for social interaction was 9.0 (SD: 2.1).

Table 2.2. shows descriptive statistics of the three autistic samples used in Study 1, 3, and 4. IQ was measured with the two subtest Wechsler Abbreviated Intelligence Scale, 2nd edition (WASI-II, Wechsler 2011). Because only two subtests were administered instead of four, separate measurements for verbal intelligence and performance intelligence cannot be given. Instead, the (age adjusted) T-scores of the subtests are reported. The scores of the subtests of vocabulary and matrix reasoning provide a reliable and validated basis for an estimation of full scale IQ (Wechsler, 2011). Autistic traits were measured with the AQ (Baron-Cohen et al., 2001), and the scores of the five subscales are reported here. Alexithymia was measured with the TAS-20 (Bagby et al., 1994), and in addition to the mean scores, the number of participants scoring above 61 is reported. A score of above 61 indicates alexithymia. As can be seen, half of the ASD participants may be considered alexithymic, in all three samples. This is in line with the prevalence of alexithymia observed in other studies (e.g. Hill, Berthoz, & Frith, 2004; Samson, Huber & Gross, 2012).

## **2.3. Ethical declaration**

## All participants received a participant information sheet before their participation. Consent was sought twice; once before their completing the questionnaires on-line, and once more in the beginning of the experimental sessions. Participants were informed of their right to withdraw. A debrief was given after completion. All studies received ethical approval from the faculty ethics committee at Anglia Ruskin University, and conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

*Table 2.1. ADOS-2 (module 4) results of the ASD participant pool*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Participant | ADOS total | ADOS communication | ADOS social interaction | Participant | ADOS total | ADOS communication | ADOS social interaction |
| 1 | 17 | 7 | 10 |  | 23 | 9 | 0 | 9 |
| 2 | 18 | 9 | 9 |  | 24 | 18 | 7 | 11 |
| 3 | 17 | 5 | 12 |  | 25 | 17 | 9 | 8 |
| 4 | 21 | 8 | 13 |  | 26 | 14 | 4 | 10 |
| 5 | 13 | 6 | 7 |  | 27 | 12 | 4 | 8 |
| 6 | 9 | 6 | 3 |  | 28 | 21 | 9 | 12 |
| 7 | 8 | 3 | 5 |  | 29 | 21 | 8 | 13 |
| 8 | 16 | 6 | 10 |  | 30 | 15 | 6 | 9 |
| 9 | 14 | 6 | 8 |  | 31 | 13 | 7 | 6 |
| 10 | 15 | 6 | 9 |  | 32 | 14 | 5 | 9 |
| 11 | 17 | 8 | 9 |  | 33 | 13 | 5 | 8 |
| 12 | 13 | 5 | 8 |  | 34 | 16 | 8 | 8 |
| 13 | 18 | 8 | 10 |  | 35 | 14 | 5 | 9 |
| 14 | 15 | 3 | 12 |  | 36 | 17 | 7 | 10 |
| 15 | 15 | 7 | 8 |  | 37 | 12 | 4 | 8 |
| 16 | 23 | 10 | 13 |  | 38 | 16 | 7 | 9 |
| 17 | 15 | 4 | 11 |  | 39 | 10 | 3 | 7 |
| 18 | 14 | 7 | 7 |  | 40 | 9 | 2 | 7 |
| 19 | 14 | 4 | 10 |  | 41 | 11 | 2 | 9 |
| 20 | 7 | 0 | 7 |  | 42 | 15 | 4 | 11 |
| 21 | 10 | 0 | 10 |  | 43 | 11 | 3 | 8 |
| 22 | 14 | 5 | 9 |  |  |  |  |  |

*Table 2.2. Descriptive statistics of the three autistic samples of Study 1, 3 and 4.*

|  |  |  |  |
| --- | --- | --- | --- |
|  | Study 1 | Study 3 | Study 4 |
|  | N = 20 (7 female) | N = 26 (7 female) | N = 22 (8 female) |
|  | M (SD) | M (SD) | M (SD) |
| Age | 25.4 (9.8) | 25.9 (7.3) | 27.0 (9.0) |
| IQ | 112.2 (17.3) | 113.8 (12.0) | 110.1 (13.0) |
| Vocabulary T-score |  58.5 (14.2) |  58.1 (9.5) |  57.0 (11.5) |
| Matrix reasoning T-score |  55.7 (10.11) |  56.9 (7.6) |  54.7 (7.0) |
| AQ (autistic traits) | 32.5 (8.6) | 31.1 (9.3) | 33.3 (7.3) |
| Social skills |  6.1 (2.9) |  5.8 (2.8) |  6.2 (2.2) |
| Attention Switching |  8.2 (1.9) |  8.0 (2.2) |  7.5 (1.9) |
| Attention to detail |  6.1 (1.7) |  6.3 (2.1) |  7.1 (1.7) |
| Communication |  7.0 (2.3) |  6.2 (2.6) |  7.1 (1.8) |
| Imagination |  5.0 (2.5) |  4.8 (2.6) |  5.6 (1.8) |
| TAS-20 (Alexithymia) | 60.2 (8.2) | 59.5 (15.9) | 61.6 (11.4) |
| N scoring > 61 (%) |  10 (50%) |  13 (50%) |  11 (50%)  |

# Chapter 3

Differences on three dimensions of interoceptive processing:

the heartbeat evoked potential, interoceptive accuracy and interoceptive sensibility in ASD

## **3.1 Introduction**

The conscious and unconscious processing and perception of internal bodily signals is multi-faceted, and includes the processing of signals originating from the body in the brain, the accurate perception of bodily signals, as well as cognitive and affective processes related to the perception of internal states (Cameron, 2001; Mehling et al., 2012). Garfinkel and colleagues identified three different, dissociable psychological dimensions of interoception: interoceptive sensibility, interoceptive accuracy and interoceptive awareness (Garfinkel, S. N. & Critchley, 2013; Garfinkel, Tiley, O'Keeffe, Harrison, Seth, & Critchley, 2016; Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015). Research into different dimensions of interoception in ASD is still in its infancy. So far, there is mixed evidence that interoceptive sensibility is altered in ASD (Garfinkel et al, 2016; Mul, Stagg, Herbelin, & Aspell, 2018; Palser, Fotopoulou, Pellicano, & Kilner, 2018; Schauder, Mash, Bryant, & Cascio, 2014), converging evidence of reduced interoceptive accuracy in ASD (Garfinkel et al., 2016; Mash, Schauder, Cochran, Park, & Cascio, 2017; Mul et al., 2018; Palser et al., 2018; Shah, Catmur, & Bird, 2016), and some evidence of reduced interoceptive metacognitive awareness in ASD (Garfinkel et al., 2016; Palser et al., 2018). However, the cortical processing of signals, measured using the heartbeat evoked potential (HEP), has not been examined in ASD. If an altered HEP is found in ASD, this may provide further evidence that altered interoceptive processing can be measured not just on behavioural levels of analysis, but is also evident on a psychophysiological level of analysis. This study addresses this gap in the literature.

 Interoceptive signals enter the brain via multiple pathways which include the spinothalamic pathway, the glossopharyngeal nerve, the vagus nerve, chemosensory pathways and somatosensory pathways. Many bodily signals converge in the brainstem in the nucleus of the solitary tract, from which there are projections to the thalamus and hypothalamus, before they are relayed to the cerebral cortex where they are mapped and re-represented in the somatosensory cortices, the insular cortex, the anterior cingulate cortex and the ventromedial prefrontal cortex (Cameron, 2001; Critchley, 2005; Palma & Benarroch, 2014). The HEP, the neural response to the heartbeat in the cortex, can be measured by electroencephalogram (EEG). The HEP is made evident by time-locking the EEG to the R-peaks of the cardiac electrical activity measured by electrocardiogram (ECG), before averaging the EEG over the 800ms time segment following the R-peaks. Each R-peak represents the occurrence of a heartbeat, and therefore averaging EEG activity time-locked to the R-peaks will show heartbeat related activity, while mostly cancelling out activity and noise due to other causes.

 The HEP is an index of afferent cardiac processing in the brain, and has been used as an objective measure of interoceptive processing. The amplitude of the HEP has been shown to be larger in individuals with better interoceptive accuracy (Mai, Georgiou, & Pollatos, 2016; Mai, Wong, Georgiou, & Pollatos, 2018; Pollatos & Schandry, 2004a; Schandry, Rainer & Montoya, 1996; Yuan, Yan, Xu, Han, & Yan, 2007) and can be enhanced by attention (Pollatos & Schandry, 2004a; Schandry, Sparrer, & Weitkunat, 1986) and arousal (Luft & Bhattacharya, 2015). The HEP amplitude appears to be strongest in fronto-central regions of the brain and can also be observed in parietal regions (Gray et al., 2007; Schandry, Rainer & Montoya, 1996). It is thought to reflect activity of interoceptive processing in the insula, the anterior cingulate cortex and the somatosensory cortex, amongst other regions (Kern, Aertsen, Schulze-Bonhage, & Ball, 2013; Park et al., 2017; Pollatos, Kirsch, & Schandry, 2005). Apart from their visceral sensory role, these structures are also involved in emotion processing (Craig, 2009; Craig, 2002) and self processing (Babo-Rebelo, Richter, & Tallon-Baudry, 2016; Babo-Rebelo, Buot, & Tallon-Baudry, 2019; Moriguchi et al., 2006; Northoff et al., 2006). It is therefore not surprising that in emotion disorders, interoception appears to be affected. For example, increased interoceptive accuracy and increased interoceptive sensibility are both associated with anxiety symptoms (Ehlers & Breuer, 1996; Pollatos, Traut-Mattausch, Schroeder, & Schandry, 2007) and may be reflected in an increased HEP (Judah et al., 2018), whereas in depression, interoceptive accuracy tends to be reduced (Dunn, Dalgleish, Ogilvie, & Lawrence, 2007; Furman, Waugh, Bhattacharjee, Thompson, & Gotlib, 2013; Terhaar, Viola, Bär, & Debener, 2012) and patients with depression have shown reduced HEP amplitudes (Terhaar et al., 2012).

It has been shown that in autistic individuals, the key brain regions involved in interoceptive processing show some differences compared to non-autistic individuals: the insula and ACC are integral to the so-called salience network, which determines which internal and external stimuli to attend to, and in which the insula is proposed to function as a switching node between other brain networks such as the default-mode network and the executive-control network (Sridharan, Levitin, & Menon, 2008; Uddin & Menon, 2009). In ASD, reduced connectivity within the salience network has been found as well as reduced connectivity of the salience network with the executive control network, (Abbott et al., 2016; Di Martino et al., 2009; Ebisch et al., 2011; Uddin & Menon, 2009) and with nodes in the default-mode network (Abbott et al., 2016; Guo et al., 2019). Within the default network itself, reduced connectivity has been shown in ASD (Cherkassky, Kana, Keller, & Just, 2006; Monk et al., 2009; Weng et al., 2010). This network includes the cingulate cortex, precuneus, medial prefrontal cortex and the angular gyrus and is active during wakeful rest, i.e. in the absence of a cognitive task, and may therefore to some extent reflect homeostatic (interoceptive) activity (Jerath & Crawford, 2015). These functional differences in the brain have been linked with some autistic traits, such as difficulties in emotion processing and social functioning (Abbott et al., 2016; Di Martino et al., 2009; Murdaugh et al., 2012). It is expected that these functional differences will be reflected in the HEP of people with ASD, and also in behavioural measures of interoceptive processing: interoceptive accuracy and interoceptive sensibility.

There is scarce qualitative evidence that individuals with ASD have altered interoceptive sensibility. Elwin and colleagues report hyposensitivity to sensations like temperature, hunger or thirst in two qualitative studies that were focused on exteroceptive sensory differences in ASD (Elwin, Ek, Schröder, & Kjellin, 2012; Elwin, Ek, Kjellin, & Schröder, 2013). Using quantitative methods, there is mixed evidence to answer the question whether individuals with ASD have lower or higher interoceptive sensibility, and this appears to depend on the questionnaire that is used. Using the Body Perception Questionnaire (BPQ - (Porges, 1993). Garfinkel et al. (2016) and found higher interoceptive sensibility in adults with ASD, but Palser et al (2018) found no difference in their sample of children, while Fiene and Brownlow (2015) reported lower interoceptive sensibility using the Body Awareness Questionnaire (Shields, Mallory, & Simon, 1989) and a thirst awareness measure (Fiene & Brownlow, 2015) and Mul and colleagues (2018 – see chapter 3) reported lower interoceptive sensibility using the Multidimensional Assessment of Interoceptive Awareness (MAIA; (Mehling et al., 2012). The BPQ focuses on negative body sensations (e.g. pain) and responses may be confounded by the prevalence of these sensations or a bias of focus on negative experiences, which may not be the same for different populations. The BAQ and the MAIA on the other hand incorporate positive, neutral and negative body sensations in their questions.

For interoceptive accuracy, which has been measured with the heartbeat tracking task (Schandry, 1981) in some of the studies above, there is more convergence: Garfinkel et al. (2016), Palser et al. (2018) and Mul et al. (2018) found reduced interoceptive accuracy (see chapter 3), while Schauder et al. (2015) found no difference in their sample of children with ASD. In another sample of children, Mash et al. (2017) found that interoceptive accuracy decreases with age in children with ASD, but increases in typical children, and this relationship is moderated by IQ. Finally, Shah et al. (2016a) found a trend for lower interoceptive accuracy (non-significant after correction for multiple comparisons) in their sample of ASD participants compared to their non-ASD participants, who, importantly, were matched on alexithymia. Alexithymia is a condition characterised by a poor ability to identify, distinguish and describe one’s own emotions (Nemiah, 1977). Shah et al.’s (2016a) analysis provides support for the hypothesis that reduced interoceptive ability is associated with alexithymia rather than autism (Bird & Cook, 2013; Shah, Hall, Catmur, & Bird, 2016), and suggests that findings of reduced interoceptive ability in autism may reflect the much higher prevalence of alexithymia in the autistic population than the typical population (Hill, Berthoz, & Frith, 2004).

Two studies measured meta-cognitive interoceptive awareness in ASD, as measured by calculating the congruence of a person’s interoceptive sensibility and interoceptive accuracy (Garfinkel, et al., 2016; Palser et al., 2018). Both studies found reduced interoceptive awareness in ASD; the discrepancy between interoceptive accuracy measured by the heartbeat tracking task (Schandry, 1981) and interoceptive sensibility measured by the BPQ (Garfinkel, 2016; Palser et al., 2018) was greater in ASD than in non-ASD participants. Garfinkel and colleagues (2016) suggest that this metacognitive dimension of interoception reflects how well individuals can predict their own interoceptive states, and could conceptually be understood as a behavioural measure of prediction error. This relates to a predictive coding account of interoception, that proposes that conscious representations of bodily feelings and emotions emerge as a product of resolving discrepancies (prediction errors) between top-down predictions of body state with bottom-up interoceptive signals (Barrett, 2017; Seth. & Critchley, 2013; Seth, & Friston, 2016). They suggest that these results may be viewed as evidence that dysfunctional predictive inference of interoceptive signals may contribute both to anxiety and certain autistic traits, like reduced empathy. However, the BPQ gives opposite interoceptive sensibility results to the MAIA or BAQ with autistic participants (Mul et al., 2018; Fiene & Brownlow, 2015), and the discrepancy might therefore be a consequence of chosen questionnaire, rather than reflecting a genuine discrepancy between accuracy and sensibility (see also Discussion). It is of note that there are no studies that have used a confidence rating in combination with interoceptive accuracy measurements as a measure of metacognitive interoceptive awareness.

This study addresses the lack of research into the HEP in autism, and extends previous experimental research which has only utilised behavioural measures of interoception. Investigating the three dimensions of interoception (processing of cardiac signals in the brain, heartbeat perception accuracy and interoceptive sensibility) in the same participants may resolve some of the contradictory results that have been found previously. The HEP was investigated in a sample of adults with ASD and a control group without ASD. Based on previous research that shows reduced connectivity of crucial interoceptive regions in the brain in ASD (Di Martino, Ross et al., 2009; Di Martino et al., 2009; Guo et al., 2019; Uddin & Menon, 2009), reduced interoceptive accuracy in ASD (Garfinkel et al., 2016; Mul et al., 2018; Palser et al., 2018; Shah et al., 2016) and the links between interoceptive accuracy and HEP amplitude in the typical population (Mai, Georgiou, & Pollatos, 2016; Mai, Wong, Georgiou, & Pollatos, 2018; Pollatos & Schandry, 2004; Schandry, Rainer & Montoya, 1996; Yuan, Yan, Xu, Han, & Yan, 2007), it was expected that the HEP amplitude in ASD would be attenuated compared to controls. This study investigated relationships of the HEP with severity of autistic traits, empathy and alexithymia, reflecting emotional understanding of others and self, expecting that a greater HEP amplitude would be related to higher empathy scores, and lower scores on autistic traits and alexithymia. Additionally, as a secondary goal, other measures of interoceptive ability were employed in order to replicate previous studies; the heartbeat tracking task (Schandry, 1981) was used to measure interoceptive accuracy and two subscales of the Multidimensional Assessment of Interoceptive Awareness (MAIA (Mehling et al., 2012) were used to measure interoceptive sensibility. It was expected that participants with ASD would be impaired on the interoceptive measures compared to neurotypical participants.

## **3.2. Methods**

### **3.2.1. Participants**

Forty-five participants (11 female) between the ages of 18 and 52, (mean 25.1 years, *SD* 8.4) took part in the study, of which 21 (7 female) had previously received a diagnosis of high functioning autism or Asperger syndrome by a clinician independent from the current study. Participants received a financial compensation for their time, or course credit for participation. A diagnosis of high functioning autism or Asperger’s syndrome was accepted for inclusion in the ASD group. Twenty participants with ASD attended an Autism Diagnostic Observation Schedule (ADOS) diagnostic interview (Lord et al., 2000) with a psychologist trained in the use of ADOS (second supervisor SS) to confirm their diagnosis of ASD. Sixteen of those met the diagnostic criteria for autism and three met the criteria for autism spectrum disorder according to ADOS guidelines. One participant did not meet the ADOS criteria for ASD and was excluded from the analysis. One participant who was unable to partake in the ADOS interview scored well above the screening cut-off point of 32 on the Autism Quotient screening questionnaire (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001).

The two groups were matched on IQ (*t* (27.6) = 1.02, *p* = .32) measured with the Wechsler Abbreviated Intelligence Scale, 2nd edition (Wechsler, 2011), and on age (*t* (42) = 0.11, *p* = .92). The two groups did not significantly differ on sex, χ2 ,*p* = .16. See Table 3.1 for demographic details.

*Table 3.1*. Participants’ characteristics of age, IQ and autistic traits (AQ).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Age | IQ | AQ |
|  | N | M (SD) | M (SD) | M (SD) |
| ASD | 20 (7 female) | 25.4 (9.8) | 112.2 (17.3) | 32.5 (8.6) |
| Non-ASD | 24 (4 female) | 25.1 (7.3) | 107.4 (10.1) | 14.5(6.0) |

### **3.2.2. Materials and Procedure**

### **3.2.2.1Interoceptive sensibility**

Participants completed the Multidimensional Assessment of Interoceptive Awareness (MAIA; (Mehling et al., 2012) questionnaire, measuring awareness of internal bodily sensations. The MAIA has 8 subscales and is not designed to provide a single summated score of interoceptive awareness. The subscale ‘Noticing’, which measures awareness of comfortable, uncomfortable and neutral body sensations, and the subscale ‘Attention Regulation’, which measures the ability to sustain and control attention to body sensations when they are competing with exteroceptive signals were of primary interest for their conceptual relevance to interoceptive ability and multisensory integration considering the known differences in sensory processing in ASD (Crane, Goddard, & Pring, 2009; Klintwall et al., 2011; Leekam, Nieto, Libby, Wing, & Gould, 2007), and the analyses focus on these.

### **3.2.2.2. Interoceptive accuracy**

Participants did the heartbeat tracking task (Schandry, Rainer, 1981), measuring the accuracy with which they perceive their heartbeat. The participant was seated upright, and was asked to count their own heartbeats and indicate how many heartbeats had occurred during a specific short time interval, whilst their heartbeat was recorded by an electrocardiogram (ECG). To this end, participants had three disposable surface electrodes with conductive hydrogel attached to their chest, and cardiac activity was relayed through shielded wires to the Powerlab Data Acquisition unit (AD Instruments, Germany). Participants were offered a practice trial, followed by 4 experimental trials of 25, 35, 45 and 55 seconds, presented in random order. The experimenter gave a verbal start and stop sign for each experimental trial. Participants were not told the duration of the trials, were asked not to take their pulse, and they did not receive any feedback on their performance. An accuracy score was calculated using the formula IA = {1⁄4 Σ [1 - (|recorded heartbeats – counted heartbeats|/recorded heartbeats)]} as in Schandry, 1981. The ECG was also used to determine the participant’s average heart rate (beats per minute – BPM)

### **3.2.2.3. Questionnaires**

The study consisted of 4 well-established and validated questionnaires, measuring autistic traits, interoceptive sensibility, empathy, and alexithymia. All participants completed the Autism Quotient (Baron-Cohen et al., 2001) measuring autistic traits, the Toronto Alexithymia Scale (Bagby, Parker, & Taylor, 1994) measuring alexithymia, and the Questionnaire of Affective and Cognitive Empathy (Reniers, Corcoran, Drake, Shryane, & Völlm, 2011) measuring empathy. The questionnaires are described in Chapter 2.

### **3.2.2.4. Heartbeat Evoked Potential (HEP) procedure**

Participants were seated in a sound-attenuated, electrically shielded Faraday cage and were fitted with an EEG cap (ActiCAP – Brain Products GmbH, Munich, Germany) on which 29 active Ag/AgCl electrodes were mounted to record the participants’ electroencephalogram (EEG) from the following positions: FP1, FP2, F7, F8, F3, Fz, F4, FC5, FC1, Fz, FC2, FC6, T7, C3, Cz, C4, T8, TP9, CP5, CP1, CP2, CP6, TP10, P7, P3, Pz, P4, P8, PO9, PO10. Three Ag/AgCl electrodes were attached to the participant’s chest to record the participant’s electrocardiogram (ECG): one electrode was placed under the right clavicle, one under the left clavicle and one on the left on the lower edge of the rib cage. Conductive hydrogel was inserted between each electrode and the scalp/skin. Electrode impedance was kept below 5 kΩ. The sampling rate of the continuous EEG/ECG recording was 500Hz.

 During the EEG recording, in order to maintain their attention on their heartbeats (which enhances the HEP (Montoya, Schandry, & Müller, 1993; Pollatos & Schandry, 2004; Schandry et al., 1986), participants performed a heartbeat counting task, consisting of 2 blocks with a 5 minute break in between. Block 1 lasted for 8 minutes and block 2 lasted for 9 minutes. Each block consisted of 4 counting phases. Participants were asked to count their own heartbeat silently for 130 beats, start counting at 1 for the next 110 beats, then return to 1 and count again for the next 140 heartbeats, and again for the next 100 heartbeats in the first block. This was repeated in the second block for 160, 100, 140, and 110 heartbeats (similar to Pollatos & Schandry, 2004; Pollatos et al., 2005). Participants were told that they should not take their pulse, but if they lost count or had difficulty perceiving their heartbeat they should nevertheless keep focusing on their heartbeat and try to continue counting in a rhythm that they felt was their heartbeat rhythm. Performance on this task was not measured. After explaining the heartbeat counting task to the participant, the experimenter retreated to the adjacent room, with communication established through an intercom system and live video feed (one-way). The beginning and end of each block was indicated verbally through the intercom system.

### **3.2.2.5. HEP processing and analysis**

The evoked potential in response to a stimulus (here, the heartbeat) can be distinguished from other brain activity by repeating the stimulus many times and then averaging the activity time-locked to the stimulus. The averaging cancelled out other unrelated brain activity, and makes the activity related to the stimulus visible in the EEG.

 Preprocessing and analysis of the EEG/ECG data was performed using EEGLAB (Delorme & Makeig, 2004) in MATLAB R2017b software (MathWorks Inc, Natick, MA, USA). Off line, the data was down-sampled to 250Hz, and filtered from 1-40 Hz. The EEGLAB plugin FMRIB 1.21(Niazy, Beckmann, Iannetti, Brady, & Smith, 2005) was used to identify the onset of the R-wave of the heart beat in the three ECG channels. The FMRIB QRS detection tool uses a combination of adaptive thresholding, the Teager energy Operator and a correction algorithm to identify the onset of the R-wave with an average sensitivity and specificity of 99% (Niazy et al., 2005). Independent component analysis (ICA) (Delorme & Makeig, 2004) was used to visually identify and then remove components reflecting eye movements, eye blinks, and cardiac field artefacts (CFA). ICA has been shown to be effective in removing components representing CFA, a procedure necessary for a reliable identification of the HEP because averaging activity around the QRS-wave of the heart beat would amplifies these artefacts and can interfere with any observed HEP activity (Luft & Bhattacharya, 2015). The ECG activity recorded by the three chest electrodes was checked after components removal: it should no longer show a recognisable QRS-wave after components representing CFA were sufficiently removed. Each data file was visually inspected for any malfunctioning electrodes, followed by, where necessary, the interpolation of the corresponding channels (mean: 0.75 channels, range: 0-4, median: 0), by computing averages of neighbouring electrodes. Subsequently, epochs were created around the previously identified R-waves of the heartbeat activity, starting 200ms before the R-wave until 800ms after the R-wave. The 200ms before the R-wave was used as the baseline for a baseline correction, before the data was re-referenced to an average of all channels. Automatic artefact rejection was applied to reject any epochs with activity below -120 μV or above 120 μV. A final visual inspection of the data was carried out to ensure all artefacts were adequately removed. The data of one non-ASD participant was excluded on the basis that more than 50% of epochs were rejected. Of the data of the remaining participants, an average of 3.8% of epochs were rejected, ranging from 0 to 14.6% across participants. Although the final number of epochs per participant varied, depending on the participant’s heart rate, a minimum of 800 epochs per average evoked potential was achieved for all participants.

 HEP grand averages were calculated for all electrodes. From the grand averages, the mean amplitude over the time window 200-350ms after the R-peak was calculated, the latency at which previous research has found strong HEP activity (Fukushima, Terasawa, & Umeda, 2011a; Gentsch, Sel, Marshall, & Schütz‐Bosbach, 2018; Judah et al., 2018; Mai et al., 2018; Pollatos & Schandry, 2004; Yuan et al., 2007). The HEP amplitude has been found to be most pronounced over frontal and central electrodes (Gentsch et al., 2018; Leopold & Schandry, 2001; Mai et al., 2018; Pollatos & Schandry, 2004a; Pollatos et al., 2005) Therefore three regions of interest were investigated in the analysis: left frontal (FP1, F7, F3, FC5), central (Fz, FC1, FC2, Cz) and right frontal (FP2, F8, F4, FC6). Group differences in mean amplitude were analysed with a 2 x 3 (Group x Regions of Interest) ANOVA, followed up with two-tailed *t-*tests where appropriate. Where assumptions of sphericity were violated, Greenhouse-Geisser corrected values are reported.

In an additional check that cardiac activity did not affect the measured brain activity, Pearson correlations between ECG amplitude and HEP amplitude in the time window were also assessed. The relationships between the HEP, heartbeat perception accuracy and questionnaire responses were assessed with Spearman correlations.

## **3.3. Results**

### **3.3.1. Interoceptive Sensibility**

ASD participants scored similarly to non-ASD participants on the MAIA subscale of noticing; ASD *M* (*SD*) = 2.9 (0.9), non-ASD *M* (*SD*) = 3.1 (1.0), Mann-Whitney *U* = 214.5, *p* = .39. ASD participants scored significantly lower on the MAIA subscale of attention regulation; ASD *M* (*SD*) = 2.3 (0.7), non-ASD *M* (*SD*) = 2.8 (1.0), Mann-Whitney *U* = 131, *p* = .02.

### **3.3.2. Interoceptive Accuracy**

Statistical checks (independent two-tailed *t*-tests) were made to ensure there was no significant difference between groups in their heart rates, measured in beats per minute (BPM), *t* (42) = 1.42, *p* = .16, nor BMI, *t* (42) = 1.10, *p* = .28, and that participants’ BPM and BMI did not correlate with accuracy at the heartbeat tracking task, *r* (BPM) = -.26, *p* = .09 and *r* (BMI)= -.25, *p* = .11.

A two-tailed independent *t*-test showed that ASD participants were significantly poorer at tracking their own heartbeat, *M* (*SD*) = 0.58 (0.2) than non-ASD participants, *M* (*SD*) = 73.2 (0.17), *t* (42) = 2.67, *p* = .01.

### **3.3.3. Heartbeat Evoked Potential**

Statistical checks showed that the mean amplitudes of the HEP in the three RoIs were not related to participants’ BPM or BMI; all *r* < ⎮0.18⎮, *p* > .23. Statistical analysis of the mean amplitude using a 3 x 2 (Region x Group) Anova revealed there was no main effect of region, *F* (2, 41) = .0.25, *p* = .78, and no main effect of group, *F* (2, 41) = 0.19, *p* = .67, but there was a significant interaction effect of region and group, *F* (2, 41) = 3,82, *p* = .026. Post-hoc *t-*test revealed that only in the central region there was a significant difference between non-ASD and ASD participants, *t* (41) = 2.15, *p* = .038, with the non ASD group showing a negative amplitude of greater magnitude than the ASD group, see Figures 3.1., 3.2. and 3.3.

We checked for the possibility that the observed difference in heartbeat evoked potential may be due to differences in ECG activity between groups by comparing the mean amplitude of cardiac activity (as measured by the ECG) in the time window 200ms -350ms of the two groups, and this showed to be non-significant for all three heartbeat channels recorded, *t* (41) < 1.08, *p >* .28. Additionally, the HEP amplitude did not correlate with ECG amplitudes of the three ECG channels in this time window, all *r* < .14, *p* > .36, providing additional evidence that the cardiac field was adequately removed and could not explain HEP amplitude.

0 200 400 600 800

Figure 3.1. The waveform of grand-averaged HEP in the central region of interest for non-ASD and ASD participants. The shaded area shows the analysed time window 200ms – 350 ms after the R-peak of the ECG.

Figure 3.2. The waveform of the grand-averaged HEP in the left frontal region of interest for non-ASD and ASD participants. The shaded area show the analysed time window 200ms-350ms after the R-peak of the ECG.

Figure 3.3. The waveform of the grand-averaged HEP in the right frontal region of interest for non-ASD and ASD participants. The shaded area show the analysed time window 200ms-350ms after the R-peak of the ECG.

### **3.3.4. Questionnaire responses and relationships with interoceptive measures**

Participants with ASD scored significantly higher on autistic traits than non-ASD participants (*p* < .001). They scored significantly lower on empathy (*p* < .001), which was driven by cognitive empathy – affective empathy scores of ASD participants were similar to those of non-ASD participants. There was a trend for ASD participants to score higher on alexithymia. See Table 3.2.

*Table 3.2*. Means, standard deviations and comparisons between groups of questionnaire responses measuring autistic traits (AQ), alexithymia (TAS-20), empathy (QCAE), cognitive empathy (subscale of QCAE), affective empathy (subscale of QCAE)

|  |  |  |  |
| --- | --- | --- | --- |
|  | Non-ASD | ASD | Difference |
| Measure | *M* (*SD*) | *M* (*SD*) | Mann-Whitney U | *p* |
| Autistic traits | 9.9 (4.1) | 29.8 (6.2) | 1.50 | < .001\* |
| Alexithymia | 48.9 (13.1) | 60.2 (12.7) | 149 | .02 |
| Empathy | 89.8 (9.2) | 73.7 (13.2) | 92.5 | < .001\* |
|  Cognitive empathy | 60.2 (8.2) | 43.4 (6.2) | 57.5 | < .001\* |
|  Affective empathy | 29.6 (3.8) | 30.3 (5.8) | 219 | .45 |

Note: \* significant at the Bonferroni corrected alpha-level of *p* < .01

Only MAIA attention regulation correlated significantly and negatively with autistic traits, as measured by the AQ, after Bonferroni correction. None of the other measures of interoception correlated significantly with autistic traits, empathy or alexithymia, taking Bonferroni correction into account. Note that due to the negative voltage of the HEP amplitude in this time window, a positive correlation with the HEP means that a higher (less negative) voltage of the HEP - i.e. a HEP amplitude of reduced absolute magnitude - is related to higher questionnaire scores. A trend of such an attenuated amplitude of the HEP in the right frontal region being related to higher scores on autistic traits (AQ) and alexithymia (TAS20) can be observed. There is also a trend in better noticing of body sensations and a better ability to regulate attention to bodily sensations (MAIA subscales) to be related to higher empathy scores (QCAE). See Table 3.3.

*Table 3.3. Spearman correlations between the three HEP regions of interest, heartbeat tracking accuracy and responses to the questionnaires: AQ (autistic traits), QCAE (empathy), and TAS20 (alexithymia).*

|  |  |  |  |
| --- | --- | --- | --- |
| Questionnaire | AQ | QCAE | TAS20 |
| Interoceptive measure | *r (p)* | *r (p)* | *r (p)* |
| HEP Left Frontal | 0.26 (.09) | -0.08 (.44) | 0.14 (.38) |
| HEP Right Frontal | 0.37(.01) | -0.30(.06) | 0.36 (.02) |
| HEP Central | 0.03 (.85) | -0.12 (.45) | 0.05 (.76) |
| Heartbeat Tracking | -0.32(.04) | 0.08 (.62) | -0.16 (.31) |
| MAIA Noticing | -0.28 (.07) | 0.37 (.02) | -0.28 (.06) |
| MAIA Attention regulation | -0.47 (.002)\* | 0.38 (.01) | -0.31 (.04) |

Note: \* Significant at the Bonferroni corrected alpha level of *p* < .002.

Additionally, the three levels of interoceptive processing measured (HEP, interoceptive accurcay and interoceptive sensibility) did not correlate significantly with each other: The mean amplitudes of the three HEP regions did not significantly correlate with heartbeat tracking accuracy, all *r* < ⎮0.13⎮, *p* > .39, nor with the subjective measures of interoceptive processing, the two domains of the MAIA questionnaire, Noticing and Attention Regulation, all *r* < ⎮0.32⎮, *p* > .04. Neither did heartbeat tracking accuracy correlate significantly with the MAIA noticing, *r* = .12, *p* = .44, but there was a trend towards a positive correlation between interoceptive accuracy and MAIA attention regulation *r* = 0.36, *p* = .02, not surviving Bonferroni correction. See Table 3.3.

## **3.4. Discussion**

A cortical index of cardiac interoception, the HEP, was investigated in people with and without ASD, to determine if the emerging behavioural evidence that interoceptive processing is altered in ASD is supported by differences in an electrophysiological measure. The results showed that in the fronto-central brain region, the average HEP amplitude in a time window from 200-350ms was significantly attenuated in adults with ASD compared to adults without ASD. This finding dovetails with the other findings, that individuals with ASD have lower interoceptive sensibility and lower interoceptive accuracy than non-ASD individuals, measured by a questionnaire and a heartbeat tracking task, respectively. These results suggest that on average, individuals with ASD show lower interoceptive processing on at least three dimensions; a less pronounced HEP amplitude, lower objectively measured interoceptive accuracy, and lower subjectively reported interoceptive sensibility. These results are in line with previous studies that have found reduced interoceptive ability in ASD (Fiene & Brownlow, 2015; Garfinkel et al., 2016; Palser et al., 2018) and this study is the first to report that weaker interoceptive ability in ASD is reflected in the brain by an attenuated HEP amplitude. This study is therefore an important addition to the growing evidence that interoceptive processing is altered, and that this is evident not just on the behavioural level, but also via measures of cortical processing.

Research with other clinical samples show the same pattern that was found here: a reduced HEP appears to occur in clinical samples with reduced interoceptive accuracy and reduced emotional awareness, while a more pronounced HEP is associated with clinical populations who have anxiety related symptoms and increased interoceptive accuracy (Paulus & Stein, 2010): in line with characteristics of anhedonia in depression, a less pronounced HEP amplitude has been found in depressed people (Terhaar et al., 2012), while patients with obsessive-compulsive disorder showed an increased HEP amplitude (Yoris et al., 2017). Social anxiety has also been associated with an increased HEP amplitude (Judah et al., 2018), as has worrying about body sensations (Baranauskas, Grabauskaitė, & Griškova-Bulanova, 2017), although people with panic disorder did not show an increased HEP (Yoris et al., 2017). The present study extends findings that differences in interoception may be associated with certain aspects of mental health, by showing they can also associated with characteristics of ASD, a developmental disorder. Controlling for levels of depression and anxiety in the ASD participants (which were not measured for this study) would improve further HEP research and confidence in this interpretation.

 The early part of the HEP waveform (<300ms after the R-peak) is thought to reflect primary processing of heartbeat related signals (Park et al., 2017) by the posterior and mid insula, the mid cingulate cortex, and the primary somatosensory cortex that receive signals directly from the thalamus ((Craig, 2003; Kern et al., 2013; Palma et al., 2014). The later part of the waveform (>300ms after the R-peak) may additionally reflect higher order processing of signals originating from primary sources (Park et al., 2017), although it is thought that primary processing for other (exteroceptive) modalities occurs <200ms after the stimulus (Garrido, Kilner, Kiebel, & Friston, 2007; Tallon-Baudry & Bertrand, 1999). Higher order processing would involve multimodal integration and processing by the association cortices. However, given the findings of Park and colleagues (2017), it is likely that the time window that was investigated here reflects primary processing of the signals as well as higher order processing. It has been shown that during the time window of 200-350ms after the R-peak heartbeat detection becomes possible (Brener & Kluvitse, 1988), and conscious awareness of the heartbeat involves processing by the anterior insula and the ACC (Craig, 2009; Craig, 2002). Weaker interoceptive signalling might affect the outcome of this process (Pollatos & Schandry, 2004) and could partly explain why the heartbeat perception of ASD participants is less accurate than that of non-ASD participants.

No differences were observed in the fronto-left or fronto-right regions of interest between ASD participants and non-ASD participants, but only in the central region. This could mean that in this time window, central brain structures such as the cingulate cortex could underly this difference in activity. A source analysis of high-density EEG data or an fMRI study would be needed to confirm this. The ACC and insular cortex are co-activated during interoceptive processing, which is in line with the idea that feeling states underlie conscious awareness of self (Babo-Rebelo et al., 2016; Babo-Rebelo et al., 2019; Chiu et al., 2008; Critchley, 2005) and support the understanding of others’ emotional states (Lamm & Singer, 2010; Mundy, 2003; Silani et al., 2008).

Previous HEP source analyses have indicated the insula and the anterior cingulate cortex (ACC) as viscerosensory and visceromotor centres involved in interoception and form a closely connected circuit (Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004; Kern et al., 2013; Pollatos et al., 2005). The left anterior insula is associated with low-level cortical registration and processing of interoceptive signals, while the right anterior insula is thought to be involved in higher order processing of interoceptive states, e.g. subjective awareness and evaluation of bodily sensations (Craig, 2009; Craig, 2002; Critchley et al., 2004). The ACC is involved in the integration of self-related information with exteroceptive sensory signals originating from others (Craig, 2002) underpinning social behaviours such as joint attention (Mundy, 2003). Previous research has found a relationship between state empathy and HEP amplitude in the frontocentral region (Fukushima, Terasawa, & Umeda, 2011). Additionally, it has been shown that the HEP amplitude is reduced during the processing of angry faces (Gentsch, Sel, Marshall, & Schütz‐Bosbach, 2018; Marshall, Gentsch, Schröder, & Schütz-Bosbach, 2018).

Although both a less pronounced HEP in ASD as well as reduced interoceptive accuracy were found, a correlation between heartbeat accuracy and the HEP was not. This suggests that factors that affect the individual performance and variability in interoceptive accuracy may be different from those that affect the magnitude of the cortical response to the heartbeat measured by the HEP. For example, it has been suggested that heartbeat perception relies mostly on signals that originate in mechanoreceptors, located not only in muscle tissue of the heart itself but also in muscles and skin near the heart which signal the pressure the beating of the heart exerts on these tissues. Others have suggested that the contribution of chemoreceptors, thermoreceptors and osmoreceptors that detect cardiac activity is unlikely to be involved in interoceptive sensibility as inputs from these rarely reach consciousness (Cameron, 2001). As such, heartbeat perception could involve relatively more somatosensory processing, while the HEP might reflect afferent input from more sources, although this is speculative and the relative contributions of different pathways to either interoceptive sensibility or HEP remain unknown (see Park & Blanke, (2019), for a review on likely pathways for HEP activity). Khalsa and colleagues (2009) found that a patient with insular damage could perceive their own heartbeat, but could no longer do so when the skin on his chest was anesthetised, suggesting that there is a somatosensory pathway contributing to interoceptive sensibility independently from an interoceptive pathway involving the insular cortex (Khalsa, Rudrauf, Feinstein, & Tranel, 2009). Alternatively, or additionally, accuracy of heartbeat perception might be affected by existing knowledge of or beliefs about one’s heartrate and other cognitive processes (Desmedt, Luminet, & Corneille, 2018; Jones, 1994; Phillips, Jones, Rieger, & Snell, 1999; Ring, Brener, Knapp, & Mailloux, 2015; Ring & Brener, 2018).

In a predictive coding account of brain functioning, sensory experience is the result of a generative process of active inference in which predictions about the causes of sensory stimuli (prior probability estimates based on past experience) are constrained and modulated by current sensory inputs to create updated posterior probabilities about the causes of these inputs (Friston, 2005; Friston, Mattout, & Kilner, 2011; Seth, Suzuki, & Critchley, 2012). So instead of functioning as a stimulus-response organ, the brain actively anticipates sensory signals which get “checked” against actual incoming sensory signals. The brain aims to minimize the difference between its predictions and sensory input (the prediction error) which it does by either driving the body to match the predicted sensation, by modifying the prediction, or by changing the sampling of or attention to the incoming sensations (Barrett & Simmons, 2015; Friston, 2005; Friston et al., 2011). The attenuation process of prediction errors is thought to be impaired in ASD (Brock, 2012; Lawson, Rees, & Friston, 2014; Palmer, Lawson, & Hohwy, 2017; Pellicano & Burr, 2012; Van Boxtel & Lu, 2013). This may be caused by an impairment in estimating the reliability and precision of sensory information, which makes it harder to control which sensory information to attend to or to ignore (Lawson et al., 2014; Palmer et al., 2017). This may explain many difficulties people with ASD have, from hypersensitivity to sounds, touch or light, to difficulty in coping with unexpected events and the need for sameness (Lawson et al., 2014; Palmer et al., 2017).

The predictive processing account of interoceptive signals proposes that top-down priors are naturally weighed more than bottom-up signals, firstly because homeostasis operates within strict limits and can’t be volatile and is therefore best based on prior probability, and secondly because the attenuation of bottom-up prediction errors allows for top-down predictions to elicit (or “command”) sympathetic and parasympathetic autonomic reflexes and other (e.g. sensorimotor) responses in anticipation of a future bodily state and well before the bodily state requires urgent action (Barrett & Simmons, 2015; Pezzulo, Rigoli, & Friston, 2015; Seth et al., 2012; Seth & Critchley, 2013). Interoceptive perception is therefore more a reflection of the beliefs about the state of the body, which are merely kept in check by signals from the body, than a reflection of the actual state of the body. Homeostatic regulation and interoceptive perception are balanced in such a way as is most useful to the organism (Seth & Tsakiris, 2018). This may be an additional explanation why the group differences in interoceptive sensibility and interoceptive accuracy dovetail with group differences in the HEP amplitude, while they do not correlate. There may be a different balance of regulatory and perceptual “usefulness” to the ASD body than the neurotypical body, arising from life-long, but individually varying, sensory processing differences.

Interoceptive predictions originate in the anterior insula and ACC, from where they are not only fed downwards along efferent interoceptive channels which include the amygdala and hypothalamus, but also integrated with signals from the other modalities (Barrett & Simmons, 2015; Palma & Benarroch, 2014). A failure to attenuate interoceptive as well as exteroceptive prediction errors will impair the ability to associate interoceptive predictions with incoming exteroceptive information, which may result in the development of weaker interoceptive expectations integral to the processing of exteroceptive, and particularly social, stimuli (Quattrocki & Friston, 2014; Seth & Friston, 2016b). This suggests a development of interoception in ASD from hypersensitivity in infancy and childhood to hyposensitivity in adulthood. In line with this, hyperconnectivity of the insula and the ACC in children with ASD has been reported (Uddin et al., 2013), while hypoconnectivity has been found in adults (Caria & de Falco, 2015; Di Martino et al., 2009; Ebisch et al., 2011; Guo et al., 2019). Furthermore, recently a study showed that interoceptive accuracy decreases during childhood for children with ASD, but increases for typically developing children (Mash et al., 2017). The reduced interoceptive processing observed in adults with ASD in the present study may be the outcome of a developmental path of less effective attenuation of prediction errors, less effective and fewer opportunities for associative learning about interoceptive cues (Quatroccki & Friston, 2014), and a brain development towards hypoconnectivity for interoceptive processing hubs (Caria & de Falco, 2015; Di Martino et al., 2009; Ebisch et al., 2011; Guo et al., 2019; Uddin et al., 2013).

There may be additional causes for reduced HEP activity, such as differences in various neurotransmitter levels and their receptors, which have been reported in ASD (Chugani, 2012). For example, reduced levels of gamma-aminobutyric acid (GABA) in the insula have been associated with decreased activity in the insula during interoception (Wiebking et al., 2014). Of particular interest in regard to interoception is the neurotransmitter and hormone oxytocin (Quattrocki & Friston, 2014). There is some evidence that plasma levels of oxytocin is lower in people with ASD (Green et al., 2001; Modahl et al., 1998) and that differences in oxytocin receptor genes are associated with ASD (Gregory et al., 2009; Jacob et al., 2007). Oxytocin has been proposed to play an essential role in the attenuation of bottom-up interoceptive signals so that top-down activation of autonomic responses or other action is elicited, which facilitates homeostatic regulation (Quattrocki & Friston, 2014). This would be in accordance with predictive coding accounts of autism, extending them by suggesting interoceptive processing might be included in the predictive coding hypotheses.

The finding of reduced interoceptive sensibility in the ASD participants, is in line with the findings of Fiene and Brownlow (2015) and Mul et al. (2018) (see chapter 3), and also in line with qualitative reports of reduced sensibility to interoceptive signals like temperature, hunger and thirst in ASD (Elwin et al., 2012; Elwin et al., 2013). It is, however, in contrast with the findings of Garfinkel et al. (2016) who used the BPQ (Porges, 1993) to assess subjective awareness of bodily sensations. This BPQ lists a range of bodily sensations, nearly all of which are unpleasant (e.g. pain, tension, bloatedness). Individuals who have more physical ailments, or those who have a bias to focus on negative experiences, such as people with symptoms of anxiety and depression, may therefore score high on this questionnaire (Paulus & Stein, 2010). ASD is associated with elevated levels of anxiety and depression (Mukaddes & Fateh, 2010; Skokauskas & Gallagher, 2010) and participants with ASD may therefore on this basis be expected to score higher on this questionnaire than participants without ASD. Garfinkel et al. (2016) do indeed find that their ASD participants are significantly more anxious than their non-ASD participants and they also report significant positive relationships between both state and trait anxiety and BPQ scores. In contrast, Palser et al. (2018) report no significant difference in anxiety in their sample of ASD children and typical children, nor a significant difference on interoceptive sensibility measured their child-friendly adaptation of the BPQ, while they still found the positive correlation between BPQ and anxiety. The questionnaire used in the current study - the MAIA (Mehling et al., 2012) - on the other hand, uses a concept of interoceptive sensibility that addresses neutral, as well as positive and negative sensations (e.g. “I notice changes in my breathing, such as whether it slows down or speeds up.”). Therefore, it is possible that responses to the BPQ are confounded by anxiety in an autistic sample, which may explain why Garfinkel found higher interoceptive sensibility.

The MAIA (Mehling et al., 2012) questionnaire which was utilised in this study uses a multi-dimensional concept of interoceptive sensibility that includes not only aspects of noticing, but also aspects of attention to and evaluation of bodily sensations. The questionnaire responses of different dimensions are not meant to summed (Mehling et al., 2012) but is intended to provide clinical practice with focused information of which aspects of interoceptive awareness are compromised in certain patient or population groups, so that appropriate and targeted measures might be taken. Certain items are reverse coded, so that maladaptive responses to bodily signals (such as worrying) result in lower scores. Here, the dimensions of noticing and attention regulation were looked at specifically. Attention regulation, a dimension that assesses how well one can maintain/switch attention to bodily sensations when competing with external stimuli, was chosen because of known differences in sensory processing in ASD (Crane et al., 2009; Elwin et al., 2013; Klintwall et al., 2011; Leekam et al., 2007; Robertson & Baron-Cohen, 2017) and because bodily self-awareness is at a fundamental level dependent on the integration of multisensory information from internal and external sources (Blanke, 2012; Damasio, 2000; Damasio, 2012). It is interesting that no significant difference in the MAIA subscale of noticing was found, whereas a significant difference between the ASD participants and control participants on the MAIA subscale of attention regulation was. The ability to effectively integrate and regulate attention to bodily sensations when competing with other sensations is one of the functions of the anterior insula, in its central role in the saliency network (Sridharan et al., 2008).

The finding of reduced interoceptive accuracy in adults with ASD is in line with previous research which also found reduced interoceptive accuracy in adults with ASD (Garfinkel, 2016; Mul et al., 2018; Palser et al., 2018) and is also in line with the trend found by Shah et al. (2016). Schauder et al. (2015) found no difference in interoceptive accuracy on the heartbeat tracking task in their sample of children. This finding may not be in conflict with the results from the present study when one considers Mash et al.’s finding (Mash et al., 2017) that interoceptive accuracy increases with age in typical children, but appears to decrease for children with ASD, except for those of high intelligence (IQ > 115).

Previous research suggests that interoceptive ability is related to the experience of emotional feelings (Dunn et al., 2010; Herbert, Pollatos, & Schandry, 2007; Pollatos et al., 2005; Wiens, Mezzacappa, & Katkin, 2000). Many individuals with ASD have difficulty in identifying, describing and distinguishing their own emotions (Hill et al., 2004), and understanding those of others (Baron-Cohen & Wheelwright, 2004; Lawrence, Shaw, Baker, Baron-Cohen, & David, 2004; Lombardo, Barnes, Wheelwright, & Baron-Cohen, 2007). It has been suggested that an impairment in detecting and processing bodily signals in ASD may contribute to a reduced ability to use these signals to learn about social interactions (Quattrocki & Friston, 2014). Impaired social functioning is a key characteristic of ASD. Support for this hypothesis was found in the group differences on the three dimensions of interoception (all three lower in participants with ASD). There was also evidence for a relationship between autistic traits and interoceptive sensibility: the ability to regulate one’s attention to bodily sensations (MAIA attention regulation) was significantly and negatively related to severity of autistic traits, and consciously noticing bodily sensations (MAIA noticing) and MAIA attention regulation showed a trend for a positive relationship with empathy (QCAE). On the other dimensions, of interoceptive accuracy and the HEP in the right frontal region, trends were observed that indicate relationships in the same predicted pattern: lower interoceptive accuracy may be linked with higher autistic traits, and similarly, a less pronounced HEP in the right frontal regions tended to be related to higher autistic traits and higher alexithymia, although these relationships were not significant after correction for multiple correlations. This could be due to a lack of power; a bigger sample size might give more power to find significant relationships.

The observed reduced interoceptive abilities in ASD may contribute to a better understanding of certain behaviours seen in individuals with ASD. Parents, carers, teachers and therapists might consider that their son or daughter, pupil or patient needs help recognising their internal states, whether it’s hunger, thirst or temperature (Elwin et al., 2012; Elwin et al., 2013) or arousal and emotions (Hill et al., 2004; Milosavljevic et al., 2015). For example, difficulties with emotion regulation may be compounded by a lower insight into one’s internal feelings and less effective self-monitoring (Rieffe et al., 2011; Samson et al., 2014; Samson, Huber, & Gross, 2012). Recently it was shown that a 9-month intervention program with typical adults aimed at improving bodily awareness in combination with socio-affective and socio-cognitive mental training resulted in improved interoception as measured by the heartbeat tracking task, and improved emotional awareness as measured by the TAS-20 (Bornemann & Singer, 2017), with the participants who had scores approaching the clinical threshold of alexithymia improving their emotional awareness the most. The authors suggest that these improvements might have beneficial knock-on effects, such as better coping with pain or healthier eating habits. It would be valuable to find out if for adults and children with ASD improved interoceptive and emotional awareness would result in better emotion regulation or improvements in social functioning. The results of this study and those of others (Garfinkel et al, 2016; Mul et al, 2018) cautiously suggest that this might be a worthwhile avenue to explore.

This study has some limitations. Levels of anxiety or depression in the participants were not measured and could therefore not be controlled for this in the analyses. Anxiety is associated with increased interoceptive accuracy (Pollatos, Traut‐Mattausch, & Schandry, 2009) and increased awareness of bodily sensations, in particular negative ones (Dunn et al., 2010b; Paulus & Stein, 2010), while depression is associated with reduced interoceptive accuracy (Furman et al., 2013; Pollatos et al., 2009) and increased subjective awareness of negative body sensations (Paulus & Stein, 2010). If there were participants with anxiety or depression in the sample, this may have affected the results. Another limitation concerns the use of the heartbeat tracking task to measure interoceptive accuracy. This task has been criticised as being confounded by beliefs about heartrate (Ring et al., 2015) Ring & Brener, 1996; Knapp et al., 1997) While participants were specifically instructed to report the number of heartbeats they counted and did not give feedback on participants’ performance during the task, it is possible that existing knowledge or beliefs about their heartrate influenced their performance. Also, recently a suggestion has been made that time estimation ability is associated with heartbeat perception (Wittmann, 2013), which was not controlled for. A final limitation is that the control group did not have similar levels of alexithymia as the ASD group. It has been suggested that alexithymia, not autism, is associated with impaired interoception (Brewer, Happé, Cook, & Bird, 2015; Shah et al., 2016). This means that it is not certain if the observed differences are a consequence of high alexithymia in the ASD group, or autism. However, the number of people with clinical levels of alexithymia in the ASD group was in line with previously reported levels of alexithymia in the autistic population (50%), as was the number of people in the control group with alexithymia (~10%) (Hill et al, 2004), and this sample may therefore be considered representative of the autistic population as well as the typical population with respect to alexithymia.

 Future work could better assess whether the ability to adjust the precision of interoceptive prediction errors is affected in ASD by comparing a condition of heartbeat counting with a condition of rest, and/or a condition of focus on an exteroceptive stimulus. Attention to the heartbeat should increase the weight of the prediction error associated with it, and result in a more pronounced HEP compared to rest or an exteroceptive focus (Petzschner et al., 2018). Similarly, a repeated presentation of an angry face has been shown to attenuate the visual evoked potential as well as the HEP in typical adults (Marshall, Gentsch, Jelinčić, & Schütz-Bosbach, 2017). If aberrant weighting of prediction errors occurs in individuals with ASD for interoceptive as well as exteroceptive stimuli, there should be an absence of or a reduced suppression effect of repetition on both evoked potentials in participants with ASD.

 In summary, this study has provided further evidence that individuals with ASD have impaired interoception on a number of levels on interoceptive processing. Specifically, for the first time, that individuals with ASD show an attenuated HEP amplitude in the frontocentral region of the brain, a result that accords with the findings of reduced interoceptive accuracy and lower interoceptive sensibility in ASD. This may be the consequence of anomalous predictive processing in the autistic brain, where the weight and therefore salience that is given to interoceptive signals is altered compared to the brains of neurotypical individuals. The HEP is thought to reflect activity in interoceptive centres like the insula and the ACC, which are also involved in self-processing and emotion processing. Individuals with ASD show behavioural deficits in these domains, which suggests that improving interoceptive ability may be a worthwhile avenue to explore to reduce difficulties that arise from these deficits, such as improving the understanding of one’s own emotions and those of others.

# Chapter 4

Interoceptive processing and the relationship with alexithymia and empathy in ASD**[[1]](#footnote-1)**

## **4.1 Introduction**

One of the main characteristics of Autism Spectrum Disorders (ASD) is impairment in reciprocal social behaviour. An important psychological explanation that may partly explain this deficit is that it arises from a limited understanding of other people’s point of view, intentions and beliefs and is known in the literature as a deficit in Theory of Mind (ToM) (Baron-Cohen, Leslie, & Frith, 1985). The understanding of others’ emotions is also affected, with studies showing reduced empathy in ASD (Baron-Cohen et al., 1985; Baron-Cohen & Wheelwright, 2004; Baron-Cohen et al., 2005). However, in recent years it has been recognised that empathy is a multifaceted process with an affective component, where a feeling of sharing the emotion with another (affective empathy) may arise from the apprehension or comprehension of another’s emotional state (cognitive empathy) (Bird, Geoffrey & Viding, 2014; Eisenberg, 2000) as well as from bottom-up processes that result in the vicarious experience of an emotion observed in another, through mirroring mechanisms (Bird, Geoffrey & Viding, 2014; Gallese, 2001; Keysers & Gazzola, 2009). Several studies have shown that cognitive empathy, which involves inferring the emotions of others, may be reduced in ASD (e.g. (Demurie, De Corel, & Roeyers, 2011; Golan & Baron-Cohen, 2006), whereas affective empathy (the ability to share the emotions of others) may not be adversely affected (Dziobek et al., 2008; Rogers, Dziobek, Hassenstab, Wolf, & Convit, 2007; Rueda, Fernández-Berrocal, & Baron-Cohen, 2014).

Given growing evidence for important links between the detection of internal bodily states (interoception), emotion processing and empathy (Craig, 2008; Craig, 2002; Damasio, 2000; Grynberg & Pollatos, 2015; Herbert, Pollatos, & Schandry, 2007; Terasawa, Moriguchi, Tochizawa, & Umeda, 2014), the present study will investigate relationships between these factors in participants with ASD.

 Interoception – the sense of the physiological state of the body (Craig, 2002) – has been proposed to play an important role in emotion processing (Cannon, 1927; Craig, 2002; Damasio, 2000; James, 1894) and may also play a part in the process of empathy. There is some evidence that people who are more sensitive to their bodily feelings tend to have a better understanding of their emotions (Critchley, 2005; Herbert, Herbert, & Pollatos, 2011), and experience emotions more intensely. Studies have found a relationship between interoceptive accuracy and cognitive and affective empathy for pain (Singer, et al., 2004), and a cortical index of interoceptive sensitivity - the heartbeat evoked potential - is related to self-reported empathic concern (Fukushima, Terasawa, & Umeda, 2011). Furthermore, neuroimaging studies show that the primary brain region involved in interoception - the insula - is also activated during the subjective awareness of feelings, including anger, disgust, pain, and empathy (Craig, 2008; Ernst, Northoff, Böker, Seifritz, & Grimm, 2012; Ochsner et al., 2008; Singer, Critchley, & Preuschoff, 2009; Zaki, Davis, & Ochsner, 2012), and insula activation during empathy tasks can be increased by raising interoceptive awareness beforehand (Ernst et al., 2012).

The above studies suggest that interoceptive processing is recruited both during emotion processing and empathy. This is in line with the simulation hypothesis of empathy, which proposes that empathy may partly be the result of the vicarious experience of an emotion observed in another through mirroring mechanisms (Baird, Scheffer, & Wilson, 2011; Bastiaansen, Thioux, & Keysers, 2009; Gallese, 2001; Keysers & Gazzola, 2009). Facial motor mirroring occurs automatically when observing others’ emotion. For example, facial motor mirroring occurs automatically when observing others’ emotions. Electromyography studies have shown that the corrugator muscles in the forehead that are used for frowning show increased activation during the observation of an angry face (compared to a smiling face), while observing a smiling face increases the activation of the zygomaticus muscle in the cheek used for smiling (Dimberg, Thunberg, & Elmehed, 2000; Dimberg, 1982; Dimberg, Andréasson, & Thunberg, 2011). This motor mirroring may contribute to the understanding of the observed emotion through the vicarious experience of the emotion that is elicited by the mirrored bodily state. Mirroring has also been shown in the brain: similar brain activity occurs during the experience of emotions and observing others’ emotions (Botvinick et al., 2005; Hennenlotter et al., 2005; Jabbi, Bastiaansen, & Keysers, 2008; Wicker et al., 2003), which suggests that the brain draws on representations of one’s own emotions to generate understanding of others’ emotions (Keysers & Gazzola, 2009; Preston & De Waal, 2002; Singer, 2009). Better emotional self-understanding is related to higher empathy levels (Grynberg, Luminet, Corneille, Grèzes, & Berthoz, 2010; Moriguchi, Y. et al., 2007; Moriguchi, Yoshiya et al., 2006; Terasawa et al., 2014). Additionally, learned associations between interoceptive signals and emotions observed in others may contribute to empathy (Bird, Geoffrey & Viding, 2014; Quattrocki & Friston, 2014). Bird and Viding (2014) have proposed the Self to Other Model of Empathy (SOME – see Appendix 1) in which interoceptive cues (partly generated by a mirroring mechanism) and the representation of emotion, together with a situation understanding system and ToM, provide the basis for empathy when the experience of emotion is recognised as having been elicited by the emotions of others. Having an internal representation of one’s own emotions is an integral part of this empathy model.

 In this light, it is important to note that ASD is a disorder that is highly co-morbid with alexithymia (Hill, Berthoz, & Frith, 2004), a condition characterised by a reduced ability to recognise, describe and understand one’s own emotions (Nemiah, 1977). Alexithymia is considered to be a character trait that is prevalent in around 10% of the general population (Linden, Wen, & Paulhus, 1995), but prevalent in ~50% of the ASD population (Hill et al., 2004; Samson, Huber, & Gross, 2012). Indeed, the high prevalence of alexithymia in the autistic population may explain mixed results in emotion research, as study findings may differ depending on the proportion of ASD participants in any particular sample who have co-morbid alexithymia (Bird & Cook, 2013; Cook, Brewer, Shah, & Bird, 2013). For example, differences in the recognition of facial expressions may be related to alexithymia, not autism (Cook et al., 2013; Grynberg et al., 2012), as may be differences in the understanding of vocal affect (Heaton et al., 2012) and emotional decision making (Shah, Catmur, & Bird, 2016). In other studies, differences between people with and without ASD in insula activation during empathy tasks were not significant after accounting for alexithymia (Bird et al., 2010; Silani et al., 2008). Similarly, differences in brain networks associated with empathy were also associated with alexithymia (Bernhardt et al., 2014). Given these results, it is important to take alexithymia levels into account when investigating empathy and other traits in ASD.

 Providing a possible explanation for the relationship between interoception and empathy, it has been suggested that the social difficulties of ASD arise from malfunctions in the ‘oxytocin-interoception system’ (Quattrocki & Friston, 2014), a system that influences the saliency of interoceptive signals, emotions and sense of self, from infancy. However, Brewer and colleagues (2015) have convincingly pointed out that alexithymia may be a consequence of a compromised ‘oxytocin-interoceptive system’ not ASD (Brewer, Happé, Cook, & Bird, 2015), and a recent study confirmed individuals with high alexithymia tended to rely less on interoceptive respiratory cues and showed reduced accuracy on muscle feedback even after controlling for autistic traits (Murphy, Catmur, & Bird, 2018). The latter is also in line with the Bird and Viding’s empathy model, who propose that low empathy in autism is caused by impairments in the ToM and situation understanding parts of the Self to Other Model of empathy (SOME), whilst alexithymia may be the result of impairments in the affective representation system of the SOME (Bird & Viding, 2014).

 Following on from the research in chapter 3, which found that interoceptive processing is impaired on three dimensions in ASD, the research presented in this chapter aims to further investigate the relationships of interoception with alexithymia and empathy in ASD. This chapter describes two studies; an exploratory questionnaire study (Study 2) with non-ASD participants, and a behavioural study (study 3) comparing participants with ASD and a control, neurotypical group. In addition to the questionnaires used in the exploratory study, the ASD participants and control group also completed an empathy task, two heartbeat perception tasks, and a facial mimicry task to test the simulation hypothesis of empathy. This theory led to the prediction that levels of mirroring activity may contribute to empathy. The simulation hypothesis also implies that alexithymia may fulfil a mediating role in the relationship between interoception and empathy, supported by research that shows alexithymia to be an explanatory factor of low levels of empathy in ASD (Bird & Cook, 2013; Bird et al., 2010). For Study 2, it is predicted that there will be a negative relationship interoceptive sensibility and alexithymia, a negative relationship between interoceptive sensibility and empathy, and that aspects of interoceptive sensibility contribute to both. It is also expected that higher levels of autistic traits are related to higher levels of alexithymia and lower levels of empathy. For study 3 it is expected that people that people with ASD will have lower interoceptive awareness and accuracy, which contribute to higher levels of alexithymia, which, in turn contributes to lower empathy. Therefore it is predicted that the individuals with ASD who also have alexithymia, will have lower levels of empathy than those without alexithymia.

## **4.2. Methods Study 2**

**4.2.1 Participants**

205 participants, recruited amongst staff and students of Anglia Ruskin University, completed the study. Participants were recruited by advertising at the university. Participants were given to opportunity to enter into a prize draw for a £25 Amazon voucher as compensation for their participation, and participants who were psychology students at ARU received course credit for their participation. 27 participants were excluded from the study because they reported they had a diagnosis of Autism Spectrum Disorder or another psychiatric diagnosis (e.g. depression, anxiety disorder). The data of the remaining 178 participants (109 female) was analysed. Participants were between 18 and 54 years old (*M* = 22.2, *SD* = 6.8). The study was approved by the ethics panel at the Faculty of Science and Technology, Anglia Ruskin University and conducted in accordance with the ethical standards of the 1964 declaration of Helsinki. All participants gave written informed consent to participate.

### **4.2.2. Materials and Procedure**

The study consisted of 4 questionnaires, measuring autistic traits, interoceptive sensibility, empathy, and alexithymia. The questionnaires that were used were The Autism Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) which measures severity of autistic traits, the Questionnaire of Cognitive and Affective Empathy (QCAE) (Reniers, Corcoran, Drake, Shryane, & Völlm, 2011) which was used to measure affective empathy and cognitive empathy and The Toronto Alexithymia Scale (TAS-20) (Bagby, Parker, & Taylor, 1994) was used to assess alexithymia. The Multi-dimensional Assessment of Interoceptive Awareness (MAIA) (Mehling et al., 2012) was used to measure the level of sensibility to bodily sensations. The questionnaires are described in Chapter 2.

### **4.2.3. Data analysis**

A median split on AQ scores will be used to identify two groups in the sample; those with high autistic traits and low autistic traits. Group differences in interoceptive sensibility, alexithymia an empathy will be investigated. Using the whole sample, correlation and multiple regression analyses will be used to investigate the relationships between interoceptive sensibility on the one hand, and empathy and alexithymia on the other.

## **4.3. Results Study 2**

Descriptive statistics (Table 4.1) showed that there was a significant difference between men and women on the QCAE affective empathy subscale, with women scoring higher than men. There was a trend for women to have lower levels on the MAIA subscale of Not-worrying, which was non-significant after Bonferroni correction for multiple comparisons to .002. There were no other differences between men and women. Using a median split on AQ scores, differences between participants with low autistic traits and those with high autistic traits were examined. The only significant difference between participants with low autistic traits and those with high autistic traits after Bonferroni correction was that participants with low autistic traits had significantly lower scores on alexithymia. Additionally, there was a trend for participants with low autistic traits to have higher scores on empathy, see Table 4.2.

 Correlation analyses were conducted to explore the relationships between the variables (Table 4.2). Looking at the relationships of interoceptive sensibility and the variables of empathy, autistic traits and alexithymia, significant negative correlations between MAIA self-regulation and autistic traits, MAIA self regulation and alexithymia, MAIA attention regulation and alexithymia and MAIA trusting and alexithymia were found (Bonferroni corrected alpha level *p* < .001). There were also significant positive correlations between MAIA noticing and empathy, MAIA attention regulation and empathy, MAIA self regulation and empathy, and MAIA body listening and empathy. Additionally, alexithymia was significantly and positively related to autistic traits, and negatively to empathy. Autistic traits were significantly and negatively related to empathy. See Table 4.2.

 Subsequently, the shared variance of autistic traits, alexithymia and empathy in the relationships with interoceptive sensibility was investigated. Statistically, the causality of the relationships is irrelevant and therefore 8 multiple regressions were conducted, in which entered autistic traits, alexithymia and empathy were entered as simultaneous predictor variables, and each subscale of the MAIA as the outcome variable. See Table 4.2 for beta-values (β). After taking the contributions of empathy and alexithymia into account, autistic traits were only predictive of MAIA self-regulation, such that higher autistic traits are associated with lower self-regulation of bodily sensations. Empathy was predictive of MAIA self-regulation, in the opposite direction: Higher empathy was associated with higher levels of self-regulation. Empathy was also positively related to MAIA noticing, MAIA attention regulation and MAIA body listening. Alexithymia was negatively related to MAIA not-worrying and MAIA trusting, after taking contributions of autistic traits and empathy into account.

*Table 4.1.* Descriptive statistics and sex differences for autistic traits, empathy, alexithymia and interoceptive sensibility of non-ASD participants (Study 2)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Mean (*SD*) |  |  | Mann-Whitney *U* | Mean (*SD*) |  | Mann-Whitney *U* |
|  | Overall | Men (n = 69) | Women (n = 109) |  | Low autistic traits | High autistic traits |  |
| Autistic traits (AQ) | 16.2 (5.4) | 17.0 (5.4) | 15.7 (5.4) | 3180 | 12.2 (3.0) | 20.1 (3.5) | 0\*\*\* |
| Empathy (QCAE) | 91.5 (9.6) | 90.9 (9.2) | 91.8 (9.9) | 3603.5 | 93.3 (8.4) | 89.4 (10.5) | 3044\*\* |
| Cognitive empathy | 59.9 (9.1) | 60.4 (9.0) | 59.6 (9.3) | 3599.5 | 61.44 (8.2) | 58.1 (9.9) | 3073.5\* |
| Affective empathy | 30.4 (3.8) | 29.0 (3.7) | 31.3 (3.5) | 2454.5\*\*\* | 30.8 (3.7) | 29.9 (3.8) | 3396 |
| Alexithymia (TAS-20) | 48.6 (11.0) | 48.5 (9.8) | 48.7 (11.8) | 3709.5 | 45.7 (11.2) | 52.2 (9.8) | 2561\*\*\* |
| Interoceptive sensibility (MAIA) |  |  |  |  |  |  |  |
| Noticing | 3.16 (1.0) | 3.24 (1.0) | 3.11 (1.0) | 3594 | 3.24 (1.0) | 3.10 (1.0) | 3469 |
| Not-Distracting | 2.23 (1.0) | 2.23 (1.0) | 2.23 (1.0) | 3726 | 2.22 (1.0) | 2.25 (1.0) | 3866.5 |
| Not-Worrying | 2.41 (0.9) | 2.66 (0.9) | 2.26 (0.9) | 2881\*\* | 2.34 (0.9) | 2.50 (0.9) | 3543.5 |
| Attention Regulation | 2.79 (0.8) | 2.82 (0.9) | 2.78 (0.9) | 3635 | 2.89 (0.9) | 2.69 (0.8) | 3328 |
| Emotional Awareness | 1.78 (0.7) | 1.82 (0.8) | 1.74 (0.6) | 3586 | 1.75 (0.7) | 1.81 (0.7) | 3749.5 |
| Self Regulation | 1.94 (0.8) | 2.07 (0.9) | 1.86 (0.8) | 3246.5 | 2.07 (0.8) | 1.79 (0.9) | 3149.5\* |
| Body Listening | 2.0 (1.3) | 2.11 (1.3) | 1.92 (1.2) | 3505.5 | 1.98 (1.2) | 2.01 (1.3) | 3863 |
| Trusting | 2.82 (1.1) | 2.87 (1.0) | 2.78 (1.1) | 3650 | 3.01 (1.0) | 2.56 (1.1) | 3105.5\* |

Note: \* *p* < .05; \*\* *p* < .01; \*\*\* *p* < .001

*Table 4.2.* Relationships between autistic traits (AQ), empathy (QCAE), alexithymia (TAS-20) and the dimensions of interoceptive sensibility (MAIA), Study 2

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| r (β) |  |  |  |  |
|  |  | Autistic traits | Empathy | Alexithymia |
| Autistic traits |  |  | -.26\*\*\* | .42\*\*\* |
| Empathy |  | -.26\*\*\* |  | -.31\*\*\* |
| Alexithymia |  | .42\*\*\* | -.31\*\*\* |  |
| Interoceptive sensibility (MAIA) |  |  |  |  |
| Noticing |  | -.10 (.04) | .36\*\*\* (.34\*\*\*) | -.19\* (-.12) |
| Not-Distracting |  | .05 (.05) | -.11 (-.15) | -.04 (-.10) |
| Not-Worrying |  | .03 (.03) | -.08 (-.15) | -12.5 (-.20\*) |
| Attention Regulation |  | -.18\* (-.02) | .33\*\*\* (.29\*\*\*) | -.24\*\* (-.15) |
| Emotional Awareness |  | .08 (.11) | .07 (.16) | .03 (.04) |
| Self Regulation |  | -.28\*\*\* (-.19\*) | .25\*\* (.17\*) | -.27\*\*\* (-14) |
| Body Listening |  | -.06 (-.02) | .30\*\*\* (.30\*\*\*) | -.04 (.06) |
| Trusting |  | -.21\*\* (-.12) | .12 (.04) | -.26\*\*\* (-.21\*) |

Note: \* *p* < .05; \*\* *p* < .01; \*\*\* *p* < .001

*r*(β): correlation coefficient *r,* and Beta-value in multiple regression with autistic traits, empathy and alexithymia as simultaneous predictor variables and each dimension of the MAIA as outcome variable.

## **4.4 Discussion Study 2**

Participants without ASD completed four questionnaires measuring interoceptive sensibility, autistic traits, empathy, and alexithymia, in order to assess the relationships between those factors. Results showed that there are significant small to moderate correlations between all of the factors. As expected, the relationship between autistic traits and empathy was negative: participants with higher autistic traits scored lower on the empathy questionnaire. Interestingly, there was a trend for participants with high autistic traits to score significantly lower on cognitive empathy, but not on affective empathy, than participants with low autistic traits (not significant after correction of the alpha level for multiple comparisons). This echoes a pattern also found in autistic participants: cognitive empathy has been found to be impaired in ASD, whilst affective empathy appears to be intact (Blair, 2005; Dziobek et al., 2008; Rueda et al., 2014). Moreover, the relationship between alexithymia and autistic traits was positive in this non-autistic sample; participants with higher autistic traits tended to also score higher on the alexithymia questionnaire. And as expected, participants with higher alexithymia tended to score lower on empathy. Furthermore, interoceptive sensibility was correlated with autistic traits, empathy and alexithymia on several dimensions. Interestingly, two dimensions of interoceptive sensibility were related to all three other variables. Participants with higher levels higher levels of self regulation (the ability to regulate distress by attending to and regulating bodily responses) and attention regulation (the ability to attend to bodily sensations when they are competing with other stimuli) tended to have lower autistic traits, lower empathy and higher alexithymia. Of interest is also the direction of association that can be observed in the significant relationships: Interoceptive sensibility was positively related to empathy, but negatively related to autistic traits and alexithymia. For some dimensions of interoceptive sensibility, this relationship remained even when controlling for the other character traits; when ruling out shared variance between autistic traits, alexithymia and empathy as an explanation. This suggests that interoceptive sensibility contributes to empathy independently from what it contributes to autistic traits independently and alexithymia independently.

These results cautiously suggest that the ‘alexithymia hypothesis’ of autism (Bird & Cook, 2013; Brewer et al., 2015) and the ‘oxytocin-interoception system’ hypothesis of autism (Quattrocki & Friston, 2014) may both be correct, and are perhaps not mutually exclusive. The ‘alexithymia hypothesis’ proposes that emotional deficits in autism (including reduced empathy) are better explained by alexithymia than autism (Bird & Cook, 2013). The ‘oxytocin-interoception system’ hypothesis proposes that, amongst other sensory, autonomic, cognitive and behavioural effects, reduced levels of oxytocin in infancy cause an impaired ability to associate interoceptive signals with exteroceptive stimuli, particularly socially important ones. This results in difficulties to acquire a generative model of an emotional and social ‘self’, which may set the autistic infant off on a path of reduced learning (and consequent altered brain development) about emotions and social communication (Quattrocki & Friston, 2014).

The learning aspect is implicitly captured in the SOME (Bird, Geoffrey & Viding, 2014 – see appendix 1) which supposes many direct and indirect, as well as reciprocal relationships between the constituting systems that collectively generate empathy. The affective representation system can be influenced and influences the ToM system and the situation understanding system, and vice versa. Affective cues (bodily sensations) feed into all three other systems (affective representation system, ToM system and the situation understanding system) directly and indirectly, and can itself be triggered by the situation understanding system. In other words, there is more than one pathway to understanding (and learning about) other people’s emotions and experiencing empathy. The authors propose that alexithymia is caused by a malfunction in the affective representation system, while in autism the ToM system is primarily compromised (Bird & Viding, 2014). This accords with the finding that participants high in autistic traits have lower cognitive empathy (which arguably is a form of ToM where the inferred mental state of others pertains to the emotions of others) but unaffected affective empathy. However, because the systems influence each other, empathy may be affected when any system is not functioning optimally in some people. In this respect, the model suggests a way how interoceptive sensibility may ultimately affect the ToM system: affective cues (bodily sensations) feed into the ToM system directly, and indirectly via the situation understanding system and via the affective representation system. Reduced interoceptive sensibility may affect empathy in ASD even in the absence of alexithymia, and these pathways may therefore explain the correlation between interoceptive sensibility and autistic traits as well as the correlation between interoceptive sensibility and alexithymia. Furthermore, one might expect individuals with ASD and co-occurring alexithymia to have greater difficulty with generating empathy than those who only have one of the conditions. Study 3 was designed to further investigate the relationships between interoception, alexithymia and empathy in an autistic sample.

## **4.5. Methods Study 3**

### **4.5.1. Participants**

Fifty-two participants (14 female) took part in the study, of which 26 (7 female) had previously received a diagnosis of high functioning autism or Asperger syndrome by a clinician independent from the current study. Participants received a financial compensation for their time, or course credit for participation. A diagnosis of high functioning autism or Asperger’s syndrome was accepted for inclusion in the ASD group. Twenty-three participants with ASD attended an Autism Diagnostic Observation Schedule (ADOS) diagnostic interview (Lord et al., 2000) with a psychologist trained in the use of ADOS (second supervisor SS) to confirm their diagnosis of ASD. They all met the diagnostic criteria for ASD according to ADOS guidelines. Written, informed consent was obtained from all participants and the study was approved by the ethics panel at the Faculty of Science and Technology, Anglia Ruskin University.

 All participants completed the Autism Quotient questionnaire (Baron-Cohen et al., 2001). The participants for whom we were unable to obtain ADOS diagnostic results for scored well above the screening cut-off point of 32 on the AQ. The two groups were matched on sex (7 female and 19 male in each group), and on IQ (*t* (50) = 0.83, *p* = .41) measured with the Wechsler Abbreviated Intelligence Scale, 2nd edition (Wechsler, 2011), and on age (*t* (50) = 0.15, *p* = .88). Five participants with ASD reported a diagnosis of co-morbid anxiety or mood disorder. None of the members of the control group reported any mental disorders. See Table 4.3 for demographic data.

*Table 4.3.* Group demographics

|  |  |  |
| --- | --- | --- |
| Measure, Mean (SD) | ASD | Non-ASD |
| Age | 25.9 (7.3) | 25.4 (7.6) |
| FSIQ-2 | 113.8 (12.0) | 110.9 (13.5) |
| AQ | 31.1 (9.3) | 16.7 (6.4) |

*Note*. FSIQ-2 – Wechsler Abbreviated Scale of Intelligence (2-subtest version);

AQ – Autism Quotient

### **4.5.2. Materials**

##### **(i) Alexithymia measure**

Participants completed the 20 item Toronto Alexithymia Scale (TAS-20 – (Bagby et al., 1994), which assesses alexithymia. See Chapter 2 for a description (Parker, Taylor, & Bagby, 2003).

##### **(ii) Empathy measures**

Empathy was measured in two ways: with a behavioural measure of affective empathy and an empathy questionnaire designed to measure affective and cognitive empathy separately. The Questionnaire of Cognitive and Affective Empathy (QCAE - Reniers et al., 2011) assesses cognitive empathy, defined as “the ability to construct a working model of the emotional states of others”, and affective empathy, defined as “the ability to be sensitive to and vicariously experience the feelings of others” (Reniers et al., 2011). See Chapter 2 for a description of the questionnaire.

 The English core version of the Multifaceted Empathy Test (MET - Dziobek et al., 2008) provided a behavioural measure of affective empathy. This version consists of 40 images displaying an individual in an emotional state in a naturalistic environment, which were presented one by one on a 17” computer screen using E-prime 2.0 software (Psychology Software Tools, Pittsburgh, PA). The emotions shown varied in valence and intensity, and the individuals depicted varied in age, gender and ethnicity. The emotions displayed were complex (e.g. desperate, relieved, content) rather than simple (angry, happy, sad). Participants completed two tasks: In one task participants were asked to infer the emotion the person depicted is experiencing by choosing one of four words that best described the emotion displayed. A list with synonyms and an example sentence for each of the mental state words used in the task was available to the participant to consult if they were unsure of the meaning of a word. The second task (measuring affective empathy) was to indicate on a scale of 1 to 9 how much they empathized with the person depicted, with empathizing being defined as feeling the same emotion as the one the person on the screen is showing. The keyboard was used for entering responses. The pictures were shown in random order in eight blocks of ten, and the blocks alternated between emotion recognition and empathizing.

##### **(iii) Interoceptive tasks**

The accuracy with which participants perceived their heartbeat was measured. There are two widely used heartbeat perception tasks: one tasks measures the performance at heartbeat discrimination and the other at heartbeat tracking. At the time this study was designed, no research into interoception in ASD had been published, and there is still no consensus in the field as to which is a better measure of interoception; both have their advantages and disadvantages and measure interoception in somewhat different ways (Jones, 1994). The tracking task requires internal monitoring of heartbeats over short time intervals which may be affected by by time estimation ability and beliefs about heart rates (Knoll & Hodapp, 1992; Ring, Brener, Knapp, & Mailloux, 2015; Wittmann, 2013), whereas the discrimination task requires cross-sensory matching of the timing of internal and external events (Brener & Kluvitse, 1988). Nevertheless, both tasks are widely regarded as measuring interoceptive accuracy (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015; Ring & Brener, 2018) and so it is not inconceivable that they should be complementary in the present study. It was difficult to predict, however, at which of the two measures participants with ASD would perform differently (if at all), so both tasks were employed.

During the heartbeat tracking task (Schandry, 1981) the participant was seated upright, and was asked to count their own heartbeat and indicate how many heartbeats had occurred during a specific short time interval, whilst their heartbeat was recorded by an electrocardiogram (ECG). To this end, participant had three disposable surface electrodes with conductive hydrogel attached to their chest, and cardiac activity was relayed through shielded wires to the Powerlab Data Acquisition unit (AD Instruments, Germany) connected to PC, which recorded the activity with a sample frequency of 1000 Hz. There were 4 trials of 25, 35, 45 and 55 seconds, presented in random order. Participants were asked not to take their pulse and they did not receive any feedback on their performance

 A second measure of interoceptive accuracy - a version of the heartbeat discrimination task (Whitehead, Drescher, Heiman, & Blackwell, 1977) - was also administered. This version was previously used by Piech and colleagues (Piech et al., 2017). During this task, ECG provided the input for in-house developed ExpyVR software (http://lnco.epfl.ch/expyvr), which produced a brief auditory tone triggered by the R-wave of the ECG in the synchronous condition, or it produced brief tones at a speed of either 80% or 120% of the frequency of the participant’s preceding two R-waves to create the asynchronous condition. Participants were exposed to 20 tones per [synchronous or asynchronous] trial and indicated after each trial whether they thought the tones were in time with their heartbeat or not in time. Four synchronous trials and four asynchronous trials (two faster and two slower than the participant’s heartbeat) were administered in random order. Again, participants were not allowed to take their pulse during the task and no feedback was given on the participant’s performance. The order of the two heartbeat tasks was counterbalanced across participants.

 Subjective interoceptive sensibility was measured with the 32-item Multidimensional Assessment of Interoceptive Awareness questionnaire (MAIA - (Mehling et al., 2012), see further details in Chapter 2.

##### **(iv) Automatic facial mimicry**

Two disposable 1 cm Ag/AgCl electrodes with conductive hydrogel were attached 1 cm apart to the participant’s left cheek, two immediately above the left eyebrow, and one to the central forehead near the hairline (ground) (cf.Fridlund & Cacioppo, 1986). Muscle activity was relayed through shielded wires to the Powerlab Data Acquisition unit connected to a PC, which continuously recorded the activity with a sample frequency of 2000 Hz, a high-pass filter of 10 Hz, a low-pass filter of 500 Hz and a mains filter of 50 Hz. The raw EMG signal was rectified and integrated with a time constant of 100ms by the application Chart for Windows (AD Instruments, Germany).

Participants were then seated in front of a computer monitor and were told they were going to be shown a series of pictures of faces displaying an emotion. The stimulus material for this task consisted of the faces of 5 white male and 5 white female individuals chosen randomly from the Karolinska Directed Emotional Faces database (KDEF – Lundqvist, Flykt, & Öhman, 1998) in the happy and angry emotional expression, creating 20 trials. The presentation of the faces was controlled by E-prime 2.0 software. The faces were presented one by one for a duration of 6 seconds on a 17” monitor, with a random inter-stimulus interval of 8, 10 or 12 seconds. During the inter-stimulus interval a fixation cross was presented centrally on the screen. 3 seconds before the presentation of the face a 500ms beep was sounded to alert the participant to the upcoming presentation. There were 2 blocks of 5 happy faces and 2 blocks of 5 angry faces. Happy and angry blocks were alternated and the order counterbalanced across participants. Within the blocks the faces were presented in a random order. Before the experiment started participants were asked to simply look at the face while it was on the screen and informed that no active response was required in this task.

### **4.5.3. Data Analysis**

Differences between groups were analysed with two-tailed independent *t*-tests (Controls-ASD) or with one-way Anovas (Controls/ASD non-alexithymia/ASD alexithymia). Spearman correlations were conducted between the relevant variables.

##### **(i) Alexithymia**

A comparison between TAS-20 scores of ASD participants were conducted using a 2-tailed *t-*test. Spearman correlation analyses between TAS-20 scores and the empathy measures were conducted. The ASD group was split into participants with and without alexithymia, according to the high alexithymia cut-off score of 62 (Bagby et al., 1994), for the analyses investigating the effect of alexithymia on empathy.

##### **(ii) Empathy measures**

A 2 x 2 (empathy type x ASD status) mixed Anova and a 2 x 3 (empathy type x ASD-alexithymia status) mixed Anova was used to investigate differences in empathy between groups on the QCAE data. Post-hoc two-tailed *t*-tests were conducted, where appropriate, with the alpha-level adjusted to .017.

##### **(iii) Interoceptive tasks**

One participant with ASD was excluded from the analyses for interoceptive accuracy due to not following instructions. For the heartbeat tracking task an accuracy score was calculated using the formula Interoceptive Accuracy = {⅟₄ Σ [1 - (|recorded heartbeats – counted heartbeats|/recorded heartbeats)]} as in Schandry, 1981. Accuracy scores of the heartbeat discrimination task were calculated as percentage correct.

The MAIA has 8 subscales that provide a profile of interoceptive sensibility and is not intended to provide a summated score of IA (Mehling et al., 2012). Multidimensional scaling of the MAIA responses was undertaken, using the PROXCAL algorithm in SPSS, in order to reduce the 8 dimensions of the MAIA and increase power. Multidimensional scaling is a way of mapping clusters of responses in a two-dimensional space, with the distance representing correlations between them, which may also be interpreted as the extent of similarity between the dimensions.

##### **(iv) Automatic facial mimicry**

Off-line, for each trial, a baseline of EMG activity was established by calculating the mean activity of 10 epochs of 100ms immediately preceding stimulus onset. EMG activity in the 2000ms immediately following stimulus onset was also calculated in 100ms epochs. Activity change was calculated for each 100ms epoch by subtracting the baseline from the post-stimulus activity. To be able to compare data across sites and to minimise the effect of personal differences in reactivity, the data was log transformed and standardised. Trials with extreme activity that was due to voluntary movement (yawning, swallowing, talking, etc.) or electrical artefacts were removed. Less than 5% of the trials were removed. The data of two participants (one with ASD and one without ASD) were excluded due to having more than 50% of trials of at least one emotion showing signs of voluntary movement or electrical artefacts. Additionally, the corrugator trials of one participant with ASD suffered from equipment malfunction, and the data of another participant with ASD was excluded, as they had not followed procedures during recording.

Post-stimulus activity was analysed in terms of total activity, peak activity (defined as highest level of activity in a 100ms epoch from 300ms post-stimulus onwards followed by a decline in activity of at least 0.1 Z) and peak latency (the epoch in which the peak occurred) (Oberman, Winkielman, & Ramachandran, 2009).

Automatic imitation data will be analysed using two 2 x 2 x 2 mixed Anovas (muscle x emotion x ASD status for the first 1000ms and the second 1000ms) and Spearman correlations with interoception and empathy measures will be conducted.

##### **(v) Relationships between interoception, alexithymia and empathy, and the role of ASD**

If correlations are found between any of the interoception measures and alexithymia, and alexithymia and the empathy measures, a mediation analysis will be conducted using PROCESS (Hayes, 2013) in SPSS, using a multiple regression approach. The relevant interoception measure will be entered as predictor in a mediation model, alexithymia will be entered as the mediator, and empathy as the outcome variable. In a separate analysis, ASD status will be entered as a moderating variable in the relationship between interoception and alexithymia. If the moderated mediation proved significant, it would mean that there was an interaction effect of ASD; the relationship of interoception with alexithymia would be different for participants with ASD than for control participants.

With PROCESS it is possible to enter a single predictor variable as well as multiple predictors, making it possible to examine the relationship of each MAIA cluster with alexithymia and empathy whilst taking the other clusters into account, effectively using a multiple regression approach. Mediation by alexithymia is qualified as a significant indirect effect of interoception on empathy, i.e. via alexithymia. The indirect effect of of the predictor(s) on empathy via alexithymia is quantified as the product (*ab*) of two effects: the direct effect of the predictor(s) on alexithymia (*a*) and the direct effect of alexithymia on empathy (*b*). Whilst controlling for the direct effect of the predictor(s) on empathy (c’), the effect *a* is estimated as the regression coefficient predicting alexithymia from the predictors, and the effect *b* is estimated as the regression coefficient predicting empathy scores from alexithymia. There may or may not be a significant direct effect (*c’*) of interoception on alexithymia as well, which would indicate a relationship traditionally thought of as partial or full mediation respectively.

PROCESS uses confidence intervals generated by bootstrapping (repeated replacement and resampling from the dataset) to produce inferential statistics (see Hayes, 2013 for more information). 95% confidence intervals that do not include zero indicate that the effect is likely a real effect (different from zero) and significant at the .05 alpha level. Because the indirect effect is a product, it is not necessary that both effects *a* and *b* should be significant for the indirect effect *ab* to be significant, although often this will be the case.

## **4.6****. Results Study 3**

### **4.6.1. Alexithymia**

Only two individuals without ASD reached the high alexithymia cut-off point of 62 (Bagby et al., 1994), whereas 13 individuals from the ASD group (50%) had scores of 62 or above. ASD participants scored significantly higher on alexithymia (M = 59.5, SD = 15.9) than control participants (M = 46.2, SD = 11.1) on the TAS-20 questionnaire, *t* (50) = 3.51, *p* = .001. In further analyses where a distinction is made between ASD participants with alexithymia and ASD participants without alexithymia, the two control participants with alexithymia were excluded from the control group.

Alexithymia scores showed a moderate negative correlation with MET affective empathy scores (*r* = -.46, *p* < .001), and a strong negative correlation with QCAE scores (*r* = -.58, *p* < .001). The two subscales of the QCAE (cognitive and affective empathy) both correlated negatively with alexithymia: QCAE cognitive *r* = -.57, *p* < .001 and QCAE affective *r* = -.40, *p* = .003.

### **4.6.2. Empathy measures**

For the QCAE, there was a significant between-subjects effect of ASD status, F (1, 50) = 15.96, *p* < .001, indicating that ASD participants (M = 72.6, SD = 16.3) scored significantly lower on the total QCAE scores than control participants (M = 89.1, SD = 13.3). An interaction effect of ASD status and empathy type, *F* (1,50) = 16.27, *p* < .001, indicated a different effect per empathy type depending on ASD status. On cognitive empathy, ASD participants scored significantly lower (M = 43.1, SD = 12.6) than the control participants (M = 58.0, SD = 5.8), *t* (50) = 4.35, *p* < .001, d = 1.20, but the affective empathy scores did not significantly differ between groups (ASD M = 29.5, SD = 5.8; controls M = 32.1, SD = 5.0), *t* (50) = 1.74, *p* = .09, d = 0.48.

A 2 x 3 mixed Anova showed a significant between-subjects effect, *F* (2, 47) = 16.77, *p* < .001, indicating differences between the control participants, ASD participants without alexithymia and ASD participants with alexithymia. An interaction effect of empathy x group, *F* (2, 47) = 12.34, *p* < .001, indicated that differences between groups were different for the two empathy types. ASD participants with alexithymia had significantly lower affective empathy on the QCAE (M = 26.9. SD = 5.7) compared to the control group (M = 32.0, SD = 5.1), *t* (35) = 2.78, *p* = .009, d= 0.94, and lower affective empathy (approaching significance) compared to ASD participants without alexithymia, *t* (24) = 2.48, *p* = .02, d = 0.97, although the effect size is large and non-significance may be attributed to the small sample size (n = 13). There was no difference in affective empathy between ASD participants without alexithymia (M = 32.1, SD = 4.8) and the control participants, *t* (35) = .02, *p* = .98, d = 0.01. On cognitive empathy, ASD participants with alexithymia scored significantly lower (M = 36.0, SD = 10.97) than control participants (M = 57.5, SD = 10.4), *t* (35) = 5.90, *p* < .001, d = 2.00, and lower than ASD participants without alexithymia (M = 50.2, SD = 10.0), *t* (24) = 3.43, *p* = .002, d = 1.34. ASD participants without alexithymia scored lower on cognitive empathy than the control participants, *t* (35) = 2.09, *p* = .04, d = 0.71, approaching the Bonferroni-corrected significance level of .017. The effect size is medium to large. See Figure 4.1.

There were ASD participants and control participants showed similar levels of empathizing in levels of affective empathy as measured by the MET (ASD M = 4.6, SD = 1.7; controls M = 5.0, SD = 1.8), *t* (50) = 0.84, *p* = .40, d = 0.23). Accounting for the alexithymia status in the ASD group, a significant difference between groups, *F* (2, 47) = 4.05, *p* = .03, was found. ASD participants with alexithymia scored significantly lower than ASD participants without alexithymia, (ASD M = 3.7, SD = 1.5) *t* (24) = 2.97, *p* = .007, d = 1.16, who scored similar to control participants without alexithymia, (ASD M = 5.5, SD = 1.5, controls M = 5.1, SD = 1.8), *t* (35) = 0.66, *p* = .51, d = 0.22. See Figure 4.1.

ASD participants were equally accurate at identifying an emotion displayed on the screen (M = 0.67, SD = 0.08) as the control participants (M = 0.67, SD = 0.1), *t* (50) = 0.12, *p* = .91, d = 0.03, in the MET emotion recognition task, in the MET emotion recognition task. Alexithymia status of the ASD participants did not alter these results, *F* (2, 47) = 0.17, *p* = .84.

*Figure 4.1.* Scores on the empathy measures – the cognitive empathy subscale and the affective empathy subscale of the QCAE and scores on the MET affective empathy task – for control participants, ASD participants without alexithymia and ASD participants with alexithymia. Error bars denote 1 standard error. \**p* < .05

### **4.6.3. Interoceptive tasks**

### **Interoceptive accuracy**

Statistical checks (independent two-tailed *t*-tests) were made to ensure there was no significant difference in heart rate or Body Mass Index between ASD participants and control participants. Nor were there any significant correlations between heart rate and autistic traits, and BMI and performance. Only on the heartbeat tracking task was there a trend towards participants with higher BMI to be less accurate in tracking, *r* (46) = -.24, *p* = .07.

 There was no significant difference in the accuracy scores for the heartbeat discrimination task between ASD participants (M = 0.56, SD = 0.17) and control participants (M =0.62, SD = 0.19), *t* (49) = 0.86, *p* = .39, *d* = 0.24. There was however a significant difference between the two groups on the heartbeat tracking task, with ASD participants being less accurate (M = 0.63, SD = 0.21) than control participants (M = 0.74, SD = 0.15), *t* (42.8) = 2.10, *p* = 0.04, *d* = 0.58. See Figure 4.2.

The scores of the heartbeat discrimination task and the heartbeat tracking task did not correlate, *r* (49) = 0.10, *p* = .49. A strong correlation between the two is often cited (Knoll & Hodapp, 1992), but is not always found in studies (e.g. (Schulz, Lass-Hennemann, Sütterlin, Schächinger, & Vögele, 2013). Sometimes a strong correlation is found only in the best performing participants (Schaefer, Egloff, & Witthöft, 2012). Indeed, this was the case here. The performances in both heartbeat tasks correlated strongly only for those with good heartbeat discrimination scores (based on a median split), *r* (9) = .70, *p* = .02.

There were no significant correlations between the interoceptive accuracy measures and empathy measures or alexithymia, see Table 4.4.

*Figure 4.2.* Interoceptive accuracy for control participants and ASD participants, measured by two heartbeat tasks. Error bars denote standard error. \**p* < .05

##### **ii. Interoceptive sensibility**

Multidimensional scaling analyses showed three clusters of MAIA dimensions (see Figure 3.3) could be identified and named, 2 (normalised raw stress = 0.035):

1. Awareness (noticing and meta-awareness of bodily sensations), which includes the MAIA dimensions of trusting, emotional awareness and noticing.
2. Active and reactive strategies with regard to bodily sensations, which includes the dimensions of not-distracting, not-worrying, self-regulation and body listening
3. Attention regulation, which is the ability to pay attention to the body in an environment of competing stimuli.



*Figure 4.3*. Two-dimensional map of the multidimensional scaling of the MAIA dimensions. The symbols indicate the three clusters of dimensions: Active and reactive strategies (triangles); Awareness (circles); Attention regulation (square).

ASD participants scored significantly lower on MAIA awareness and MAIA active and reactive strategies than control participants, but there was no significant difference on MAIA attention regulation, see Table 3.4 for all p-values. After Bonferroni correction of the alpha level to *p* = .0014, MAIA awareness had strong negative correlations with autistic traits (AQ) and alexithymia (TAS20), strong positive correlations with QCAE total scores and QCAE cognitive empathy scores, and a moderate positive correlation with MET empathizing scores. There was a moderate negative correlation of MAIA active and reactive strategies with autistic traits and a strong negative correlation with alexithymia scores, see Table 4.4.

*Table 4.4.*

Correlations between interoceptive measures and autistic traits (AQ), alexithymia (TAS-20) and empathy measures (MET and QCAE)*.*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Measure | AQ | TAS20 | MET accuracy | MET empathizing | QCAE total | QCAE cognitive empathy | QCAE affective empathy |
|  |  |  |  |  |  |  |  |
| Heartbeat tracking 1 | -0.04 | 0.14 | 0.04 | -0.14 | 0.03 | 0.15 | -0.17 |
| Heartbeat detection  | -0.29\* | -0.10 | -0.17 | 0.11 | 0.16 | 0.13 | 0.17 |
| MAIA awareness | -0.57\*\*\* | -0.57\*\*\* | 0.01 | 0.45\*\*\* | 0.56\*\*\* | 0.56\*\*\* | 0.33\* |
| MAIA strategies | -0.44\*\*\* | -0.57\*\*\* | -0.26 | 0.23 | 0.27\* | 0.33\* | 0.03 |
| MAIA attention regulation | -0.34\* | -0.36\*\* | -0.09 | -0.09 | 0.22 | -0.31\* | 0.10 |

1 Correlations were controlled for Body Mass Index

Note: \* *p* ≤.05. \*\**p* ≤ .01. \*\* *p*\*\*\**p* < .001.

In order to identify the relative magnitude of the relationship of alexithymia and autistic traits with interoceptive sensibility, partial correlations were carried out. After Bonferroni correction of the alpha level to *p* = .025, these showed that the relationship with between MAIA awareness and AQ scores was no longer significant after controlling for alexithymia, *r* = -0.28, *p* = .03, as was the relationship of MAIA active and reactive strategies and AQ, *r* = -0.10, *p* = .49. However the relationship between MAIA alexithymia was no longer significant either after controlling for AQ, *r* = -0.28, *p* = .05. On the other hand, the relationship between MAIA active and reactive strategies and alexithymia was still significant after controlling for AQ, *r* = -0.38, *p* = .005.

### **4.6.4 Automatic facial mimicry**

Two 2 x 2 x 2 mixed Anovas (emotion x muscle x ASD status) were performed on mean activity, one for each time window. This showed, as expected, a significant interaction of muscle and emotion in the first 1000ms, *F* (1, 46) = 7.66, *p* = .008, ɳp2 = .14, as well as in the second 1000ms, *F* (46, 1) = 13.43, *p* = .001, ɳp2 = .23, was found, suggesting that the activity per muscle was different depending on the emotion. Zygomaticus major activity was significantly greater after viewing happy faces than after viewing angry faces in both the first 1000ms, *t* (46) = 6.59, *p =* .005, d = 1.90, and the second 1000ms, *t* (48) = 2.4, *p* = .018, d = 0.69. On the other hand corrugator supercilii activity was significantly greater after seeing angry faces than after seeing happy faces in the second 1000ms, *t* (47) = 3.35, *p* = .002, d = 0.97, although not in the first 1000ms, *t* (47) = 1.02m, *p* = .31, d = .30. There was no interaction with ASD status in the first 1000ms time window, *F* (1, 46) = .29, *p* = .29, ɳp2 = .006, nor in the second 1000ms time window, *F* (1, 46) = .03, *p* = .88, ɳp2 = .01, suggesting that ASD participants showed the same pattern of activation as control participants, see Figure 4.4 and 4.5.

The mean peak activity of the corrugator supercilii muscle after exposure to an angry face was not significantly different between ASD participants (M = 2.2, SD = 1.84) and control participants (M = 1.79, SD = 2.4), *t* (46) = 1.62, p = .12, d = 0.47, nor was the mean epoch in which the peak occurred (ASD M = 12.4, SD = 3.7, non-ASD M = 11.22, SD = 5.05), *t* (46) = 0.93, p = .36, d = 0.27. Similarly, the mean peak activity of the zygomaticus major muscle after exposure to a happy face was not significantly different between ASD participants (M = 2.05, SD = 1.84) and control participants (M = 1.79, SD = 2.41), *t* (47) = 0.43, p = .67, d = 0.13, nor was the mean epoch in which the peak occurred (ASD M = 12.1, SD = 3.70, non-ASD M = 10.1, SD = 4.3), *t* (47) = 1.74, p = .09, d = 0.49.

 There were no significant correlations between the interoceptive measures of heartbeat tracking, heartbeat discrimination, MAIA attention regulation, MAIA active and reactive strategies, MAIA awareness on the one hand, and the EMG measures of peak latency, peak amplitude and EMG activity in the first 1000ms and EMG activity in the second 1000ms on the other hand. The EMG measures were neither related to autistic traits, nor to alexithymia scores.

Only zygomaticus major activity in the second 1000ms after exposure to a happy face was correlated with QCAE affective empathy scores, *r* (47) = .36, *p* = .01, which does not survive a Bonferroni correction of the alpha-level to .004.

*Figure 4.4.* Mean zygomaticus EMG activity change (Z-score in log µV/s) compared to baseline after seeing a happy face, for ASD and non-ASD participants, from stimulus onset to 2000ms post-stimulus onset.

*Figure 4.5*. Mean corrugator EMG activity change (Z-score in log µV/s) compared to baseline after seeing an angry face, for ASD and non-ASD participants, from stimulus onset to 2000ms post-stimulus onset.

### **4.6.5. Relationships between interoception, alexithymia and empathy, and the role of ASD**

No conditional process analyses or mediation analyses were conducted with interoceptive accuracy as predictor variable, due to the absence of significant correlations of interoceptive accuracy with alexithymia and empathy.

Mediation analyses using PROCESS (Hayes, 2013) in SPSS was conducted with the three MAIA clusters entered as predictor variables (using a multiple regression approach), alexithymia as a mediator and total QCAE score as the dependent variable, using a multiple regression approach. The analysis showed that both MAIA awareness and MAIA active and reactive strategies contribute significantly to alexithymia, while MAIA attention regulation does not contribute to alexithymia after taking the other MAIA clusters into account (see the regression coeffients *a1 , a2* , and *a3* in Table 4.5). Alexithymia contributes significantly to QCAE scores (see regression coefficient *b* in Table 3.5). This indicates that participants with lower MAIA awareness demonstrate higher alexithymia levels (negative coefficients *a1* and *a2*), and in turn participants with higher alexithymia levels tended to have lower QCAE (negative coefficient *b*). The indirect path (*ab*) of the effects of MAIA awareness and MAIA active and reactive strategies via alexithymia on QCAE scores was significant. The three MAIA clusters explain 32 percent of the variance in QCAE empathy scores. See Table 3.5 for the coefficients of the paths.

The same analysis was conducted to look at the effects of the MAIA clusters on behavioural affective empathy scores (MET empathy) through alexithymia, see Table 3.6. Similar to the effects of MAIA clusters on QCAE scores, this showed that the indirect effect of MAIA awareness through alexithymia to MET empathy was significant, as was the indirect effect of MAIA Active/Reactive strategies. The effect of MAIA attention regulation on MET empathy was not mediated through alexithymia after taking the other MAIA clusters into account. The three MAIA clusters explain 34 percent of the variance in MET empathy scores.

To answer the question of whether the path from interoceptive awareness to understanding oneself to understanding others is different in participants with ASD, a conditional process analysis was carried out (Hayes, 2013). ASD status was introduced as a moderator of the indirect path (see Figure 6), testing the hypothesis that the strength of the indirect effect of MAIA scores on empathy through alexithymia depends on whether one has ASD or not. Only the indirect effect of MAIA Active and reactive strategies on QCAE and MET empathy scores via alexithymia were moderated by ASD status (index of moderated mediation QCAE = 2.08, CI = 0.275 - 4.558; index of moderated mediation MET empathy = 0.177, CI = .028 - 0.408). This means that the increase in alexithymia due to higher active and reactive strategies scores is significantly larger for ASD participants compared to control participants, (ΔR2 = .05, *F* (1, 47) = 4.03, *p* = .05). Therefore, the final model of the relationship between the clusters of the MAIA, ASD, alexithymia and empathy can be visualised as in Figure 4.6.

*Table 4.5***.** Coefficients of the direct (*c’*) and indirect path (*a* and *b*) of the effect of self-reported interoceptive awareness (MAIA clusters)

on self-reported empathy (QCAE) through alexithymia.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | Consequent |  |  |  |  |  |  |
|  |  | *M* (TAS20) |  |  |  |  | *Y (QCAE)* |  |  |  |
| Antecedent |  | Coeff. | SE | *p* |  | Coeff. | SE | *p* | *ab*LLCI | *ab*ULCI |
|  |  |  |  |  |  |  |  |  |  |  |
| Awareness | *a1* | -2.417 | 0.69 | .0010 | *c’1* | 2.170 | 0.86 | .015 | 0.42 | 2.65 |
| Active/Reactive Strategies | *a2* | -2.876 | 0.83 | .0012 | *c’2* | -0.72 | 1.03 | .488 | 0.53 | 2.83 |
| Attention regulation | *a3* | 0.159 | 0.78 | .839 | *c’3* | -.353 | 0.86 | .684 | -0.70 | 0.57 |
| *M* (TAS20) |  |  |  |  | *b* | -.49 | 0.16 | .004 |  |  |
| Constant | *i1* | 99.72 | 7.75 | < .0001 | *i2* | 95.66 | 18.27 | < .0001 |  |  |
|  |  |  |  |  |  |  |  |  | Total effects: |
|  |  |  | *R2* =.474 |  |  | *R2* = .434 |  |  | *R2* = 0.320 |
|  |  |  | *F* (3, 47) = 14.09*p* < .0001 |  |  | F (4, 46) = 8.80, *p* < .0001 |  |  | F (3, 47) = 7.37, *p* = .0004 |

*Table 4.6***.** Coefficients of the direct (*c’*) and indirect path (*a* and *b*) of the effect of self-reported interoceptive awareness (MAIA clusters)

on affective empathy (MET scores) through alexithymia.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | Consequent |  |  |  |  |  |  |
|  |  | *M* (TAS20) |  |  |  |  | *Y (METempathy)* |  |  |  |
| Antecedent |  | Coeff. | SE | *p* |  | Coeff. | SE | *p* | *ab*LLCI | *ab*ULCI |
|  |  |  |  |  |  |  |  |  |  |  |
| Awareness | *a1* | -2.417 | 0.69 | .0010 | *c’1* | 0.283 | 0.10 | .006 | 0.248 | 0.272 |
| Active/Reactive Strategies | *a2* | -2.876 | 0.83 | .0012 | *c’2* | 0.075 | 0.12 | .531 | 0.020 | 0.267 |
| Attention regulation | *a3* | 0.159 | 0.78 | .839 | *c’3* | -0.31 | 0.10 | .003 | -0.069 | 0.054 |
| *M* (TAS20) |  |  |  |  | *b* | -.039 | 0.019 | .0431 |  |  |
| Constant | *i1* | 99.72 | 7.75 | < .0001 | *i2* | 5.05 | 2.19 | < .0001 |  |  |
|  |  |  |  |  |  |  |  |  | Total effects: |
|  |  |  | *R2* =.474 |  |  | *R2* = .402 |  |  | *R2* = 0.344 |
|  |  |  | *F* (3,47) = 14.09*p* < .0001 |  |  | F (4, 46) = 7.72, *p* = .0001 |  |  | F (3, 46) = 8.27, *p* = .0002 |



*Figure 4.6***.** Shows the final model of the relationships between the MAIA clusters and empathy, mediated by alexithymia, in which the indirect effect of MAIA active and reactive strategies on empathy via alexithymia is moderated by ASD status and is dependent on the level of active and reactive strategies. MAIA attention regulation did not significantly predict empathy levels whilst taking the other two MAIA clusters into account, and has been controlled for in the mediation analyses. Dotted lines show non-significant regression coefficients after taking the other variables into account*.*

## **4.7. Discussion Study 3**

The study sought to investigate links between interoceptive processing, alexithymia and empathy in participants with ASD. The findings suggest that interoceptive processing is attenuated in ASD participants compared to control participants, since the former were less accurate at tracking their own heartbeat and showed lower self-reported interoceptive awareness. This is in line with the results reported in Chapter 3. Contrary to expectations, interoceptive accuracy and automatic facial mimicry were not related to alexithymia and empathy. However, interoceptive sensibility was found to be related to autistic traits, alexithymia and empathy. Interoceptive sensibility contributed to empathy levels indirectly, through inverse relationships with alexithymia, suggesting that greater awareness of one’s own bodily sensations (measured via the MAIA questionnaire) the better one may be able to identify and describe one’s own emotions (measured via TAS20 score), the higher the empathy for others’ emotions. It appears then, that the level of subjective awareness and appraisal of one’s bodily feelings and emotions is more important for empathy than is basic sensitivity to one’s bodily processes. These findings can be argued to support Bird and Viding’s SOME (2014), which proposes that representations of one’s own emotions are integral to empathy. The ability to accurately *recognise* another’s emotion, often regarded as a measure of cognitive empathy (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001; Baron-Cohen & Wheelwright, 2004; Demurie et al., 2011; Golan & Baron-Cohen, 2006), was not related to interoceptive accuracy, interoceptive sensibility or alexithymia in this sample.

A difference in interoceptive accuracy was shown between the groups in one of the two heartbeat perception tasks. On average, control participants were better at tracking their own heartbeat, but there was no difference between groups in the heartbeat discrimination task. The heartbeat discrimination task is thought to be less susceptible to confounds, such as prior knowledge about heart rate, but a disadvantage of the heartbeat discrimination task is that most individuals (including current participants) perform close to chance level, resulting in a lower variance in performance across a sample (Knapp-Kline & Kline, 2005; Phillips, Jones, Rieger, & Snell, 1999). The heartbeat discrimination task relies on the discrimination of two stimuli from different modalities: one auditory and one interoceptive, and requires a temporal comparison for a judgment of synchronicity. In contrast, the heartbeat tracking task demands attention to only one (interoceptive) modality and no synchronicity judgement is required. These different demands of these tasks on sensory processing and on attention may contribute to the different results in the two tasks in this study. A dissociation between performance on the two tasks has been found before, with different populations (Kandasamy et al., 2016; Schulz et al., 2013). Performance on the heartbeat tracking task has shown to be related to performance on a time estimation task (Meissner & Wittmann, 2011), suggesting that the ability to estimate time or sustain attention may influence heartbeat tracking accuracy. However, subsequent research with ASD participants did not replicate this relationship (Shah et al., 2016a), nor did controlling for it alter the observed relationship between heartbeat tracking and alexithymia. Time estimation was not measured and could therefore not be controlled for, but based on the research of Shah and colleagues it appears that time estimation is not always a confounding variable.

The investigations into the relationships between the measured variables showed that, in line with the findings reported in chapter 3, there was no correlation between interoceptive accuracy and the empathy measures. In contrast, Grynberg and Pollatos (2015) found that interoceptive accuracy measured by the heartbeat tracking task was predictive of the level of self-reported arousal, compassion and estimated intensity of depicted pain, in response to viewing pictures of persons in painful and non-painful situation. As such, empathy was measured as empathy to pain only, which may elicit stronger feelings in the empathic observer than our stimuli, and/or only empathy accompanied by strong bodily sensations is measurably related to interoceptive accuracy, which might explain the divergent results. In support of this null-results, another study on healthy adults that measured heartbeat tracking and empathy (via the QCAE) also found no correlation between the two (Ainley, Maister, & Tsakiris, 2015).

In line with Fiene and Brownlow (2015) and qualitative studies that have reported on sensory sensitivity to sensations like hunger, temperature, and thirst (Elwin, Ek, Schröder, & Kjellin, 2012; Elwin, Ek, Kjellin, & Schröder, 2013), self-reported interoceptive awareness (measured with the MAIA questionnaire) was found to be lower for ASD participants, in two of the three clusters (comprising 7 of the 8 subscales of the MAIA): the cluster that measured noticing and meta-awareness of bodily sensations, and the cluster that measured active and reactive strategies towards bodily sensations, which encompasses self regulation of bodily feelings and the tendencies to not worry about and to not distract from bodily feelings. There was no difference between groups for MAIA attention regulation. This is in contrast to the finding reported in chapter 2, which showed reduced MAIA attention regulation in the ASD participants compared to controls, but no significant impairment in MAIA noticing. It is possible that the clustering of the MAIA dimensions in this study was successful in increasing the power to find a difference between groups, and that the power to find a difference per dimension is limited. The exploratory Study 2 with its greater number of participants showed an interesting trend in participants with high and low autistic traits in this respect: Here there was a trend (non-significant after Bonferroni correction) of individuals with high autistic traits to have lower scores on attention regulation. This trend would be in line with the study reported in chapter 2.

When taking into account the alexithymia status of the participants, this showed that ASD participants with alexithymia had lower MAIA scores than those without alexithymia in two of the three MAIA clusters. This supports the recent findings by Shah and colleagues (Shah, Hall, Catmur, & Bird, 2016; Shah et al., 2016a) that alexithymia and interoception are related, whereas interoception and autistic traits may not be. The partial correlation performed to tease out the relative relationships of autistic traits confirmed this interpretation in the case of MAIA active and reactive strategies: after controlling for alexithymia, the relationship with autistic traits was no longer significant, while the relationship with alexithymia remained significant even after controlling for autistic traits. This could not be confirmed for MAIA awareness however, where autistic traits remained significantly related to MAIA awareness after controlling for alexithymia, and vice versa. Whether this is due to our participant groups not being matched on alexithymia is hard to establish, but cannot be ruled out. Having matched groups on alexithymia would allow for a better assessment of whether the effects of alexithymia shown in the ASD population are also seen in the typical population.

 None of the MAIA clusters correlated significantly with the heartbeat perception tasks, something that was also observed in chapter 3. This confirms the view that that the experience of bodily sensations does not necessarily reflect one’s sensitivity to them (Cameron, 2001; Ceunen, Van Diest, & Vlaeyen, 2013; Garfinkel et al., 2015). This is in line with previous studies (Garfinkel et al., 2016; Garfinkel et al., 2015; Khalsa et al., 2008). These studies, as well as the ones presented here and in chapter 3, therefore reinforce the notion that in the investigation of interoceptive processes a distinction should be made between the physiological states of the body, the conscious feelings that accompany these states, and metacognition of these states (Critchley & Harrison, 2013; Damasio, 2000; Garfinkel & Critchley, 2013; Garfinkel et al., 2015; Lambie & Marcel, 2002).

The finding that ASD participants have overall lower empathy levels than participants without ASD supports previous findings (e.g., (Baron-Cohen & Wheelwright, 2004; Greimel et al., 2010; Johnson, Filliter, & Murphy, 2009). When cognitive and affective empathy were separately examined, only cognitive empathy (inferring the emotions of others) was found to be lower in ASD participants; affective empathy (the sharing of the emotions of others) was at the same level as found for control participants, in line with recent findings (Blair, 2005; Dziobek et al., 2008; Jones, Happé, Gilbert, Burnett, & Viding, 2010; Rogers et al., 2007; Rueda et al., 2014). This result was corroborated by data from the affective empathy behavioural task: there was no difference between ASD participants and controls when they were asked how much they felt the same emotion as the people shown on the monitor. This shows that a description of ASD as an empathy disorder (Gillberg, 1992) is not entirely correct, and difficulties in emotional and social functioning are more likely to reflect a deficit in the cognitive domain rather than the affective domain ((Bachevalier & Loveland, 2006). Notably, another psychiatric condition often characterised by an empathy deficit, psychopathy, shows the opposite pattern of empathic ability: intact cognitive empathy but weak affective empathy (Jones et al., 2010; Lockwood, Bird, Bridge, & Viding, 2013).

Previous research has suggested that inconsistent findings with regard to empathy levels in participants with ASD might be explained by variations in alexithymia levels among participants (Bird & Cook, 2013; Bird et al., 2010; Silani et al., 2008). Confirming this, it was found that both cognitive and affective empathy levels of the ASD participants with co-morbid alexithymia were lower than those of control participants, whereas in ASD participants without alexithymia only cognitive empathy was affected; they had similar levels of affective empathy to control participants, on both behavioural and self-reported measures. Given the high prevalence of alexithymia amongst ASD participants (here 50% - in line with earlier findings, e.g. Hill et al., 2004), there may be large subset of individuals with ASD whose experience of emotions (their own and those of others) is qualitatively different from other individuals with ASD. Furthermore, this research suggests that these individuals may have reduced access to associative learning mechanisms between interoceptive signals, their emotions and others’ emotions (Bird, Geoffrey & Viding, 2014; Murphy, Brewer, Catmur, & Bird, 2017; Quattrocki & Friston, 2014), which means that interoceptive training to accompany social and/or emotional learning for these individuals could be helpful (Bornemann & Singer, 2017; Gaigg, Cornell, & Bird, 2018; Livingston & Livingston, 2016; Shah et al., 2016). This may be a valuable insight for anyone who deals with people with ASD, from parents to teachers to therapists and is a topic that clearly warrants further research.

Conditional process analyses showed that alexithymia played a mediating role between IA and empathy, and that this relationship is partly moderated by autistic status. The indirect path, i.e. the association of IA with empathy via alexithymia, explained around a third of the variance in empathy scores. Specifically, lower scores on the MAIA clusters of awareness, and active and reactive strategies, both contributed to higher alexithymia (TAS-20) scores. Higher levels of alexithymia were in turn related to lower levels of empathy, in line with earlier findings (Grynberg et al., 2010; Guttman & Laporte, 2002).

ASD status did not moderate the relationship between the cluster of ‘awareness’ and alexithymia, but it did moderate the relationship between the cluster of ‘active and reactive strategies’ and alexithymia: If a participant had ASD, the relationship between ‘active and reactive strategies’ and alexithymia was significantly stronger than if a participant did not have ASD. The attitudinal and regulatory dimensions of IA may be more consequential for individuals with ASD than for individuals without ASD. Resulting higher levels of alexithymia and lower levels of empathy may be related to more difficulties in social functioning and emotion regulation (Garfinkel et al., 2016; Pollatos & Ferentzi, 2018; Swart, Kortekaas, & Aleman, 2009), and may affect other aspects of self-referenced cognition (Cameron, 2001; Northoff et al., 2006) and mental health (Khalsa et al., 2018; Murphy et al., 2017). For example, excessive focus on and a numbing of bodily sensations have been related to maladaptive self-referenced processing contributing to anxiety and depression respectively (Dunn et al., 2010; Paulus & Stein, 2010). Both disorders are also associated with higher alexithymia levels (Marchesi, Brusamonti, & Maggini, 2000; Paulus & Stein, 2010) and are common co-occurring conditions of ASD (Skokauskas & Gallagher, 2010).

However, some caution must be exercised with this possible interpretation for two reasons. The difference in the mediating effect of alexithymia between the ASD participants and control participants may be caused by the lack of variance in alexithymia in the control group; the number of control participants with high alexithymia levels did not match the number of ASD participants with high alexithymia. The observed moderation effect also seems to be in contradiction to the result of the partial correlations that show that the relationship between MAIA active and reactive strategies and alexithymia to be robust when controlling for autistic traits, while the relationship between MAIA active and reactive strategies and autistic traits became non-significant when controlling for alexithymia. Similarly, two recent studies in which alexithymia levels between groups was matched, found that severity of autistic traits was not related to interoceptive accuracy, whereas alexithymia was related to interoceptive accuracy (Shah et al., 2016; Shah, Catmur, & Bird, 2016). Secondly, five of the ASD participants reported co-occurring emotion disorders (depression or anxiety), three of which had high alexithymia. This cannot be excluded as a second possible explanation for the different effect in the ASD group, as levels of anxiety or depression were not measured. An inability to control for levels of anxiety or depression is a limitation of this study.

Results showed that both participants with ASD and control participants engaged in automatic mirroring of the facial expressions they were observing. Taking into account baseline activation, both groups activated the muscles of the brow (frowning) more than the muscles of the cheek when exposed to an angry face, and the muscles of the cheek (smiling) more than the muscles of the brow when exposed to a happy face, and the level of activation of the two groups was similar. This was contrary to expectations. Some previous research with ASD participants found that the facial stimuli presented caused activation of both sets of muscles to a similar extent irrespective of the emotion displayed, instead of an emotion specific activation (McIntosh, Reichmann‐Decker, Winkielman, & Wilbarger, 2006). Undifferentiated activation was also reported in response to fearful faces (Rozga, King, Vuduc, & Robins, 2013), in response to subliminally presented emotional stimuli (Mathersul, McDonald, & Rushby, 2013b) and in children with ASD (Beall, Moody, McIntosh, Hepburn, & Reed, 2008). The latter found that with age, emotion-typical activation increased. Other studies have found typical levels of mimicry in adults with ASD in response to happy and angry faces (Mathersul, McDonald, & Rushby, 2013a; Oberman et al., 2009; Rozga et al., 2013) and children with ASD (Deschamps, Coppes, Kenemans, Schutter, & Matthys, 2013). One study found that their adult high-functioning ASD group had stronger emotion-typical muscle activation than the control group for happy and fearful faces when this was accompanied by matching auditory stimuli (Magnée, De Gelder, Van Engeland, & Kemner, 2007). These divergent results could be due to slightly different methods of presenting stimuli and calculations of activity. Although the EMG experiment did not have any additional demand, perhaps it’s possible that the other tasks had drawn attention to the emotional content of the stimuli and empathy as a subject of study. If this is the case, it shows that ASD participants are capable of mimicry if motivated to pay attention to emotional content.

 In this sample, there was no difference between groups in peak latency, nor in peak amplitude of the EMG activity. Previous research has shown a latency difference between children with ASD and children without ASD, where children with ASD showed a slightly delayed peak response compared to children without ASD (Oberman et al., 2009). This was not replicated with this sample of adults with high functioning ASD. No relationship was found between the total activation in the first 1000ms, peak amplitude or peak latency of the mimicry on the one hand and autistic traits, alexithymia and empathy measures on the other. In the second 1000ms time window after exposure to a happy face, individuals with stronger zygomaticus major activity tended to have higher self-reported empathy. However, this time window is arguably not reflecting *automatic* imitation, which is thought to occur very quickly after exposure to an emotional face, ie. within the first 1000ms (Dimberg, 1982; Dimberg, Thunberg, & Elmehed, 2000). The second 1000ms was mainly included as way to test a possible delayed response in the ASD group, following Oberman and colleagues (2009), although activity in this time window may reflect voluntary movements of the facial muscles in reaction to the stimuli.

According to simulation theory, mimicry may induce a representation of the observed emotion in brain, with accompanying somatic responses, which aids the understanding of the emotion and empathic feelings (Keysers & Gazzola, 2009) This could imply that individuals who have a stronger mimicry response would have a stronger representation of the emotion in the brain, which could increase their empathy. However, the hypothesis regarding a relationship between the magnitude or timing of automatic imitation and empathy levels was not supported by the results of this study.

In conclusion, these studies have found evidence of the role of several aspects of interoceptive sensibility in empathy, such that higher interoceptive sensibility is related to higher levels of both cognitive and affective empathy. Study 3 showed that this relationship was mediated by alexithymia, which has an inverse relationship with both interoceptive awareness and empathy. Based on the results it appears that the magnitude of a psycho-physiological process such as automatic mimicry, or mere sensitivity to one’s heartbeat does not, or is not sufficient, to explain individual differences in understanding one’s own emotions or empathy. This study suggests that cognitive processes contributing to the subjective experience of bodily feelings contributes to that link, which is supportive of Bird and Viding’s SOME and the role of its ‘affective representation system’ (Bird, Geoffrey & Viding, 2014).

It was found that participants with high functioning ASD have lower interoceptive sensitivity and lower interoceptive awareness than participants without ASD. However, it is proved difficult to unequivocally establish whether the relationship between interoceptive sensibility and alexithymia is unique to autism or also occurs in the typical population, because the control group in Study 3 lacked individuals with high alexithymia. Despite this, this research contributes to the growing evidence that within the ASD population there is a large subgroup of individuals with high levels of alexithymia (Hill et al., 2004). These individuals have lower levels of cognitive and affective empathy than the typical population and individuals with ASD without alexithymia. The present and related recent findings may therefore impact on ASD diagnosis since they show the potential importance of distinguishing between symptoms and characteristics that are linked to ASD and those that are linked to alexithymia. Finally, a focus on interoceptive training and in particular, promoting a beneficial (mindful) attentional style towards bodily sensations may be fruitful avenues for future research.

# Chapter 5

# Multisensory bodily self-consciousness and peripersonal space

# in ASD**[[2]](#footnote-2)**

## **5.1. Introduction**

Autism has long been described as a disorder of self (Asperger & Frith, 1991; Frith, 2003; Kanner, 1943). Many studies have shown altered self processsing in ASD, for example, weaker auto-biographical memory (Crane & Goddard, 2008) and self-referenced memory (Henderson et al., 2009), deficits in emotional self-awareness (Hill, Berthoz, & Frith, 2004), lower recognition and display of ‘self-conscious’ emotions (Heerey, Keltner, & Capps, 2003), atypical use of personal pronouns (Lee, Hobson, & Chiat, 1994), and impairments in other aspects of self-referential cognition (Lombardo, Barnes, Wheelwright, & Baron-Cohen, 2007; Mundy, Gwaltney, & Henderson, 2010; Gillespie‐Smith, Ballantyne, Branigan, Turk, & Cunningham, 2017).

At the root of a cognitively ‘higher level’ sense of self is a more basic, non-conceptual sense of self that is grounded in neural representations of the body (Bermúdez, 2018; Damasio, 2012). Some representations and mappings of the body arising from interoceptive signals may be manifested as visceral sensations and emotions (Craig, 2009; Damasio, 2012). In the previous chapters it was shown that there are differences between participants with ASD and without ASD in dimensions of interoception. However, exteroceptive modalities also contribute to representations of the body in the brain (Blanke, 2012; Botvinick & Cohen, 1998). Specifically, bodily self-consciousness – the feeling that we exist as and within a body that we own and control, which takes up space, and provides the first-person perspective from which we experience the world (Blanke, 2012; Maselli & Slater, 2013; Serino et al., 2013) - emerges from the integration of sensory signals, within and across different modalities (Blanke, 2012; Botvinick & Cohen, 1998), exteroceptive and interoceptive (Aspell et al., 2013). Surprisingly, given the above-mentioned differences in higher level self processing, the bodily self in ASD has received little research attention to date. This chapter reports on a study that investigated multisensory bodily self-consciousness and peri-personal space in ASD using multisensory experimental paradigms, and embodied perspective taking.

The bodily self has been extensively studied using different paradigms in which multisensory conflicts are used to manipulate bodily self-consciousness, resulting in changes of body ownership and self-location, i.e., the rubber hand illusion and full body illusion (Botvinick & Cohen, 1998; Ehrsson, 2007; Lenggenhager, Tadi, Metzinger, & Blanke, 2007), and audio-tactile integration tasks that measure peripersonal space (PPS; Canzoneri et al., 2013; Serino et al., 2013; Serino et al., 2018)). Supported by studies that show that PPS and FBI arise from multisensory integration processes (Aspell, Palluel, & Blanke, 2012; Avillac, Deneve, Olivier, Pouget, & Duhamel, 2005; Bernasconi et al., 2018), these experiments importantly suggest that the bodily self is flexible and malleable. For example, in the rubber hand illusion (RHI), participants are asked to look at a dummy hand, which is positioned next to the participant’s hand on the table. The hand of the participant is kept out of sight. Subsequently, feeling one’s own hand being brushed and seeing a dummy hand being brushed in synchrony, elicits the illusion that their own hand is located closer to the dummy hand, and can make participants feel as if the dummy hand is their hand (i.e., change in body-part ownership). Similarly, in the full body illusion (FBI), viewing a virtual body being stroked whilst feeling synchronous stroking on one’s own body, results in a feeling of ownership for (self-identification with), referral of touch to and a drift in self-location towards the virtual body (Aspell, Lenggenhager, & Blanke, 2009; Lenggenhager et al., 2007). Recently, it has also been shown that peripersonal space (PPS) - the space immediately around the body, which mediates our interaction with external objects that come within reach or should be avoided -(Rizzolatti, Fadiga, Fogassi, & Gallese, 1997) - is extended towards the virtual body during the FBI, confirming that the PPS is ‘the space of the bodily self’ (Noel, Pfeiffer, Blanke, & Serino, 2015; Salomon et al., 2017; Riva, 2018; Rizzolatti et al., 1997).

Differentiation between self and other underlies the development of social interaction, through the representation of self and an other who is distinct yet similar (Decety & Chaminade, 2003; Gallagher & Meltzoff, 1996; Neisser, 1991; Palmer & Tsakiris, 2018). Indeed, in ASD, observed differences in the ‘higher level’ aspects of self may be related to some of the social deficits seen in ASD (Gillespie‐Smith, Ballantyne, Branigan, Turk, & Cunningham, 2017; Henderson et al., 2009; Lombardo et al., 2007). However, bodily self-consciousness in ASD and its possible relationship with impairments in social interaction have not been investigated.

Susceptibility to body illusions may be an indirect measure of the tendency to blur the distinction between self and other. People who tend to feel other people’s pain more easily are also more susceptible to the RHI (Derbyshire, Osborn, & Brown, 2013). Highly empathic persons show higher susceptibility to the RHI and experience more vicarious pain when a sharp object is administered to the rubber hand (Seiryte & Rusconi, 2015). Other multisensory illusion paradigms have shown that synchronous stroking of oneself and another can result in an increased perception of similarity with the other (Paladino, Mazzurega, Pavani, & Schubert, 2010; Tajadura-Jiménez, Grehl, & Tsakiris, 2012). The size of the PPS also appears to reflect the differentiation between self and other, as shown by the expansion of the PPS towards an other in social interactions (Cardellicchio, Sinigaglia, & Costantini, 2012; Teneggi, Canzoneri, di Pellegrino, & Serino, 2013), and even a remapping of another person’s PPS onto one’s own when sensory experiences are shared (Maister, Cardini, Zamariola, Serino, & Tsakiris, 2015). Finally, the ability to suspend the first-person perspective and adopt the perspective of another is essential for effective social interaction and communication (Duran, Dale, & Galati, 2016; Schober, 1993). Together, these results are supportive of the hypothesis that the multisensory representation of the body contributes to representations of self and other, and to social functioning, and suggest that altered bodily self-consciousness in ASD may underpin at least some of the social impairments seen in ASD.

Key aspects of bodily self-consciousness – self-identification with one’s entire body, self-location, and embodied first-person perspective (Blanke, 2012) – have not been researched in autism. To date, only three studies have investigated body ownership, in relation to body *parts*, using the RHI (Cascio, Foss-Feig, Burnette, Heacock, & Cosby, 2012; Paton, Hohwy, & Enticott, 2012) and the ‘numbness illusion’ (NI) in ASD (Guerra, Spoto, Parma, Straulino, & Castiello, 2017). Cascio and colleagues (2012) found that children with ASD required a much longer stroking duration for the illusion to establish, whilst Paton and colleagues (2012) found that both (adult) groups experienced the illusion, but the ASD group displayed reduced proprioceptive drift towards the rubber hand. Guerra and colleagues (2017) found that the NI occurred for ASD participants in both the synchronous and asynchronous conditions, whilst control participants only experienced it in the synchronous condition. The FBI, an illusion that manipulates body ownership (self-identification) and self-location, is arguably a more effective and conceptually appropriate way of investigating the bodily self than the RHI and NI - in which ownership of a single body part is altered - since one identifies one’s self with one’s whole body, rather than with a body part (Blanke & Metzinger, 2009), yet the FBI has not been investigated in ASD.

It has been shown that the FBI can also be elicited by the manipulation of interoceptive and exteroceptive (cardio-visual) integration (Aspell et al., 2013; Heydrich et al., 2018), suggesting that the representation of internal bodily processes (interoception) crucially contributes to the bodily self (Damasio, 2000). Following on from the studies reported in chapter 3 and 4, which confirmed previous evidence that a large proportion of individuals with ASD have impaired interoception (Fiene & Brownlow, 2015; Garfinkel et al., 2016; Palser, Fotopoulou, Pellicano, & Kilner, 2018; Schauder, Mash, Bryant, & Cascio, 2014; Shah, Hall, Catmur, & Bird, 2016; Shah, Catmur, & Bird, 2017), there is reason to suspect that people with ASD may have an altered bodily self. Additionally, given the reduced sensitivity to the RHI and the alterations in higher level aspects of self in ASD discussed previously, it is hypothesised that an altered bodily self may be expected to manifest as a reduced susceptibility to the FBI in ASD participants.

 PPS has also not been investigated in people with ASD before, although it has been suggested - based on previous results with the RHI (Cascio et al., 2012; Paton et al., 2012) that show reduced flexibility of the representation of the bodily self - that the PPS of individuals with ASD may be sharper and smaller than in the typical population (Noel, Cascio, Wallace, & Park, 2017). This might manifest as a steeper gradient from self to other: a reduced distance over which multisensory stimuli approaching PPS are integrated, reflecting less flexibility in the PPS when interacting with the external world (Noel et al., 2017). This is in line with reports of individuals with ASD having difficulty respecting the personal space of others (Kennedy & Adolphs, 2014) and as more likely to bump into, or approach other individuals too closely (Asada et al., 2016; Parsons, Mitchell, & Leonard, 2004). It may also be inferred from these behaviours that the size of their PPS is smaller than in typical individuals.

Lastly, bodily self-consciousness also comprises the first person perspective, the sense that we perceive the world from the perspective our body affords (Blanke, 2012). Humans also have a well developed ability to mentally adopt and understand anothers’ points of view. Spatial perspective taking is a cognitive process of inferring another person’s mind at a basic level, which involves mentally disembodying one’s own body, and embodying another’s (Arnold & Auvray, 2017; Kessler & Thomson, 2010). To measure embodied perspective taking, the graphesthesia task (Arnold & Auvray, 2017), which has not been used in conjunction with the FBI before, nor with an ASD sample, was used. This task investigates spontaneous perspective taking in reaction to a tactile stimulus: an ambiguous letter (e.g. the letter d, which is a mirror image of the letter b) traced (by a finger, or paintbrush) onto the body, usually the forehead. The participant can adopt a disembodied perspective to interpret the letter, i.e. taking the perspective of the experimenter to recognise the letter as a ‘d’, or an embodied perspective, interpreting the letter as a ‘b’, as if their forehead is a screen they look at from an ‘inner eye’ located behind their forehead. In the typical population, individuals predominantly adopt the embodied position to interpret the letter (Arnold, Spence, & Auvray, 2017). Although research on perspective taking in ASD is mixed (see Pearson, Ropar, & Hamilton, 2013 for a review), based on the apparent difficulty children with ASD and individuals with high autistic traits have in adjusting for angle in visual perspective taking (Brunyé et al., 2012; Hamilton, Brindley, & Frith, 2009; Tan & Harris, 1991), and based on the difficulty they have with embodying fake body parts (Cascio et al., 2012; Paton et al., 2012), the hypothesis was that they may be less prone than individuals without ASD to adopt a disembodied perspective.

To summarize, this chapter will report on a study that, for the first time, investigates multisensory bodily self -consciousness in individuals with ASD using the FBI, PPS and graphesthesia tasks. We expected to find evidence of altered bodily self-consciousness in individuals with ASD, manifesting as a reduced susceptibility to the FBI, a smaller PPS with steeper gradient, and a reduced tendency to choose a disembodied perspective. We also expected there would be a positive relationship between empathy and susceptibility to the FBI, supporting previous suggestions that the representation of the bodily self contributes to social functioning. Additionally, based on the literature outlined in previous chapters, the relationships of multisensory bodily self-consciousness (FBI and PPS) with alexithymia and interoceptive sensibility were analysed. It was expected that a reduced susceptibility to the FBI and a steeper gradient in the PPS would be related to reduced interoceptive sensibility and increased alexithymia.

## **5.2 Methods**

### **5.2.1. Participants**

Twenty-two participants with ASD and 29 participants without ASD, making a total of 51 participants (30 male), were recruited (mean age 27.1, age range 18-53), of whom 47 participants completed all parts and 4 (control) participants completed the PPS task only. Twenty-two participants had a formal diagnosis of ASD given by a clinician independent of this study (14 male, 8 female); 19 of these participants attended an ADOS diagnostic interview (Lord et al., 2000) with the second supervisor Dr Steven Stagg, and four met the threshold point for an autism spectrum diagnosis, while 15 met the threshold for autism. The three participants who were not able to attend the ADOS interview scored well above the ASD cut-off point of 32 on the AQ screening questionnaire (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). Participants were matched on age, ASD *M* (*SD*)= 27.0 (9.0); non-ASD *M* (*SD*) = 27.2 (6.7), *t* (49) = 0.11, *p* = 0.91), and IQ, (ASD *M* (*SD*)= 110.1 (13.0); non-ASD *M* (*SD*) = 112.7 (12.2), *t* (45) = 0.70, *p* = 0.49), as measured with the WASI II (Wechsler, 2011).

### **5.2.2. Materials and Procedure**

#### **5.2.2.1 Questionnaires**

All participants completed the Autism Quotient (Baron-Cohen et al., 2001) measuring autistic traits, the Toronto Alexithymia Scale (Bagby, Parker, & Taylor, 1994) measuring alexithymia, the Questionnaire of Affective and Cognitive Empathy (Reniers, Corcoran, Drake, Shryane, & Völlm, 2011) measuring empathy, and the Multidimensional Assessment of Interoceptive Awareness (MAIA - Mehling et al., 2012) measuring awareness of internal bodily sensations. The subscale ‘Noticing’, which measures awareness of comfortable, uncomfortable and neutral body sensations, and the subscale ‘Attention Regulation’, which measures the ability to sustain and control attention to body sensations when they are competing with exteroceptive signals, were the focus in the analyses.

#### **5.2.2.2. Full Body Illusion (FBI)**

Participants wore an Oculus Rift CV1 VR head mounted display (HMD) and were positioned 2.3m in front of a video camera in the body condition. In the object condition, participants stood 1.0m to the side of a tall cardboard box with a height and width similar to a person’s body. The box was positioned 2.3m in front of the camera, such that the participant was out of view of the camera. The HMD displayed the body of the participant from the back in the body conditions, or the box in the object conditions (see Figure 5.1).

Real body

Real object

A

Virtual body

Camera

2.3m

2.3m

Participant’s view

 through HMD

Participant’s view

 through HMD

Virtual object

Camera

B

*Figure 5.1.* FBI set-up for the body condition (A) and the object condition (B).

A custom-made program in Unity software was used to control the timing of the visual feed from the camera to the HMD. Four conditions were presented in random order: body synchronous, body asynchronous, object synchronous and object asynchronous. In the asynchronous conditions, the visual feed was delayed by 400ms, while there was no discernable delay (<50ms) in the synchronous condition). In the body conditions, the experimenter tapped and stroked the back of the participant for two minutes with a bamboo back scratcher. In the object conditions, the experimenter tapped and stroked the back of the participant and the cardboard box simultaneously in a spatially congruent manner for two minutes, using two bamboo back scratchers. The experimenter was out of view of the camera in all conditions. In each condition, at the end of the two minutes, participants were asked to close their eyes, and the HMD was taken off. They were guided by the experimenter to walk backwards by a distance of 1.5m in very small steps, and then asked to return to their original position in normal steps, while still keeping their eyes closed. The drift in self-location was measured as the distance in centimetres between the original position and the estimated position. The graphesthesia task was then administered (see below), and afterwards participants were guided to a desk (so as not to see their estimated location) where they could open their eyes and complete a questionnaire about the experience. The FBI questionnaire (Lenggenhager et al., 2007) contained seven statements with which participants could agree/disagree with on a seven point Likert scale from --- to +++. The midpoint was assigned zero. There were three illusion items, which rated touch perception (Q1 and Q2) and self-identification (Q3), and four control items (see Table 4.1). The order of the items was randomised to avoid order effects.

*Table 5.1.* FBI Questionnaire items. Q1, Q2 and Q3 are illusion items and Q4-Q7 are control items.

|  |  |
| --- | --- |
|  | StatementsDuring the experiment there were times when: |
| Q1 | It seemed as if I were feeling the touch of the stick in the location where I saw the virtual body touched. |
| Q2 | It seemed as though the touch I felt was caused by the stick touching the virtual body. |
| Q3 | It felt as if the virtual body was my body. |
| Q4 | It felt as if my (real) body was drifting towards the front (towards the virtual body). |
| Q5 | It seemed as if the touch I was feeling came from somewhere between my own body and the virtual body. |
| Q6  | It appeared (visually) as if the virtual body was drifting backwards (towards my body). |
| Q7 | It seemed as if I might have more than one body. |

#### **5.2.2.3. Peripersonal space**

Peripersonal space was measured prior to the FBI experiment – using an audiotactile integration task (Canzoneri, Magosso, & Serino, 2012). A custom-built small tapper attached to the right middle finger was used to administer a small tap (the drop of a 4mm magnet) to the finger. Participants were seated blindfolded in a chair and asked to respond as fast as possible to the tap by pressing a button with their left hand. Participants were told to ignore a sound (a pink noise) that was presented in each trial. This sound was emitted from two loudspeakers, one next to the participant’s right hand and one 1 m further away, on the same table. Automatic modulation of the volume of the sound through the two loudspeakers resulted in the impression of the sound moving towards them (Maister et al., 2015). Taps were administered at 300ms, 800ms, 1500ms, 2200ms and 2500ms after sound onset. Arduino board and LabView 8 (National Instruments, Austin, TX) software were used to control the sound, onset delay of the tap and recording of reaction times (RTs). There were 65 randomised trials in total, 10 for each onset delay, and 15 no-tap catch trials.

#### **5.2.2.4. Graphesthesia task**

After each condition of the FBI, after the self-location drift measurement, and while they still had their eyes closed, participants were told the following: “Here are two letters: a lower case ‘b’ and a lower case ‘d’. Which one do you experience?” A letter ‘d’ or ‘b’ was then traced on the participant’s forehead with a cotton bud. The experimenter noted down whether the answer given was from the participant’s perspective (embodied - e.g. if the experimenter traced a ‘b’ but the participant reported a ‘d’) or from the experimenter’s perspective (disembodied – if the experimenter traced a ‘b’ and the participant reported a ‘b’).

## **5.3. Results**

### **5.3.1. Empathy, Alexithymia and Interoception Questionnaires**

Non-ASD and ASD participants scored significantly higher on the questionnaires that measured autistic traits (AQ) and alexithymia (TAS20), and significantly lower on the questionnaires that measured empathy (QCAE), cognitive empathy (QCAEcog), and the MAIA subscale of attention regulation. No differences between groups were observed for affective empathy (QCAEaff) nor the other MAIA subscales, taking into account a Bonferroni corrected alpha level of .007 (see Table 5.2).

*Table 5.2.* Means, standard deviations and comparisons between groups of questionnaire responses measuring autistic traits (AQ), alexithymia (TAS-20), empathy (QCAE), cognitive empathy (subscale of QCAE), affective empathy (subscale of QCAE), and interoceptive sensibility (subscales of MAIA).

|  |  |  |  |
| --- | --- | --- | --- |
|  | Non-ASD | ASD | Difference |
| Measure | *M* (*SD*) | *M* (*SD*) | Mann-Whitney U | *p* |
| Autistic traits | 14.5 (5.8) | 33.3 (7.3) | 7.0 | < .001\* |
| Alexithymia | 43.9 (12.9) | 61.6 (11.4) | 90 | < .001\* |
| Empathy | 96.2 (10.2) | 73.9 (10.7) | 39.5 | < .001\* |
|  Cognitive empathy | 61.5 (8.2) | 40.9 (6.2) | 39 | < .001\* |
|  Affective empathy | 34.6 (4.4) | 33.0 (6.2) | 220.5 | .24 |
| MAIA noticing | 3.4 (0.9) | 2.7 (1.2) | 175.5 | .03 |
| MAIA attention regulation | 2.9 (0.7) | 2.0 (1.1) | 131 | .002\* |

Note: \* *p* < .007 (Bonferroni corrected alpha-level)

### **5.3.2. Full Body Illusion - Drift**

Participant’s drift in self-location was measured as the distance of the participant’s estimated self-location from the original position where they stood during the stroking. Subsequently, the difference in self-location drift between synchronous and asynchronous conditions was calculated by subtracting the drift in self-location of the participant in the asynchronous condition from the drift in self-location of the participant in the synchronous condition. The subtracted drift measurement was calculated because of the large variance between participants in the estimates: there were some participants who did not reach the original position in any condition, while there were other participants who passed the original position by quite some distance.

Participants without ASD showed an average subtracted (synch- asynch) self-location drift in body conditions of 12.8 cm (*SD* = 29.6). For ASD participants subtracted drift measurement for body conditions was 0.3 cm (*SD* = 16.1). In the object conditions, non-ASD participants’ subtracted drift measurement was -4.9 cm (*SD* = 5.4) whereas ASD participants’ subtracted drift measurement was 2.7 cm (*SD* = 8.2).

For the body condition the subtracted self-location drift measurement of non-ASD participants compared to that of ASD participants was significant, *t* (45) = 1.77, *p* = .04, while for the object conditions, the difference in the subtracted drift measurement between non-ASD participants and ASD participants was non-significant, *t* (45) = 0.80, *p* = .43. See Figure 5.2.

*Figure 5.2.* Subtracted drift (self-location in the asynchronous condition subtracted from self-location in the synchronous condition) for ASD participants and non-ASD participants in the body and object display conditions. \* p < .05. Error bars denote SE.

### **5.3.3.Full Body Illusion – questionnaire**

The scale of the questionnaire was transformed from --- to +++ into a scale from 1 to 7, with the ‘neutral’ mid-point acquiring a value of 4. For the analysis of the questionnaire scores, we assessed a possible response bias by calculating, per participant, an average score for the responses to the four control items for each condition, and we did the same for the three illusion items (as in, e.g. Ehrsson, 2007). For all main ANOVA analyses, the data was transformed using ARTool aligned rank transform software (Wobbrock Findlater, Gergle & Higgins, 2011) to be able to do nonparametric factorial analysis using ANOVA in SPSS and correctly assess interaction effects.

A four-way ANOVA (Question type x Synchrony x Display x ASD status) showed a main effect of Question type (illusion vs control), *F* (1, 45) = 92,27, *p* < .001, ηp2 = 0.67, a main effect of Synchrony, *F* (1, 45) = 15.80, *p* < .001, ηp2 = 0.26, a main effect of Display, *F* (1, 45) = 9.30, *p*  = .004, ηp2 = 0.17, and no main effect of ASD status, *F* (1, 45) = .09, *p* = .77, ηp2 = 0.002.

There were several significant interaction effects: an interaction effect of Question type and Synchrony *F* (1, 45) = 30.36, *p* < .001, ηp2 =0.40, an interaction effect of ASD status and Synchrony, *F* (1, 45) = 4.43, *p*  = .04, ηp2 = 0.09, and an interaction effect of Question type and Display, *F* (1, 45) = 11.51, *p*  = .001, ηp2 = 0.20. One three-way interaction, ASD x Question type x Synchrony, approached significance, *F* (1, 45) = 3.38, *p* = .07, ηp2 = 0.07. The remaining interactions were non-significant: Question type x ASD x Synchrony x Display, *F* (1, 45) = 1.63, *p* = .21, ηp2 =0.04; ASD x Synchrony x Display, *F* (1, 45) = .08, *p* = .79, ηp2 = 0.06, ASD x Question type, *F* (1, 45) = .02, *p* = 0.88, ηp2 < 0.001; ASD x Display, *F* ( 1, 45) = 1.35. *p* = .25, ηp2 = 0.03; ASD x Question type x Display *F* (1,45) = 0.003, *p* = .95, ηp2 < 0.001; Display x Synchrony, *F* (1,45) = 0.27, *p* = .61, ηp2 = 0.006.

In order to check for differences in response bias in the two groups, we conducted a 2 x 2 x 2 (ASD x Synchrony x Display) mixed Anova on the control questions only. This showed there was no significant main effect of ASD *F* (1, 45) = 0.95, ηp2 = 0.001, and no interaction of Display x ASD, *F* (1, 45) = 0.67, *p* = .57, ηp2 = 0.01, nor Synchrony x ASD, *F* (1, 45) = 0.16, *p* = .16, ηp2 = 0.004, nor a three-way interaction of Synchrony x Display x ASD, *F* (1, 45) = 0.14, *p =* .94, ηp2 = 0.003, indicating that the two groups responded in a similar way to the control questions and a correction for a response bias was unnecessary.

 Planned comparisons with Wilcoxon signed ranks tests showed that for the non-ASD participants, the average ratings for the illusion questions in the synchronous body condition was significantly higher, *M* (*SD*) = 5.53 (1.12), than in the asynchronous body condition, *M* (*SD*) = 3.97 (1.70), *Z* = 3.33, *p* = .001. On the other hand, ASD participants’ ratings in the synchronous body condition, *M* (*SD*) = 4.63 (1.64) were not significantly different from their ratings in the asynchronous body condition, *M* (*SD*) = 4.26 (1.64), *Z* = .64, *p* = .52. Concerning the average ratings for illusion items in the object conditions, non-ASD participants’ ratings were significantly higher in the synchronous condition, *M* (*SD*) = 4.4 (1.4) than the asynchronous condition, *M* (*SD*) = 3.1 (1.4), *Z* = 3.60, *p* = .001. ASD participants also had significantly higher scores in the synchronous condition *M* (*SD*) = 4.3 (2.0) than in the asynchronous condition, *M* (*SD*) = 3.5 (2.0), *Z* = 2.78, *p* = .005, in the object condition.

To further explore the data we examined differences in ratings for the ‘self-identification’ question, Q3 (‘It felt as if the body/object was my body’). Wilcoxon signed ranks tests were planned per group for Q3, comparing the synchronous vs asynchronous for the body and object. The alpha-level was Bonferroni corrected to 0.012.

In response to Q3 Wilcoxon signed ranks tests showed that the response of non-ASD participants in the synchronous body condition, *M* (*SD*) = 5.76 (1.39), was significantly higher than in the asynchronous body condition, *M* (*SD*) = 4.32 (2.10), *Z* = 3.07, *p* = .001. However, for ASD participants, the difference between the synchronous body condition, *M* (*SD*) = 3.86 (2.42) and the asynchronous body condition, *M* (*SD*) = 4.68 (2.01) was not significant, *Z* = 0.64, *p*  = .52. In the object conditions, non-ASD participants showed a significant difference, showing higher ratings in the synchronous condition *M* (*SD*) = 3.40 (2.24) than in the asynchronous condition, *M* (*SD*) = 2.40 (1.76), *Z* = 2.64, *p* = .008. In contrast, ASD participants showed similar levels of self-identification with the object in the synchronous condition *M* (*SD*) = 3.50 (2.58) as in the asynchronous condition *M* (*SD*) = 2.91 (2.16), *Z* = 1.08, *p* = .28 (see Figure 5.3).



*Figure 5.3.* Group medians (horizontal lines) and interquartile ranges of questionnaire responses to Q3 “It felt as if the virtual body/object was my body”. Whiskers denote 1st and 4th quartile range. \* p < .012 (Bonferroni corrected alpha level).

### **5.3.4. Peripersonal Space (PPS)**

Participants’ RTs were recorded per tapping delay after sound onset. Per participant, trials that were faster or slower than 2.5 SD of their average RT for that onset delay were removed. In total, fewer than 5% of all trials were removed. Additionally, the data of two control participants was rejected due to equipment malfunction.

A 2 x 5 mixed ANOVA, with ASD status (ASD vs non-ASD participants) as the between subjects factor, and Tap Delay after sound onset as the within subjects factor (300ms, 800ms, 1500ms, 2200ms, 2500ms) was run. Results revealed a significant main effect of Tap Delay, *F* (1, 47) = 25.51, *p* < .001, ηp2 = 0.35 and a significant main effect of ASD status, *F* (1, 47) = 7.11, *p* = .01, ηp2 = 0.13: ASD participants tended to have slower RTs than control participants and RTs tended to become faster with each consecutive delay (see Table 5.3). Importantly, a significant interaction ASD status x Tap Delay was found, *F* (1, 47) = 3.47, *p* = .04, ηp2 = 0.07, which means that the effect of Delay on RTs was different for each group. To test the robustness of the interaction effect specifically, we calculated log-transformed RT value and repeated the ANOVA with these new values. The interaction effect was borderline significant with the transformed date, *F* (1, 47) = 2.95, *p* = .05, ηp2 = 0.06.

To analyse this further, in each group, we ran four paired samples *t*-tests to compare RTs between each consecutive delay i.e. we compared RT at 300ms with RT at 800ms, RT at 800ms with RT at 1500ms etc. The alpha-level was Bonferroni corrected to *p* = .006 for multiple comparisons. For ASD participants, RTs at 1500ms were significantly faster than the RTs at 800ms, *t* (21) = 3.62, *p* = .002, but there was no significant difference between RTs at 300ms and 800ms, *t* (21) = 1.86, *p* = .08, between RTs at 1500 and 2200ms, *t* (21) = 2.49, *p* = .02, and between RTs at 2200ms and 2500ms, *t* (21) = 1.14, *p* = .27. For non-ASD participants, RTs at 800ms were significantly faster than RTs at 300ms, *t* (26) = 3.16, *p*  = .004, but there was no significant difference between RTs at 800ms and 1500ms, *t* (26) = 1.61, *p* = .12, between RTs at 1500 and 2200ms, *t* (26) = 0.82, *p* = .42, and between RTs at 2200ms and 2500ms, *t* (26) = 2.66, *p* = .01. This means that in the two groups, tactile processing is differently boosted by co-occurring dynamic sounds, with a facilitation effect of sound on RTs occurring between 800 and 1500ms for ASD participants, whereas for non-ASD participants the facilitation occurred between 300 and 800ms. See Figure 5.4. In this way, if we take the critical distance where the sound speeds up tactile RTs as a proxy of the PPS boundary (Canzoneri et al., 2012; Teneggi et al., 2013), we can conclude that the PPS size of ASD participants is smaller than that of non-ASD participants.

*Table 5.3.* Reaction time (in ms) at tap delay after sound onset, for ASD and control participants.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Tap Delay | 300ms*M* (*SD*) | 800ms*M* (*SD*) | 1500ms*M* (*SD*) | 2200ms*M* (*SD*) | 2500ms*M* (*SD*) |
| Non-ASD | 1109 (107) | 1070 (104) | 1043 (80) | 1037 (74) | 1017 (73) |
| ASD | 1272 (286) | 1220 (216) | 1147 (218) | 1112 (198) | 1093 (183) |

Using a MATLAB curve fitting tool, we fitted the data of the two groups to a linear function to assess if the slope of the PPS gradient as the sound approached was steeper for ASD participants than for control participants, as suggested by Noel and colleagues (2017). The linear function was described by the following equation: y(x)= y0 + kx, where x represents the tap delay, y the RT, y0  the intercept at x = 0, and k the slope of the function. After removing the data of individuals with a poor fit (adjusted R2 < 0.2, 6 participants in each group) the ASD linear equation could be described as y = 1340 – 0.11x, and the non-ASD linear equation could be described at y = 1142 – 0.05x. Importantly, the slope of the function was significantly different for the two groups, *t* (33) = 2.67, *p* = .01, with the slope of ASD participants being steeper (k = -0.11) than the slope of non-ASD participants (k = -.05). See Figure 5.4.



 *Figure 5.4.* Reaction time of participants in response to taps after sound onset. Dotted lines depict the linear function. Error bars denote 1SE. \* p < .006 (Bonferroni corrected alpha level)

### **5.3.5. Graphesthesia task**

Per group, the number and proportion of participants who responded as though adopting an embodied perspective with respect to the letter traced on the forehead were calculated per FBI condition (see Table 5.4).

Chi-Square test of independence showed no relationship between Synchrony and ASD status for the body condition χ2 (2, N= 54) = 0.004, *p* > .05, nor for the object condition, χ2 (2, N= 52) = .08, *p* > .05.

*Table 5.4.* Number and proportion of participants who chose the embodied perspective, per synchrony and display condition, for non-ASD and ASD participants.

|  |  |  |
| --- | --- | --- |
|  | Body  | Object  |
|  | Synch | Asynch | Synch | Asynch |
| Non-ASD | 14 (56%) | 15 (60%) | 14 (56%) | 15 (60%) |
| ASD | 12 (54%) | 13 (59%) | 12 (54%) | 11 (50%) |

### **5.3.6 Correlations**

Relationships between illusion strength, PPS slope and questionnaire measures of interoceptive awareness, autistic traits, empathy and alexithymia were investigated with Spearman correlations for the full sample of participants. Illusion strength – calculated as the subtracted score (synch – asynch) for Q3 (self-identification) in the body condition – showed a significant negative correlation with severity of autistic traits and a significant positive correlation with empathy. The latter was mainly driven by scores of the cognitive empathy subscale (see Table 5.5).There were no significant correlations between the PPS slope, nor of the subtracted self-location (synch – asynch) measurement in the body conditions with the two MAIA subscales, AQ, TAS-20, nor QCAE, all *ps* > .06. The subtracted score (synchronous-asynchronous) of the mean ratings for the aggregate of the Illusion Questions in the body condition did not correlate significantly with any of the questionnaires either, taking into account a Bonferroni corrected level of significance of .002.

*Table 5.5.* Spearman’s correlations and p-values of the subtracted FBI scores (synchronous – asynchronous) for self-location drift and combined illusion questions ratings in the body condition, Question 3 (self-identification), and PPS slope, with scores measuring autistic traits (AQ), alexithymia (TAS20) and empathy (QCAE) and interoceptive awareness (MAIA subscales)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Drift | Illusion Questions  | Q3 | PPS slope |
|  | *rho* | *p* |  *rho* | *p* | *rho* | *p* | *rho* | *p* |
| Autistic traits | 0.23 | .11 | -0.27 | .07 | -0.46 | .001\* | -0.10 | .51 |
| Alexithymia | -0.08 | .59 | -0.27 | .08 | -0.26 | .06 | -0.11 | .48 |
| Empathy | 0.26 | .08 | 0.37 | .01 | 0.49 | < .001\* | 0.05 | .75 |
|  Cognitive Empathy | 0.25 | .09 | 0.36 | .01 | 0.47 | < .001\* | 0.12 | .45 |
|  Affective Empathy | 0.07 | .64 | 0.13 | .37 | 0.18 | .22 | -0.19 | .20 |
| MAIA Noticing | -0.07 | .67 | 0.21 | .16 | 0.22 | .14 | -0.06 | .69 |
| MAIA Attention regulation | .11 | .46 | 0.18 | .23 | 0.27 | .07 | 0.12 | .44 |

Note: *\* p* < .002 (Bonferroni corrected alpha level)

To address the hypothesis that bodily self-consciousness may contribute to empathy, a stepwise multiple regression was conducted, with the predictor variables of autistic traits (AQ scores), alexithymia (TAS-20 scores), IQ scores and the scores of FBI self-identification (Q3), and with empathy scores (QCAE) as the dependent variable. This showed that autistic traits and FBI self-identification are significant predictors of empathy, *F* (2, 44) = 42.27, *p* < .001, explaining 66% of the variance of empathy. The relationship between autistic traits and empathy is negative, while the relationship between self-identification and empathy is positive. Alexithymia and IQ do not significantly explain any additional variance of empathy after the AQ and Q3 scores were modelled. See Table 4.6 for the regression co-efficients.

*Table 5.6*. Regression model showing the contributions of autistic traits (AQ) and FBI self-identification (Q3) to empathy (QCAE).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | B | *SE* B | *β* |
| Step 1 |  |  |  |  |
|  | Constant | 110.55 | 3.24 |  |
|  | AQ | -1.06 | 0.13 | -.78\*\*\* |
| Step 2 |  |  |  |  |
|  | Constant | 100.32 | 5.44 |  |
|  | AQ | -0.95 | 0.13 | -.71\*\*\* |
|  | Q3 | 1.58 | 0.69 | .22\* |

Note: \* *p* < .05; \*\*\**p* < .001

R2 = .62, *p* < .001 for Step 1. ΔR2  = .04, *p* = .03 for Step 2.

## 5.4. Discussion

In this study bodily self-consciousness, peripersonal space and embodied first person perpsective in ASD was investigated, by measuring responses to the full body illusion, the extent of PPS, and responses in the graphesthesia task. Overall the results show that individuals with ASD are much less susceptible to the FBI than are typical control participants. Consistent with this, the data also show that the PPS of ASD participants is smaller and shows a steeper gradient at its boundary, indicating a less flexible, more pronounced self-other distinction in ASD. The representation of the bodily self therefore seems to be less malleable in ASD participants and these ‘low-level’ differences in self may relate to (and partly underlie) the ability to empathise with others. We did however find no difference in embodied perspective taking between the groups. These findings support previous suggestions that ASD is a disorder of the self and support the hypothesis that self-representation in ASD is altered at its foundational levels.

 The FBI data show that agreement with illusion statements was significantly higher in synchronous than asynchronous body conditions in the non-ASD group – as found many times previously (e.g., Aspell et al., 2013; Cowie, McKenna, Bremner, & Aspell, 2017; Ionta et al., 2011; Lenggenhager et al., 2007) - but did not differ in the ASD group. Moreover, non-ASD participants showed signficantly greater self-identification with the virtual body in the synchronous condition and a greater self-location drift towards the virtual body during the synchronous condition, but this was not found for ASD participants. In keeping with this, findings include a strong and highly significant negative correlation of autistic traits with self-identification ratings.

 Surprisingly, non-ASD participants also responded with higher ratings after synchronous stroking on the summated illusion questionnaire items and on the self-identification item Q3, in the object condition. However, that the actual score of control participants in the object condition on Q3 indicated negative agreement with the statement (lower than 4 which equates to the zero/neutral point on the scale), and only in the body condition did control participants rate the experience of self-identification with positive agreement, as expected. Similarly, ASD participants appeared to experience an illusion in the object condition, as shown by higher scores in the synchronous condition than the asynchronous condition for the summated illusion scores. But when looking at their score on Q3, the score in the synchronous object condition was below 4, and therefore a negative agreement. In summary, only non-ASD participants identified more with the virtual body after synchronous stroking, while neither group identified with the object more after synchronous stroking. This suggests that, whereas non-ASD participants had a tendency to embody the virtual body and localise their self closer to it following synchronous visuo-tactile stimulation, ASD participants did not appear to have a bodily self representation that adapts to changes in multisensory input so readily. This is in line with previous body-part illusion studies, in which ASD participants have shown a reduced susceptibility to the RHI (Cascio et al., 2012; Paton et al., 2012), and suggests that ASD participants have an altered bodily self representation that encompasses their whole body.

 Confirming the other hypotheses, and in line with the prediction that Noel and colleagues recently made about the slope of PPS in ASD (Noel et al., 2017), the results of the PPS audiotactile integration task showed that ASD participants exhibited a steeper slope in their RTs as a function of the temporal delay of the tap, as the sound was approaching their body. Also, their PPS boundary was smaller, i.e. its boundary was closer to the body than for non-ASD participants. A smaller PPS may partly underlie certain behaviours sometimes seen in individuals with ASD, such as approaching others closer than social norms would prescribe, or having difficulty considering (verbal or non-verbal) communications outside personal space as directed towards themselves (Asada et al., 2016; Kennedy & Adolphs, 2014; Parsons et al., 2004).

The reduced susceptibility to the FBI we found for ASD participants fits with the steeper PPS slope of these participants and may indicate a generally less flexible representation of the bodily self in ASD. During the FBI, non-ASD participants identified with an external virtual body and showed a drift in self-location towards the body, while ASD participants did not show the same malleability in self-identity and self-location. The slope of the PPS indicates the distance over which the facilitatory effect on RT via the integration of touch and sound manifests: it occurs over a greater distance in a shallow slope than it does in a steep slope (found for ASD participants). Therefore conceptually, the slope of the PPS may indicate the flexibility of the boundary between one’s self and an other (Noel et al., 2017). It has been shown that PPS extends towards others in social interactions (Teneggi et al., 2013) and the others’ PPS can even be remapped onto one’s own when sensory experiences are shared (Maister et al., 2015). Having a steeper, less flexible boundary between self and other would mean that the PPS boundary of individuals with ASD would not change to the same extent as the boundary of people without ASD might change in social interactions or during shared sensory experiences. Further research could explore whether this is the case. Individual differences in the flexibility of bodily self representations have recently been suggested to lie on a continuum, with autism on the one, less flexible, end, and for example schizophrenia on the opposite, more flexible end. (Noel et al., 2017; Stanghellini, 2009). In support of this, individuals with schizophrenia have shown the opposite pattern of differences with the typical population that we observed here; they tend to be more susceptible to body illusions (Peled, Ritsner, Hirschmann, Geva, & Modai, 2000; Thakkar, Nichols, McIntosh, & Park, 2011; see also Shaqiri et al., 2018 for conflicting findings).

A limition of the study, however, is that these PPS results refer to the ‘peri-hand’ PPS and not the ‘full-body’ PPS that can be measured by stimulating the trunk (Serino et al., 2015). Therefore, the conclusions about the PPS modulation in ASD participants only relate to the peri-hand portion of the space around the body. A recent paper by Serino et al (2015) showed that the PPS size changes according to the body part around which the PPS is measured, (i.e. face or hand or trunk), with the hand-PPS being the smallest, the face-PPS being larger, and the trunk-PPS the largest. This is thought to reflect the different portions of space in which a body part mostly interacts with external objects: whereas the hand interacts with objects in a very limite area, only when a hand is touching an object, the trunk is usually involved in interactions that occur over a larger area. Despite the different sizes of the body-part centred PPSs, we expect the full-body PPS in ASD participants to be modulated as the peri-hand one, that is, being smaller in ASD than in non-ASD participants. This is because the sizes of different body parts are not fully independent of each other (Serino et al., 2015), and is in line with the interpretation and previous studies, that the smaller PPS in ASD participants may reflect their often observed anomalous social interactions – such as ‘invading’ others’ personal space – where the whole body as well as the hands are similarly involved (Asada et al., 2016; Kennedy & Adolphs, 2014; Parsons, Mitchell, & Leonard, 2004)

An explanation for the reduced susceptibility to the FBI in ASD is offered by research that shows that individuals with ASD have a wider temporal binding window in which temporally close sensory signals are “bound” into a single perceived event (Greenfield, Ropar, Smith, Carey, & Newport, 2015; Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2011; Noel, Stevenson, & Wallace, 2018; Stevenson et al., 2014). A wider temporal binding window would impair the ability to integrate multisensory information and may lead to a lower ability to discriminate between the synchronous and asynchronous conditions of body illusions. This explanation is supported by the finding that on all measures, the difference between the synchronous and asynchronous condition was smaller for ASD participants.

In addition, it has been suggested – following the finding of an inverse relationship between interoceptive sensitivity and susceptibility to the RHI (Tsakiris et al. 2011) – that an individual’s bodily self is more robust and stable if interoceptive cues are more accurately/precisely represented relative to exteroceptive stimuli, making them less susceptible to body illusions (Palmer & Tsakiris, 2018; Tajadura-Jiménez & Tsakiris, 2014; Tsakiris, Tajadura-Jimenez, & Costantini, 2011). In a predictive coding approach, Palmer and Tsakiris (2018) propose that probabilistic representions of the bodily self emerge from the integration of top-down predictions and bottom-up prediction errors across all modalities, including interoceptive ones. They suggest that the balance in saliency of interoceptive relative to exteroceptive prediction errors will determine the malleability of the representation of self, with the interoceptive prediction errors providing stability and continuity of the representation of self in the face of exteroceptive uncertainty. In this account, the brains of individuals with lower interoceptive accuracy would rely less on the prediction errors generated by interoceptive senses, awarding more saliency to exteroceptive signals. Therefore, representations of self would be updated based on conflicting exteroceptive signals, thus generating stronger body illusions. The opposite would be true for individuals with high interoceptive accuracy: because less saliency is awarded to the exteroceptive prediction errors relative to the interoceptive ones, representations of self are not as easily updated, resulting in lower susceptibility to body illusions.

However, in the present study we did not find relationships between susceptibility to the FBI and interoceptive awareness. Furthermore, autistic individuals tend to have *lower* interoceptive sensitivity and awareness than the typical population (DuBois, Ameis, Lai, Casanova, & Desarkar, 2016; Mul et al., 2018; Shah et al., 2016), yet these findings are in line with previous research that shows that they are *less* susceptible to body illusions, not more (Cascio et al., 2012; Guerra et al., 2017; Paton et al., 2012). It is worth noting that an exceptionally wide temporal binding window for interoceptive and exteroceptive (cardio-visual) signals has been shown in ASD. This may affect the balance of interoceptive and exteroceptive processing in terms of saliency and integration (Noel, Lytle, Cascio, & Wallace, 2018). In line with this suggestion, it is of note that the ASD participansts scored significantly lower than the non-ASD participants on the MAIA dimension of Attention Regulation. This dimension of interoceptive awareness captures how well individuals can control or maintain focus on interoceptive sensations when they are competing with exteroceptive sensations. Attention modulates the saliency of signals (Ainley, Apps, Fotopoulou, & Tsakiris, 2016;(Montoya, Schandry, & Müller, 1993; Petzschner et al., 2018)6), and individuals with ASD may thus be less able to sustain attention to interoceptive signals.

Taken together, these findings support suggestions that the predictive coding mechanism in individuals with ASD is different from the typical population, such that the saliency of interoceptive vs exteroceptive prediction errors may differ (Noel et al., 2018), and/or that the strength of top-down predictions (priors) versus the saliency of bottom-up sensory prediction errors is different, as proposed by the so-called hypo-prior model of autism (Lawson, Rees, & Friston, 2014; Pellicano & Burr, 2012). Usually, the experience of the full body illusion results from an optimal top-down resolution (update) to the prediction errors the multisensory conflict of the illusion generates. However, it has been proposed that in ASD bottom-up sensory signals outweigh top-down priors: an inflexibility in adapting higher order cognitions to novel sensory signals results (Lawson et al., 2014; Lawson, Mathys, & Rees, 2017). This might explain both a less flexible sense of bodily self as evidenced by a reduced susceptibility to the FBI, and a reduced flexibility in self-other boundaries as suggested by the finding of a steeper slope of the PPS boundary.

It is worth noting that these findings are in line with suggestions that a low-level mechanism that differentiates between representations of self and other may be anomalous in ASD (Lamm, Bukowski, & Silani, 2016; Lombardo et al., 2010; Sowden & Shah, 2014). In particular, it is agreed that successful social interactions are reliant on the ability to flexibly switch between neural representations of self and others. This mechanism, referred to as ‘self-other control’ (Decety & Sommerville, 2003) has been hypothesised to be altered in ASD (de Guzman, Bird, Banissy, & Catmur, 2016) and plays a role in the Self-to-Other-Model of empathy described in chapter 3 (Bird & Viding, 2014). Several studies have tried to identify the neural basis of the ‘self-other control’ mechanism, with a consensus emerging that the two main areas involved are the medial prefrontal cortex and the temporoparietal junction (Brass, Ruby, & Spengler, 2009; Spengler, von Cramon, & Brass, 2009). These regions are critical in metalising, theory of mind and perspective taking, that is, in those processes for which a flexible yet well-controlled distinction betweeen self and others is needed. A dysfunction in these key regions for controlling self-other distinction may therefore underpin the observed reduced malleability of bodily self-representations in ASD participants, although this is speculative given the purely behavioural nature of this study.

Despite findings of significant group differences for the FBI and PPS measures, the graphesthesia results showed there was no significant relationship between the conditions or between groups in choosing the embodied perspective. Visual perspective taking has been previously investigated in ASD. Some studies show that children with autism have impaired perspective taking when the adoption of an embodied perspective from another’s viewpoint is required (Hamilton et al., 2009; Pearson, Ropar, & Hamilton, 2013; Tan & Harris, 1991; Yirmiya, Sigman, & Zacks, 1994). However, these perspective taking studies focused on ability, not preference, and have mainly been on children. The hypothesis that ASD participants would be less likely to abandon the normally preferred embodied perspective has not been supported. Furthermore, we did not find a differential effect of the FBI conditions on embodied perspective taking in either group. It is possible that preference in the two groups only diverges when presented with an additional challenge. For example, previous research has found that the embodied perspective is adopted less when the letter is not drawn on the forehead, but for example on the chest or back (Arnold, Spence, & Auvray, 2017). The additional difficulty of imagining an ‘inner eye’ on the inside of the trunk instead of behind the forehead which is much closer to the real position of one’s eyes, might have been more sensitive in teasing out group differences in preference, if there is one.

 The final hypothesis, that altered bodily self-consciousness would be related to social functioning in ASD is supported by the findings. The strength of the experienced illusion as indicated by the self-identification question (Q3) was negatively related to autistic traits and positively related to empathy. The multiple regression showed that both autistic traits and the tendency to self-identify with the virtual body contributed significantly to empathy scores. This link with empathy suggests that altered bodily self-consciousness has social implications. Empathy involves the understanding and sharing of the emotion of an other, a process in which one’s own emotional experience and that observed in an other are both neurally represented (Bird & Viding, 2014; Decety & Jackson, 2006; Sowden & Shah, 2014)). We can speculate that the reduced flexibility of bodily self-representation in ASD may hamper the ability to represent another flexibly as well. Indeed, the social environment provides more unpredictable and novel situations than any other, and it has been suggested that consequences of altered predictive coding in the brain are not restricted to perception, but also affect aspects of behaviour and social interaction (Balsters et al., 2016; Kilner, Friston, & Frith, 2007; Lawson et al., 2014; Palmer, Lawson, & Hohwy, 2017).

 It was somewhat surprising to find that, in this sample, autistic traits and the tendency to self-identify with the virtual body contributed both to empathy, while alexithymia did not contribute significantly to empathy once autistic traits and self-identication were taken into account in the multiple regression model. This is in contrast to previous studies (e.g. Bird et al., 2010; Shah et al., 2016), which found a relationship between alexithymia and state empathy in response to visual stimuli depicting pain, and in contrast to the results of the study reported and chapter 3, which found a relationship between alexithymia and empathy which was partly independent from autistic traits. In spite of this, these results provide additional support for the self-to-other-model of empathy (Bird & Viding, 2014) which suggests there are multiple pathways to empathy (and also more ways in which empathy may be impaired in individuals).

 This study has a number of limitations. The use of self-report measures to measure self-identification in the FBI may have produced some unreliable responses from some participants. It would be useful if future studies use an additional implicit measure of susceptibility to the FBI, such as changes in skin temperature (Salomon, Lim, Pfeiffer, Gassert, & Blanke, 2013), skin conductance response (Ehrsson et al., 2008), or cross-modal congruency effects (Aspell, Jane E., Lenggenhager, & Blanke, 2009). The relatively small sample size, and the fact that the non-ASD group did not have similar levels of high alexithymia as the ASD group, means that this study is limited in regard to conclusions that can be drawn on the contributions of alexithymia and autistic traits to empathy.

Extending the findings presented chapter 1 and 2, which showed that interoception – the sense of the physiological condition of the body - is altered in ASD, the findings of the study presented here suggest that individuals with ASD have altered bodily self-consciousness. This is likely due to differences in multisensory integration, which may have a cascading effect on social functioning. Participants with ASD showed reduced susceptibility to the FBI and had a smaller PPS with a steeper slope than non-ASD participants. These results might be explained by wider temporal binding windows in ASD and/or a hypo-prior predictive coding account of autism, and may be compounded by impairments in the mechanism underlying ‘self-other control’ (Decety & Sommerville, 2003) in autism. The observed differences may be indicative of a less flexible representation of the bodily self in ASD. The integration of interoceptive and exteroceptive signals and the contribution of these integrated signals to bodily self-consciousness may also differ in ASD, and this warrants further investigation. Lastly, further research into if and how an altered bodily self affects higher order self-processing would also be informative, as this would not only increase our understanding of autism and other disorders of self, but also deepen our insight into the nature of self.

# Chapter 6

# Overall discussion and conclusion

Recent theories of the self propose that interoception - the conscious and unconscious processing of signals originating from within the body – has an essential role in bodily self-consciousness, the basic sense of self that is rooted in the body (Bermúdez, 2018; Blanke, 2012; Craig, A. D., 2010; Damasio, 2000; Damasio, 2012; Heydrich et al., 2018; Park & Blanke, 2019; Tsakiris, M., Tajadura-Jimenez, & Costantini, 2011). Furthermore, interoceptive processes affect behaviour, emotions and cognition (Azzalini, Rebollo, & Tallon-Baudry, 2019; Craig, 2008; Critchley, 2005; Critchley & Harrison, 2013). Although differences between autistic individuals and non-autistic individuals have previously been found in different, ‘high-level’ aspects of self-processing (e.g. (Crane & Goddard, 2008; Gillespie‐Smith, Ballantyne, Branigan, Turk, & Cunningham, 2017; Heerey, Keltner, & Capps, 2003; Henderson et al., 2009; Hill, Berthoz, & Frith, 2004; Lombardo, Barnes, Wheelwright, & Baron-Cohen, 2007; Lombardo et al., 2010), as well as in sensory processing (Ben-Sasson et al., 2009; Crane, Goddard, & Pring, 2009; Elwin, Ek, Schröder, & Kjellin, 2012; Klintwall et al., 2011; Leekam, Nieto, Libby, Wing, & Gould, 2007; Marco, Hinkley, Hill, & Nagarajan, 2011), when designing this PhD research, bodily self-consciousness and interoception in ASD had not been investigated before. Growing evidence that both interoception and bodily self-consciousness are involved in emotional and social cognition (Critchley, 2005; Garfinkel & Critchley, 2013; Gray et al., 2012; Maister, Cardini, Zamariola, Serino, & Tsakiris, 2015; Quadt, Critchley, & Garfinkel, 2018; Salomon et al., 2017) - areas in which people with ASD have deficits – led to the hypotheses underpinning this thesis, that interoception and bodily self-consciousness are altered in ASD. The objective of this PhD project was therefore to investigate if there are differences in interoception and bodily self-consciousness in people with ASD compared to people from the neurotypical population, and if this is related to the understanding of one’s own emotions and those of others.

 Bodily self-consciousness is necessarily rooted in the body, and here, two approaches have been used to investigate it: the processing of bodily, interoceptive signals and the processing of multisensory body-related exteroceptive stimuli, i.e. visual, tactile and auditory. A third approach, using combinations of interoceptive and exteroceptive stimuli, e.g. cardio-visual (Aspell, et al., 2013), has not been explored in this thesis. Only very recently has a growing understanding emerged that bodily self-consciousness is most likely not emerging from either mainly interoceptive processing (e.g. Craig, 2009) or mainly multisensory exteroceptive processing (e.g. Blanke, 2012), but from both (Park & Tallon-Baudry, 2014; Park & Blanke, 2019; Seth & Tsakiris, 2018). Not many studies have combined interoceptive and exteroceptive manipulation of stimuli to show that both sensory dimensions are involved in the emergence of bodily self-consciousness (e.g. Aspell, et al., 2013; Heydrich et al., 2018; Park et al., 2016), so this offers a potentially fruitful and interesting area to explore in future research.

In chapter 3 of this thesis the findings from the experiment investigating the group differences in interoceptive sensibility, interoceptive accuracy and the heartbeat evoked potential (HEP) are reported. It was found that the participants with ASD had lower subjectively reported interceptive sensibility, lower objectively measured interoceptive accuracy and a less pronounced HEP amplitude than the neurotypical participants. Although the three measures were not correlated with each other in our sample, these results dovetail in all demonstrating reduced interoceptive processing in ASD. The finding of reduced interoceptive accuracy was replicated with a different sample of adults with ASD in the study reported in chapter 3, and the finding of reduced interoceptive sensibility was replicated twice with different samples, as reported in chapter 3 and 4, thus we can have confidence that these findings are reliable and replicable.

Chapter 4 reports on the findings of two studies that investigated the relationship between interoception and the understanding of one’s own emotions and the understanding of others’ emotions, using measures of alexithymia and empathy. Study 2 was an exploratory study using a large sample of non-ASD adults. The advantage of this was that data had enough power to look at all the subscales of the MAIA (Mehling et al., 2012), instead of choosing appropriate subscales only, or trying to cluster them. Results showed that participants with high autistic traits had significantly lower interoceptive sensibility on the dimensions of self regulation and trusting than participants with low autistic traits. Correlation analyses showed that there were dimensions of interoceptive sensibility that related to all other variables; autistic traits, alexithymia and empathy. Furthermore, the interoceptive sensibility dimensions of noticing, attention regulation, self-regulation and body listening were associated with empathy independently, i.e. while controlling for the shared variance in alexithymia, autistic traits, and empathy. Self-regulation was additionally independently associated with autistic traits, and the dimensions of not-worrying and trusting were independently associated with alexithymia.

Study 3 investigated the relationships between interoception, empathy and alexithymia in participants with ASD. Results on interoceptive sensibility were in line with the findings of Study 2 and the chapter 2 study: ASD participants scored lower than non-ASD participants on two of the three clusters of the questionnaire, comprising 7 of the 8 subscales of the Multidimensional Assessment of Interoceptive Awareness (Mehling et al., 2012). ASD participants were less accurate in perceiving their own heartbeat during the heartbeat tracking task (Schandry, 1981). However, there was no difference between groups in automatic mimicry (EMG activity), nor was there a relationship between mimicry and empathy. Self-reported interoceptive sensibility was related to autistic traits, alexithymia, and to cognitive and affective empathy measured by questionnaires, in line with the results in the non-autistic sample used in Study 2. It was also associated with affective empathy measured by the Multifaceted Empathy Task (Dziobek et al., 2008). Mediation analyses showed that alexithymia fulfilled a mediating role in the relationship between interoceptive sensibility and empathy, such that higher interoceptive sensibility contributed to lower alexithymia, which in turn contributed to higher empathy. This result was reflected in our finding that ASD participants with alexithymia had lower cognitive and affective empathy than ASD participants without alexithymia.

Chapter 5 reports on the investigation into bodily self-consciousness as underpinned by multisensory integration (Aspell, Lenggenhager, & Blanke, 2009; Blanke, 2012). The generation of multisensory conflicts to elicit the full body illusion in participants without ASD (as reported many times previously with neurotypical participants e.g. (Aspell, et al., 2009; Ehrsson, 2007; Lenggenhager, Tadi, Metzinger, & Blanke, 2007; Salomon, Lim, Pfeiffer, Gassert, & Blanke, 2013)), failed to do so in participants with ASD. ASD participants did not report self-identification with a virtual body whereas participants without ASD did, and ASD participants’ self-location did not move towards the virtual body as non-ASD participants’ did. Furthermore, self-identification with the virtual body was positively associated with empathy, and was a significant predictor of empathy even when autistic traits, alexithymia and IQ were taken into account. The results of the graphesthesia task, which was included to measure first-person perspective, failed to show group differences in the tendency to prefer an embodied first-person perspective. However, the peripersonal space task showed a difference in the ‘space of bodily self’ for ASD participants compared to those without ASD. The peripersonal space of participants with ASD was smaller and the boundary between peripersonal and extrapersonal space had a steeper slope than that of non-ASD participants.

In summary, this research shows, firstly, that interoception in ASD is reduced on multiple levels of processing compared to neurotypical participants. Secondly, it shows that reduced interoceptive sensibility is associated with increased alexithymia and reduced empathy, and that alexithymia plays a mediating role in the relationship between interoception and empathy. Thirdly, it shows that bodily self-consciousness is less malleable in ASD than it is in the neuro-typical population, and the extent to which it is malleable contributes to empathy, even when taking autistic traits and alexithymia into account. Taken together, these results suggest that sensory processing - specifically interoceptive processing and multisensory integration - is altered in ASD, affecting a basic, bodily sense of self as well as cognitive and affective functioning. The theoretical implications of these findings are discussed below.

The results of this PhD are in line with a recent model of empathy, the Self To Other Model (SOME - Bird & Viding, 2014, see Appendix 1) which proposes that contributing to empathy are multiple ‘systems’ that have reciprocal connections and thus inform each other. This means there are multiple pathways by which empathy can be achieved, and a deficit in one (or more) systems will affect the extent and character of the resulting empathy. The ‘Theory of Mind system’ is known to be impaired in autism (Baron-Cohen, Leslie, & Frith, 1985; Baron-Cohen, 1989; Baron-Cohen, 2000), which may explain the deficit in cognitive empathy and findings of intact affective empathy in ASD (Bird & Viding, 2014; Jones, Happé, Gilbert, Burnett, & Viding, 2010). Alexithymia on the other hand, may be explained by a dysfunction of the ‘affective representation system’, which means that an experienced emotional state will not be accompanied by a distinct and consciously accessible representation of an emotion. It follows that individuals with both an impaired ‘ToM system’ and an impaired ‘affective representation system’ have a double whammy of impediments against the development of empathy, something that was evident in our study in which ASD participants with co-occurring alexithymia had lower cognitive and affective empathy than their ASD counterparts without alexithymia.

These results may also be evidence of altered self-other distinction in ASD. The authors of the SOME model propose that people with ASD may also have an impaired self-other switch, a process that determines if any experienced bodily state, thought or situation should be assigned/is relevant to an other instead of one’s self, with self being the default option (Bird & Viding, 2014). They suggest that in ASD, this switch may be excessively biased towards self. The steeper slope of the peripersonal space boundary that was reported in chapter 4, when interpreted as a more limited ability to blur boundaries between self and other (Noel, Cascio, Wallace, & Park, 2017), is in line with this, although the evidence found is more on a conceptual than empirical level. Similarly, the results of the full body illusion experiment may indicate that ASD participants are less able to suspend representations of self in favour of representations of self that include an other in order to experience ownership of a virtual body.

Future studies could explore the flexibility in self-other distinction in ASD further. A variation on the peripersonal space paradigm offers an opportunity that was not exploited in this research: It has been shown that peripersonal space extends towards others in social interactions (Cardellicchio, Sinigaglia, & Costantini, 2012; Teneggi, Canzoneri, di Pellegrino, & Serino, 2013). When including social interaction as a variable in the peripersonal space paradigm, participants with ASD should show this extension to a lesser extent than those without ASD, if their steeper peripersonal space boundary slope signifies a more robust distinction between self and other than that in the typical population. Similarly, ASD participants should be less susceptible to the enfacement illusion, a paradigm in which the stroking of the participant’s face while seeing another being stroked simultaneously, alters self-recognition to include more of the other person’s face being included in the mental representation of the participant’s face (Tsakiris, Manos, 2008).

A less flexible peripersonal space in ASD tallies with the robustness of bodily self consciousness found in the full body illusion study. These results are consistent with altered predictive coding in ASD. The multisensory conflict that is responsible for eliciting the illusion (feeling tapping on the back but seeing it simultaneously on a virtual body a few metres away) can also be conceptualised as prediction error. The non-ASD group attenuated the prediction error by updating their perception of self-location (closer to the virtual body than they really were) and by adjusting their self-identification to include the virtual body to some extent. The ASD participants were not susceptible to the illusion, or in other words, they failed to attenuate the prediction error and update their perception of self-location and self-identity. This is also in line with the SOME’s self-other switch that is proposed to be more biased towards self in ASD than in neurotypical participants. There is currently a debate about what the mechanisms are for the failure to update perceptions; whether predictions are too weak to modulate sensory prediction errors into new updated perceptions (the hypo-prior account of autism (Pellicano & Burr, 2012), whether bottom-up sensory information is overweighted (Brock, 2012), whether the mechanism by which to assign weight to top-down predictions and bottom-up prediction errors is altered (Lawson, Rees, & Friston, 2014; Van de Cruys et al., 2014), and whether the volatility of sensory information is overestimated (Lawson, Mathys, & Rees, 2017). These accounts are not necessarily in contradiction with each other and could be complimentary. While the results do not provide an answer to these open questions, this research suggests that typical malleability of bodily self is impaired in ASD, which is consistent with altered predictive coding processes in ASD.

Similarly, the altered heartbeat evoked potential of our ASD participants may suggest that predictive coding processes are altered in ASD. There have been suggestions that evoked potentials reflect the attenuation of prediction errors (Friston, 2005), for example when used in paradigms which use repeat stimuli. Expected or repeated exposure to a stimulus typically yields an evoked neural response that is less pronounced, i.e. is attenuated, compared to a single or surprise exposure to a stimulus (repetition suppression (Friston, 2005; Garrido, Kilner, Kiebel, & Friston, 2007; Summerfield, Trittschuh, Monti, Mesulam, & Egner, 2008; Summerfield, Wyart, Mareike Johnen, & De Gardelle, 2011; Todorovic & de Lange, 2012). Predictive coding theory suggests that this occurs as top-down predictions resolve the ascending prediction error; once a repeat stimulus is expected, the error of the prediction is reduced. Accordingly, the HEP has been proposed to demonstrate interoceptive (cardiac) prediction error (Ainley, Apps, Fotopoulou, & Tsakiris, 2016) or top-down predictions (Gentsch, Sel, Marshall, & Schütz‐Bosbach, 2018; Marshall, Gentsch, Jelinčić, & Schütz-Bosbach, 2017). The HEP experiment did not manipulate an expectation or repetition variable, so without the contrast of a control vs experimental condition it is impossible to interpret the reduced HEP for ASD participants as a reduced prediction error or reduced top-down attenuation activity. Previous research has found attenuated evoked responses after repetition or surprise in other modalities in ASD samples (Donkers et al., 2015; Ewbank et al., 2017), although not all studies show this (Marco et al., 2011). Future research could investigate this by integrating homeostatically relevant stimuli such as angry faces with the HEP paradigm and manipulating expectations and/or repetition (e.g. cf. (Gentsch et al., 2018; Marshall et al., 2017). The predictive coding accounts for ASD (Lawson et al., 2014; Lawson et al., 2017) suggest that the effect of expectation would be reduced in participants with ASD, i.e. the attenuation of the HEP should be less for ASD participants than for non-ASD participants.

There are limitations to this research. For example, levels of depression or anxiety were not controlled for in the experiments, both of which may affect interoceptive processing. Secondly, although statistical methods were used to control for the difference in variance in alexithymia levels in the ASD participants and the non-ASD participants, it would be better if the two groups were matched on alexithymia, in order to tease out the effects of alexithymia vs the effects of autism more robustly. Thirdly, the heartbeat tracking task, although widely used, continues to be criticised for confounding variables that may affect performance (Desmedt, Luminet, & Corneille, 2018; Ring, Brener, Knapp, & Mailloux, 2015). Although behavioural measures were included in the experiments, some of the correlations between different constructs were only found for self-report measures. This may be because the behavioural measures (the heartbeat perception task, self-location measurement in the full body illusion) lack power (e.g. low number of trials). Similarly, sample sizes may have been too small to find small effects and results would be more reliable with a bigger sample. Despite using widely used questionnaires that have been tested rigorously for reliability and validity, it is impossible to exclude any biases, or, in case of the ASD participants, differences in the understanding of the statements and in self-insight. Limitations specific to each experiment were discussed further in each chapter.

The findings of this PhD research advance both the understanding of autism as well as our understanding of interoception and bodily self-consciousness. They support recently advanced propositions that altered sensory processing in ASD is not just an epiphenomenon, but may be a primary neurobiological characteristic underpinning differences at a basic level of sense of self - bodily self-consciousness – as well as the higher order deficits of ASD (Robertson & Baron-Cohen, 2017),. The importance of the awareness of one’s own bodily feelings in the understanding of one’s own emotions and others’ is a valuable insight for anyone working or living with autistic people, especially given that around 50% of people with ASD show high levels of alexithymia. The high co-occurence of alexithymia in ASD is not known widely enough, which may, for example, lead to unrealistic expectations on people with ASD in terms of how they manage or show their own emotions and empathy. However, this research points to a way in which therapy could address some of the emotional and social difficulties that people with ASD may experience. Hopefully this research will increase the general understanding of and empathy for those difficulties.

# References

Abbott, A. E., Nair, A., Keown, C. L., Datko, M., Jahedi, A., Fishman, I., & Müller, R. (2016). Patterns of atypical functional connectivity and behavioral links in autism differ between default, salience, and executive networks. *Cerebral Cortex, 26*(10), 4034-4045.

Ainley, V., Apps, M. A., Fotopoulou, A., & Tsakiris, M. (2016). 'Bodily precision': A predictive coding account of individual differences in interoceptive accuracy. *Philosophical Transactions of the Royal Society of London.Series B, Biological Sciences, 371*(1708), 10.1098/rstb.2016.0003. Epub 2016 Oct 10. doi:20160003 [pii]

Ainley, V., Maister, L., & Tsakiris, M. (2015). Heartfelt empathy? no association between interoceptive awareness, questionnaire measures of empathy, reading the mind in the eyes task or the director task. *Frontiers in Psychology, 6*, 554. doi:10.3389/fpsyg.2015.00554

American Psychiatric Association, (. (2013). *Diagnostic and statistical manual of mental disorders - DSM-V.* (5th Edition ed.). Washington, D.C.: American Psychiatric Publishing.

Arnold, G., & Auvray, M. (2017). The graphesthesia paradigm: Drawing letters on the body to investigate the embodied nature of perspective-taking. *I-Perception, 8*(1), 2041669517690163.

Arnold, G., Spence, C., & Auvray, M. (2017). A unity of the self or a multiplicity of locations? how the graphesthesia task sheds light on the role of spatial perspectives in bodily self-consciousness. *Consciousness and Cognition, 56*, 100-114. doi:10.1016/j.concog.2017.06.012

Ashwin, C., Chapman, E., Colle, L., & Baron-Cohen, S. (2006). Impaired recognition of negative basic emotions in autism: A test of the amygdala theory. *Social Neuroscience, 1*(3-4), 349-363. doi:10.1080/17470910601040772

Aspell, J. E., Heydrich, L., Marillier, G., Lavanchy, T., Herbelin, B., & Blanke, O. (2013). Turning body and self inside out: Visualized heartbeats alter bodily self-consciousness and tactile perception. *Psychological Science, 24*(12), 2445-2453. doi:10.1177/0956797613498395; 10.1177/0956797613498395

Aspell, J. E., Lenggenhager, B., & Blanke, O. (2009). Keeping in touch with one's self: Multisensory mechanisms of self-consciousness. *PloS One, 4*(8), e6488. doi:10.1371/journal.pone.0006488

Asperger, H. (1991). Autistic psychopathy in childhood. In U. Frith (Ed.), *Autism and asperger syndrome* (pp. 37-92). Cambridge: Cambridge University Press.

Atkinson, A. P. (2009). Impaired recognition of emotions from body movements is associated with elevated motion coherence thresholds in autism spectrum disorders. *Neuropsychologia, 47*(13), 3023-3029.

Avery, J. A., Drevets, W. C., Moseman, S. E., Bodurka, J., Barcalow, J. C., & Simmons, W. K. (2014). Major depressive disorder is associated with abnormal interoceptive activity and functional connectivity in the insula. *Biological Psychiatry, 76*(3), 258-266.

Azzalini, D., Rebollo, I., & Tallon-Baudry, C. (2019). Visceral signals shape brain dynamics and cognition. *Trends in Cognitive Sciences,*

Babo-Rebelo, M., Buot, A., & Tallon-Baudry, C. (2019). Neural responses to heartbeats distinguish self from other during imagination. *NeuroImage,*

Babo-Rebelo, M., Richter, C. G., & Tallon-Baudry, C. (2016). Neural responses to heartbeats in the default network encode the self in spontaneous thoughts. *Journal of Neuroscience, 36*(30), 7829-7840.

Bachevalier, J., & Loveland, K. A. (2006). The orbitofrontal–amygdala circuit and self-regulation of social–emotional behavior in autism. *Neuroscience & Biobehavioral Reviews, 30*(1), 97-117. doi:10.1016/j.neubiorev.2005.07.002

Bagby, R. M., Parker, J. D., & Taylor, G. J. (1994). The twenty-item toronto alexithymia Scale—I. item selection and cross-validation of the factor structure. *Journal of Psychosomatic Research, 38*(1), 23-32. doi:10.1016/0022-3999(94)90005-1

Baird, A. D., Scheffer, I. E., & Wilson, S. J. (2011). Mirror neuron system involvement in empathy: A critical look at the evidence. *Social Neuroscience, 6*(4), 327-335. doi:10.1080/17470919.2010.547085

Bandy, D., Chen, K., Craig, A. D., & Reiman, E. M. (2000). Thermosensory activation of insular cortex. *Nature Neuroscience, 3*, 184+. Retrieved from http://go.galegroup.com/ps/i.do?id=GALE%7CA185568853&v=2.1&u=anglia\_itw&it=r&p=AONE&sw=w&asid=1ce0ff3bda7dbdf27a8a57badae0fec7

Baranauskas, M., Grabauskaitė, A., & Griškova-Bulanova, I. (2017). Brain responses and self-reported indices of interoception: Heartbeat evoked potentials are inversely associated with worrying about body sensations. *Physiology & Behavior, 180*, 1-7.

Baron-Cohen, S. (1989). The autistic child's theory of mind: A case of specific developmental delay. *Journal of Child Psychology and Psychiatry, 30*(2), 285-297. doi:10.1111/j.1469-7610.1989.tb00241.x

Baron-Cohen, S. (2000). Theory of mind and autism: A fifteen year review. *Understanding Other Minds: Perspectives from Developmental Cognitive Neuroscience, 2*, 3-20.

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have a “theory of mind” ? *Cognition, 21*(1), 37-46. doi:10.1016/0010-0277(85)90022-8

Baron-Cohen, S., & Wheelwright, S. (2004). The empathy quotient: An investigation of adults with asperger syndrome or high functioning autism, and normal sex differences. *Journal of Autism and Developmental Disorders, 34*(2), 163-175. doi:JADD.0000022607.19833.00

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001a). The ?reading the mind in the eyes? test revised version: A study with normal adults, and adults with asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry, 42*(2), 241-251. doi:10.1111/1469-7610.00715

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001b). The "reading the mind in the eyes" test revised version: A study with normal adults, and adults with asperger syndrome or high-functioning autism.*42*, 241-251. doi:10.1111/1469-7610.00715

Baron-Cohen, S., Wheelwright, S., Lawson, J., Griffin, R., Ashwin, C., Billington, J., & Chakrabarti, B. (2005). Empathizing and systemizing in autism spectrum conditions. *Handbook of Autism and Pervasive Developmental Disorders, 1*, 628-639.

Baron-Cohen, S., Wheelwright, S., Skinner, R., Martin, J., & Clubley, E. (2001). The autism-spectrum quotient (AQ): Evidence from asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of Autism and Developmental Disorders, 31*(1), 5-17. doi:1005653411471

Barrett, L. F. (2017). The theory of constructed emotion: An active inference account of interoception and categorization. *Social Cognitive and Affective Neuroscience, 12*(1), 1-23.

Barrett, L. F., Quigley, K. S., Bliss-Moreau, E., & Aronson, K. R. (2004). Interoceptive sensitivity and self-reports of emotional experience. *Journal of Personality and Social Psychology, 87*(5), 684-697. doi:10.1037/0022-3514.87.5.684

Barrett, L. F., & Simmons, W. K. (2015). Interoceptive predictions in the brain. *Nature Reviews Neuroscience, 16*(7), 419.

Bastiaansen, J. A., Thioux, M., & Keysers, C. (2009). Evidence for mirror systems in emotions. *Philosophical Transactions of the Royal Society of London.Series B, Biological Sciences, 364*(1528), 2391-2404. doi:10.1098/rstb.2009.0058 [doi]

Beall, P. M., Moody, E. J., McIntosh, D. N., Hepburn, S. L., & Reed, C. L. (2008). Rapid facial reactions to emotional facial expressions in typically developing children and children with autism spectrum disorder. *Journal of Experimental Child Psychology, 101*(3), 206-223. doi:10.1016/j.jecp.2008.04.004

Ben-Sasson, A., Hen, L., Fluss, R., Cermak, S. A., Engel-Yeger, B., & Gal, E. (2009). A meta-analysis of sensory modulation symptoms in individuals with autism spectrum disorders. *Journal of Autism and Developmental Disorders, 39*(1), 1-11. doi:10.1007/s10803-008-0593-3

Bermúdez, J. L. (2018). *The bodily self: Selected essays* London: MIT Press.

Bernhardt, B. C., Valk, S. L., Silani, G., Bird, G., Frith, U., & Singer, T. (2014). Selective disruption of sociocognitive structural brain networks in autism and alexithymia. *Cerebral Cortex (New York, N.Y.: 1991), 24*(12), 3258-3267. doi:10.1093/cercor/bht182

Berthoz, S., & Hill, E. L. (2005). The validity of using self-reports to assess emotion regulation abilities in adults with autism spectrum disorder. *European Psychiatry, 20*(3), 291-298.

Bird, G., & Cook, R. (2013). Mixed emotions: The contribution of alexithymia to the emotional symptoms of autism. *Translational Psychiatry, 3*(7), e285. doi:10.1038/tp.2013.61

Bird, G., Silani, G., Brindley, R., White, S., Frith, U., & Singer, T. (2010). Empathic brain responses in insula are modulated by levels of alexithymia but not autism. *Brain, 133*(5), 1515-1525. doi:10.1093/brain/awq060

Bird, G., & Viding, E. (2014). The self to other model of empathy: Providing a new framework for understanding empathy impairments in psychopathy, autism, and alexithymia. *Neuroscience & Biobehavioral Reviews, 47*, 520-532. doi:10.1016/j.neubiorev.2014.09.021

Bishop, D. V. M. (2010). Overlap between autism and language impairment: Phenomimicry or shared etiology? *Behavior Genetics, 40,* 618-629. Doi: 10.1007/s10519-010-9381-x

Blair, R. J. R. (2005). Responding to the emotions of others: Dissociating forms of empathy through the study of typical and psychiatric populations. *Consciousness and Cognition, 14*(4), 698-718. doi:10.1016/j.concog.2005.06.004

Blanke, O. (2012). Multisensory brain mechanisms of bodily self-consciousness. *Nature Reviews Neuroscience, 13*(8), 556-571. doi:10.1038/nrn3292

Blanke, O., & Metzinger, T. (2009). Full-body illusions and minimal phenomenal selfhood. *Trends in Cognitive Sciences, 13*(1), 7-13. doi://dx.doi.org/10.1016/j.tics.2008.10.003

Blanke, O., & Mohr, C. (2005). Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin: Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness. *Brain Research Reviews, 50*(1), 184-199. doi://dx.doi.org/10.1016/j.brainresrev.2005.05.008

Blanke, O., Slater, M., & Serino, A. (2015). Behavioral, neural, and computational principles of bodily self-consciousness. *Neuron, 88*(1), 145-166.

Bornemann, B., & Singer, T. (2017). Taking time to feel our body: Steady increases in heartbeat perception accuracy and decreases in alexithymia over 9 months of contemplative mental training. *Psychophysiology, 54*(3), 469-482.

Botvinick, M., & Cohen, J. (1998). Rubber hands' feel'touch that eyes see. *Nature, 391*(6669), 756.

Botvinick, M., Jha, A. P., Bylsma, L. M., Fabian, S. A., Solomon, P. E., & Prkachin, K. M. (2005). Viewing facial expressions of pain engages cortical areas involved in the direct experience of pain. *NeuroImage, 25*(1), 312-319. doi:10.1016/j.neuroimage.2004.11.043

Brener, J., & Kluvitse, C. (1988). Heartbeat detection: Judgement of the simultaneity of external stimuli and heartbeats. *Psychophysiology, 25*, 554-561. doi:10.1111/j.1469-8986.1988.tb01891.x

Brewer, R., Happé, F., Cook, R., & Bird, G. (2015). Commentary on “Autism, oxytocin and interoception”: Alexithymia, not autism spectrum disorders, is the consequence of interoceptive failure. *Neuroscience & Biobehavioral Reviews, 56*, 348-353. doi:10.1016/j.neubiorev.2015.07.006

Brock, J. (2012). Alternative bayesian accounts of autistic perception: Comment on pellicano and burr. *Trends in Cognitive Sciences, 16*(12), 573-574.

Brooks, J., Zambreanu, L., Godinez, A., Craig, A. D., & Tracey, I. (2005). Somatotopic organisation of the human insula to painful heat studied with high resolution functional imaging. *NeuroImage, 27*(1), 201-209. doi://dx.doi.org/10.1016/j.neuroimage.2005.03.041

Burrows, C. A., Usher, L. V., Mundy, P. C., & Henderson, H. A. (2017). The salience of the self: Self‐referential processing and internalizing problems in children and adolescents with autism spectrum disorder. *Autism Research, 10*(5), 949-960.

Calì, G., Ambrosini, E., Picconi, L., Mehling, W., & Committeri, G. (2015). Investigating the relationship between interoceptive accuracy, interoceptive awareness, and emotional susceptibility. *Frontiers in Psychology, 6*, 1202.

Cameron, O. G. (2001a). *Visceral sensory neuroscience: Interoception* Oxford University Press.

Cameron, O. G. (2001b). Interoception: The inside story: a model for psychosomatic processes. *Psychosomatic Medicine, 63*, 697-710.

Cannon, W. B. (1927). The james-lange theory of emotions: A critical examination and an alternative theory. *American Journal of Psychology, 39*, 106-124.

Canzoneri, E., Magosso, E., & Serino, A. (2012). Dynamic sounds capture the boundaries of peripersonal space representation in humans. *PloS One, 7*(9), e44306. doi:10.1371/journal.pone.0044306

Cardellicchio, P., Sinigaglia, C., & Costantini, M. (2012). Grasping affordances with the other’s hand: A TMS study. *Social Cognitive and Affective Neuroscience, 8*(4), 455-459. doi:10.1093/scan/nss017

Caria, A., & de Falco, S. (2015). Anterior insular cortex regulation in autism spectrum disorders. *Frontiers in Behavioral Neuroscience, 9*, 38.

Cascio, C. J., Foss-Feig, J., Burnette, C. P., Heacock, J. L., & Cosby, A. A. (2012). The rubber hand illusion in children with autism spectrum disorders: Delayed influence of combined tactile and visual input on proprioception. *Autism, 16*(4), 406-419. doi:10.1177/1362361311430404

Ceunen, E., Van Diest, I., & Vlaeyen, J. (2013). Accuracy and awareness of perception: Related, yet distinct (commentary on herbert et al., 2012). *Biological Psychology, 92*(2), 426-427. doi://dx.doi.org/10.1016/j.biopsycho.2012.09.012

Ceunen, E., Vlaeyen, J. W., & Van Diest, I. (2016). On the origin of interoception. *Frontiers in Psychology, 7*, 743.

Cherkassky, V. L., Kana, R. K., Keller, T. A., & Just, M. A. (2006). Functional connectivity in a baseline resting-state network in autism. *Neuroreport, 17*(16), 1687-1690.

Chiu, P. H., Kayali, M. A., Kishida, K. T., Tomlin, D., Klinger, L. G., Klinger, M. R., & Montague, P. R. (2008). Self responses along cingulate cortex reveal quantitative neural phenotype for high-functioning autism. *Neuron, 57*(3), 463-473.

Chugani, D. C. (2012). Neuroimaging and neurochemistry of autism. *Pediatric Clinics, 59*(1), 63-73.

Cook, R., Brewer, R., Shah, P., & Bird, G. (2013). Alexithymia, not autism, predicts poor recognition of emotional facial expressions. *Psychological Science, 24*(5), 723-732. doi:10.1177/0956797612463582 [doi]

Craig, A. D. (2009). How do you feel--now? the anterior insula and human awareness. *Nature Reviews Neuroscience, 10*, 59-70. doi:10.1038/nrn2555

Craig, A. D. (2010). The sentient self. *Brain Structure and Function, 214*, 563-577.

Craig, A. D. (2008). Interoception and emotion: A neuroanatomical perspective.
. *Handbook of emotions* (pp. 272-292). New York: Guildford Press.

Craig, A. D. (2002). How do you feel? interoception: The sense of the physiological condition of the body. *Nature Reviews Neuroscience, 3*, 655-666. doi:10.1038/nrn894

Craig, A. D. (2003). A new view of pain as a homeostatic emotion. *Trends in Neurosciences, 26*(6), 303-307. doi://dx.doi.org.proxy-lib.anglia.ac.uk/10.1016/S0166-2236(03)00123-1

Crane, L., Batty, R., Adeyinka, H., Goddard, L., Henry, L. A., & Hill, E. L. (2018). Autism diagnosis in the United Kingdom: Perspectives of autistic adults, parents and professionals. *Journal of Autism and Developmental Disorders, 48,* 3761- 3772. https://doi.org/10.1007/s10803-018-3639-1

Crane, L., & Goddard, L. (2008). Episodic and semantic autobiographical memory in adults with autism spectrum disorders. *Journal of Autism and Developmental Disorders, 38*(3), 498-506.

Crane, L., Goddard, L., & Pring, L. (2009). Sensory processing in adults with autism spectrum disorders. *Autism, 13*(3), 215-228. doi:10.1177/1362361309103794

Crane, L., Pring, L., Jukes, K., & Goddard, L. (2012). Patterns of autobiographical memory in adults with autism spectrum disorder. *Journal of Autism and Developmental Disorders, 42*(10), 2100-2112.

Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature Neuroscience, 7*, 189-195. doi:10.1038/nn1176

Critchley, H. D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *Journal of Comparative Neurology, 493*, 154-166. doi:10.1002/cne.20749

Critchley, H. D., & Harrison, N. A. (2013). Visceral influences on brain and behavior. *Neuron, 77*, 624-638. doi://dx.doi.org/10.1016/j.neuron.2013.02.008

Critchley, H. D., Mathias, C. J., & Dolan, R. J. (2002). Fear conditioning in humans: The influence of awareness and autonomic arousal on functional neuroanatomy. *Neuron, 33*(4), 653-663.

Critchley, H. D., Mathias, C. J., Josephs, O., O’Doherty, J., Zanini, S., Dewar, B., . . . Dolan, R. J. (2003). Human cingulate cortex and autonomic control: Converging neuroimaging and clinical evidence. *Brain, 126*(10), 2139-2152.

Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A., & Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature Neuroscience, 7*(2), 189-195. doi:10.1038/nn1176

Dahme, B., Richter, R., & Mass, R. (1996). Interoception of respiratory resistance in asthmatic patients. *Biological Psychology, 42*(1-2), 215-229.

Damasio, A. (2000). *The feeling of what happens: Body and emotion in the making of consciousness* Harvest Books.

Damasio, A. (2012). *Self comes to mind; constructing the conscious brain*. London: Vintage.

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *Journal of Personality and Social Psychology, 44*, 113-126. doi:10.1037/0022-3514.44.1.113

Decety, J., & Jackson, P. L. (2006). A social-neuroscience perspective on empathy. *Current Directions in Psychological Science, 15*(2), 54-58. doi:10.1111/j.0963-7214.2006.00406.x

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*(1), 9-21.

Demurie, E., De Corel, M., & Roeyers, H. (2011). Empathic accuracy in adolescents with autism spectrum disorders and adolescents with attention-deficit/hyperactivity disorder. *Research in Autism Spectrum Disorders, 5*(1), 126-134. doi:10.1016/j.rasd.2010.03.002

Deschamps, P., Coppes, L., Kenemans, J. L., Schutter, D., & Matthys, W. (2013). Electromyographic responses to emotional facial expressions in 6–7 year olds with autism spectrum disorders. *Journal of Autism and Developmental Disorders,* , 1-9.

Desmedt, O., Luminet, O., & Corneille, O. (2018). The heartbeat counting task largely involves non-interoceptive processes: Evidence from both the original and an adapted counting task. *Biological Psychology, 138*, 185-188.

Di Martino, A., Ross, K., Uddin, L. Q., Sklar, A. B., Castellanos, F. X., & Milham, M. P. (2009). Functional brain correlates of social and nonsocial processes in autism spectrum disorders: An activation likelihood estimation meta-analysis. *Biological Psychiatry, 65*(1), 63-74. doi://dx.doi.org/10.1016/j.biopsych.2008.09.022

Di Martino, A., Shehzad, Z., Kelly, C., Roy, A., Gee, D., Uddin, L., . . . Milham, M. (2009). Relationship between cingulo-insular functional connectivity and autistic traits in neurotypical adults. *American Journal of Psychiatry, 166*(8), 891-899. doi:10.1176/appi.ajp.2009.08121894

Dimberg, U., Thunberg, M., & Elmehed, K. (2000). Unconscious facial reactions to emotional facial expressions. *Psychological Science, 11*(1), 86-89.

Dimberg, U. (1982). Facial reactions to facial expressions. *Psychophysiology, 19*(6), 643-647. doi:10.1111/j.1469-8986.1982.tb02516.x

Dimberg, U., Andréasson, P., & Thunberg, M. (2011a). Emotional empathy and facial reactions to facial expressions. *Journal of Psychophysiology, 25*, 26-31. doi:10.1027/0269-8803/a000029

Domschke, K., Stevens, S., Pfleiderer, B., & Gerlach, A. L. (2010). Interoceptive sensitivity in anxiety and anxiety disorders: An overview and integration of neurobiological findings. *Clinical Psychology Review, 30*, 1-11. doi://dx.doi.org/10.1016/j.cpr.2009.08.008

Donkers, F. C., Schipul, S. E., Baranek, G. T., Cleary, K. M., Willoughby, M. T., Evans, A. M., . . . Belger, A. (2015). Attenuated auditory event-related potentials and associations with atypical sensory response patterns in children with autism. *Journal of Autism and Developmental Disorders, 45*(2), 506-523.

Dumontheil, I., Apperly, I. A., & Blakemore, S. (2010). Online usage of theory of mind continues to develop in late adolescence. *Developmental Science, 13*, 331-338. doi:10.1111/j.1467-7687.2009.00888.x

Dunn, B. D., Stefanovitch, I., Evans, D., Oliver, C., Hawkins, A., & Dalgleish, T. (2010a). Can you feel the beat? interoceptive awareness is an interactive function of anxiety-and depression-specific symptom dimensions. *Behaviour Research and Therapy, 48*, 1133-1138. doi://dx.doi.org/10.1016/j.brat.2010.07.006

Dunn, B. D., Dalgleish, T., Ogilvie, A. D., & Lawrence, A. D. (2007a). Heartbeat perception in depression. *Behaviour Research and Therapy, 45*(8), 1921-1930.

Dunn, B. D., Stefanovitch, I., Evans, D., Oliver, C., Hawkins, A., & Dalgleish, T. (2010b). Can you feel the beat? interoceptive awareness is an interactive function of anxiety-and depression-specific symptom dimensions. *Behaviour Research and Therapy, 48*(11), 1133-1138. doi:10.1016/j.brat.2010.07.006

Dziobek, I., Rogers, K., Fleck, S., Bahnemann, M., Heekeren, H., Wolf, O., & Convit, A. (2008). Dissociation of cognitive and emotional empathy in adults with asperger syndrome using the multifaceted empathy test (MET). *Journal of Autism and Developmental Disorders, 38*(3), 464-473. doi:10.1007/s10803-007-0486-x

Ebisch, S. J., Gallese, V., Willems, R. M., Mantini, D., Groen, W. B., Romani, G. L., . . . Bekkering, H. (2011). Altered intrinsic functional connectivity of anterior and posterior insula regions in high‐functioning participants with autism spectrum disorder. *Human Brain Mapping, 32*(7), 1013-1028. doi:10.1002/hbm.21085

Ehlers, A. (1993). Interoception and panic disorder. *Advances in Behaviour Research and Therapy, 15*, 3-21. doi://dx.doi.org/10.1016/0146-6402(93)90001-I

Ehlers, A., & Breuer, P. (1996). How good are patients with panic disorder at perceiving their heartbeats? *Biological Psychology, 42*(1), 165-182. doi:10.1016/0301-0511(95)05153-8

Ehrsson, H. H. (2007). The experimental induction of out-of-body experiences. *Science (New York, N.Y.), 317*(5841), 1048. doi:317/5841/1048 [pii]

Eisenberg, N. (2000). Emotion, regulation, and moral development. *Annual Review of Psychology, 51*(1), 665-697.

Elwin, M., Ek, L., Kjellin, L., & Schröder, A. (2013). Too much or too little: Hyper-and hypo-reactivity in high-functioning autism spectrum conditions. *Journal of Intellectual and Developmental Disability, 38*(3), 232-241. doi:10.3109/13668250.2013.815694

Elwin, M., Ek, L., Schröder, A., & Kjellin, L. (2012). Autobiographical accounts of sensing in asperger syndrome and high-functioning autism. *Archives of Psychiatric Nursing, 36*, 420-429. doi://dx.doi.org/10.1016/j.apnu.2011.10.003

Ernst, J., Northoff, G., Böker, H., Seifritz, E., & Grimm, S. (2012). Interoceptive awareness enhances neural activity during empathy. *Human Brain Mapping, 34*, 1615-1624. doi:10.1002/hbm.22014

Eshkevari, E., Rieger, E., Musiat, P., & Treasure, J. (2014). An investigation of interoceptive sensitivity in eating disorders using a heartbeat detection task and a self‐report measure. *European Eating Disorders Review, 22*(5), 383-388.

Ewbank, M. P., Pell, P. J., Powell, T. E., von dem Hagen, Elisabeth AH, Baron-Cohen, S., & Calder, A. J. (2017). Repetition suppression and memory for faces is reduced in adults with autism spectrum conditions. *Cerebral Cortex, 27*(1), 92-103.

Eysenck, S. B., & Eysenck, H. J. (1978). Impulsiveness and venturesomeness: Their position in a dimensional system of personality description. *Psychological Reports, 43*(3f), 1247-1255. doi:10.2466/pr0.1978.43.3f.1247

Fan, Y. T., Chen, C., Chen, S. C., Decety, J., & Cheng, Y. (2014). Empathic arousal and social understanding in individuals with autism: Evidence from fMRI and ERP measurements. *Social Cognitive and Affective Neuroscience, 9*(8), 1203-1213. doi:10.1093/scan/nst101

Fiene, L., & Brownlow, C. (2015). Investigating interoception and body awareness in adults with and without autism spectrum disorder. *Autism Research, 8,* 709-716.

Fombonne, E. (2009). Epidemiology of pervasive developmental disorders. *Pediatric. Research,* *65*, 591–598. doi:10.1203/PDR.0b013e31819e7203

Foss-Feig, J. H., Kwakye, L. D., Cascio, C. J., Burnette, C. P., Kadivar, H., Stone, W. L., & Wallace, M. T. (2010). An extended multisensory temporal binding window in autism spectrum disorders. *Experimental Brain Research, 203*(2), 381-389. doi:10.1007/s00221-010-2240-4

Fridlund, A. J., & Cacioppo, J. T. (1986). Guidelines for human electromyographic research. *Psychophysiology, 23*(5), 567-589. doi:10.1111/j.1469-8986.1986.tb00676.x

Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society B: Biological Sciences, 360*(1456), 815-836.

Friston, K., Mattout, J., & Kilner, J. (2011). Action understanding and active inference. *Biological Cybernetics, 104*(1-2), 137-160.

Fukushima, H., Terasawa, Y., & Umeda, S. (2011). Association between interoception and empathy: Evidence from heartbeat-evoked brain potential. *International Journal of Psychophysiology, 79*(2), 259-265. doi:10.1016/j.ijpsycho.2010.10.015

Furman, D. J., Waugh, C. E., Bhattacharjee, K., Thompson, R. J., & Gotlib, I. H. (2013). Interoceptive awareness, positive affect, and decision making in major depressive disorder. *Journal of Affective Disorders, 151*(2), 780-785.

Gaigg, S. B., Cornell, A. S., & Bird, G. (2018). The psychophysiological mechanisms of alexithymia in autism spectrum disorder. *Autism, 22*(2), 227-231.

Gadow, K. D., Devincent, C. J., Pomeroy, J., & Azizian, A. (2005). Comparison of DSM-IV symptoms in elementary school-age children with PDD versus clinic and community samples. *Autism,* *9*, 392–415. doi:10.1177/1362361305056079

Gallagher, S. (2000). Philosophical conceptions of the self: Implications for cognitive science. *Trends in Cognitive Sciences, 4*(1), 14-21. doi://dx.doi.org/10.1016/S1364-6613(99)01417-5

Gallese, V. (2001). The shared manifold hypothesis. From mirror neurons to empathy. *Journal of Consciousness Studies, 8*(5-7), 5-7.

Garfinkel, S. N., Tiley, C., O'Keeffe, S., Harrison, N. A., Seth, A. K., & Critchley, H. D. (2016). Discrepancies between dimensions of interoception in autism: Implications for emotions and anxiety. *Biological Psychology, 114*, 117-126. doi:10.1016/j.biopsycho.2015.12.003

Garfinkel, S. N., & Critchley, H. D. (2013). Interoception, emotion and brain: New insights link internal physiology to social behaviour. commentary on:: "Anterior insular cortex mediates bodily sensibility and social anxiety" by terasawa et al. (2012). *Social Cognitive and Affective Neuroscience, 8*(3), 231-234. doi:10.1093/scan/nss140 [doi]

Garfinkel, S. N., Manassei, M. F., Hamilton-Fletcher, G., In den Bosch, Y., Critchley, H. D., & Engels, M. (2016). Interoceptive dimensions across cardiac and respiratory axes. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1708), 20160014.

Garfinkel, S. N., Seth, A. K., Barrett, A. B., Suzuki, K., & Critchley, H. D. (2015). Knowing your own heart: Distinguishing interoceptive accuracy from interoceptive awareness. *Biological Psychology, in Press,* doi:10.1016/j.biopsycho.2014.11.004

Gargaro, B. A., Rinehart, N. J., Bradshaw, J. L., Tonge, B. J., and Sheppard, D. M. (2011). Autism and ADHD: how far have we come in the comorbidity debate? *Neuroscience. Biobehavioral. Review, 35*, 1081–1088. doi:10.1016/j.neubiorev.2010.11.002

Garrido, M. I., Kilner, J. M., Kiebel, S. J., & Friston, K. J. (2007). Evoked brain responses are generated by feedback loops. *Proceedings of the National Academy of Sciences, 104*, 20961-20966.

Gebauer, L., Skewes, J., Hørlyck, L., & Vuust, P. (2014). Atypical perception of affective prosody in autism spectrum disorder. *NeuroImage: Clinical, 6*, 370-378.

Gendron, M., & Barrett, L. F. (2009). Reconstructing the past: A century of ideas about emotion in psychology. *Emotion Review, 1*, 316-339. doi:10.1177/1754073909338877

Gentsch, A., Sel, A., Marshall, A. C., & Schütz‐Bosbach, S. (2018). Affective interoceptive inference: Evidence from heart‐beat evoked brain potentials. *Human Brain Mapping,*

Georgiades, S., Szatman, P., & Boyle, M. (2013). Importance of studying heterogeneity in autism. *Neuropsychiatry, 3,* 123-125. doi: 10.2217/NPY.13.8

Gillberg, C. L. (1992). The emanuel miller memorial lecture 1991. *Journal of Child Psychology and Psychiatry, 33*(5), 813-842. doi:10.1111/j.1469-7610.1992.tb01959.x

Gillespie‐Smith, K., Ballantyne, C., Branigan, H. P., Turk, D. J., & Cunningham, S. J. (2017). The I in autism: Severity and social functioning in autism are related to self‐processing. *British Journal of Developmental Psychology, 36*, 127-141. doi:10.1111/bjdp.12219

Golan, O., & Baron-Cohen, S. (2006). Systemizing empathy: Teaching adults with asperger syndrome or high-functioning autism to recognize complex emotions using interactive multimedia. *Development and Psychopathology, 18*(02), 591-617. doi:10.1017/S0954579406060305

Gray, M. A., Beacher, F. D., Minati, L., Nagai, Y., Kemp, A. H., Harrison, N. A., & Critchley, H. D. (2012). Emotional appraisal is influenced by cardiac afferent information. *Emotion, 12*(1), 180-192. doi:10.1037/a0025083

Gray, M. A., Taggart, P., Sutton, P. M., Groves, D., Holdright, D. R., Bradbury, D., . . . Critchley, H. D. (2007). A cortical potential reflecting cardiac function. *Proceedings of the National Academy of Sciences, 104*(16), 6818-6823.

Green, L., Fein, D., Modahl, C., Feinstein, C., Waterhouse, L., & Morris, M. (2001). Oxytocin and autistic disorder: Alterations in peptide forms. *Biological Psychiatry, 50*(8), 609-613.

Gregory, S. G., Connelly, J. J., Towers, A. J., Johnson, J., Biscocho, D., Markunas, C. A., . . . Ellis, P. (2009). Genomic and epigenetic evidence for oxytocin receptor deficiency in autism. *BMC Medicine, 7*(1), 62.

Greimel, E., Schulte-Rüther, M., Kircher, T., Kamp-Becker, I., Remschmidt, H., Fink, G. R., . . . Konrad, K. (2010). Neural mechanisms of empathy in adolescents with autism spectrum disorder and their fathers. *NeuroImage, 49*(1), 1055-1065. doi://dx.doi.org/10.1016/j.neuroimage.2009.07.057

Griffin, C., Lombardo, M. V., & Auyeung, B. (2015). Alexithymia in children with and without autism spectrum disorders. *Autism Research,* doi:10.1002/aur.1569

Grynberg, D., Chang, B., Corneille, O., Maurage, P., Vermeulen, N., Berthoz, S., & Luminet, O. (2012). Alexithymia and the processing of emotional facial expressions (EFEs): Systematic review, unanswered questions and further perspectives. *PLoS One, 7*(8), e42429. doi:10.1371/journal.pone.0042429

Grynberg, D., Luminet, O., Corneille, O., GrÃ¨zes, J., & Berthoz, S. (2010). Alexithymia in the interpersonal domain: A general deficit of empathy? *Personality and Individual Differences, 49*, 845-850. doi://dx.doi.org/10.1016/j.paid.2010.07.013

Grynberg, D., & Pollatos, O. (2015). Perceiving one's body shapes empathy. *Physiology & Behavior, 140*, 54-60. doi:10.1016/j.physbeh.2014.12.026

Gu, X., Hof, P. R., Friston, K. J., & Fan, J. (2013). Anterior insular cortex and emotional awareness. *Journal of Comparative Neurology, 15*, 3371-3388. doi:10.1002/cne.23368

Guo, X., Duan, X., Suckling, J., Chen, H., Liao, W., Cui, Q., & Chen, H. (2019). Partially impaired functional connectivity states between right anterior insula and default mode network in autism spectrum disorder. *Human Brain Mapping, 40*(4), 1264-1275.

Guttman, H., & Laporte, L. (2002). Alexithymia, empathy, and psychological symptoms in a family context. *Comprehensive Psychiatry, 43*(6), 448-455. doi:10.1053/comp.2002.35905

Harrison, N. A., Gray, M. A., Gianaros, P. J., & Critchley, H. D. (2010). The embodiment of emotional feelings in the brain. *Journal of Neuroscience, 30*, 12878-12884. doi:10.1523/JNEUROSCI.1725-10.2010

Harver, A., Katkin, E. S., & Bloch, E. (1993). Signal‐detection outcomes on heartbeat and respiratory resistance detection tasks in male and female subjects. *Psychophysiology, 30*(3), 223-230. doi:10.1111/j.1469-8986.1993.tb03347.x

Hayes, A. F. (2013). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. New York: Guilford Press.

Heaton, P., Reichenbacher, L., Sauter, D., Allen, R., Scott, S., & Hill, E. (2012). Measuring the effects of alexithymia on perception of emotional vocalizations in autistic spectrum disorder and typical development. *Psychological Medicine, 42*(11), 2453-2459.

Heerey, E. A., Keltner, D., & Capps, L. M. (2003). Making sense of self-conscious emotion: Linking theory of mind and emotion in children with autism. *Emotion, 3*(4), 394-400. doi:10.1037/1528-3542.3.4.394

Henderson, H. A., Zahka, N. E., Kojkowski, N. M., Inge, A. P., Schwartz, C. B., Hileman, C. M., . . . Mundy, P. C. (2009). Self-referenced memory, social cognition, and symptom presentation in autism. *Journal of Child Psychology and Psychiatry, 50*(7), 853-861. doi:10.1111/j.1469-7610.2008.02059.x

Hennenlotter, A., Schroeder, U., Erhard, P., Castrop, F., Haslinger, B., Stoecker, D., . . . Ceballos-Baumann, A. O. (2005). A common neural basis for receptive and expressive communication of pleasant facial affect. *NeuroImage, 26*(2), 581-591. doi:10.1016/j.neuroimage.2005.01.057

Herbert, B. M., Herbert, C., & Pollatos, O. (2011). On the relationship between interoceptive awareness and alexithymia: Is interoceptive awareness related to emotional awareness? *Journal of Personality, 79*, 1149-1175. doi:10.1111/j.1467-6494.2011.00717.x

Herbert, B. M., Muth, E. R., Pollatos, O., & Herbert, C. (2012). Interoception across modalities: On the relationship between cardiac awareness and the sensitivity for gastric functions. *PLoS ONE, 7*(5), e36646. doi:10.1371/journal.pone.0036646

Herbert, B. M., Pollatos, O., & Schandry, R. (2007). Interoceptive sensitivity and emotion processing: An EEG study. *International Journal of Psychophysiology, 65*, 214-227. doi://dx.doi.org/10.1016/j.ijpsycho.2007.04.007

Heydrich, L., Aspell, J. E., Marillier, G., Lavanchy, T., Herbelin, B., & Blanke, O. (2018). Cardio-visual full body illusion alters bodily self-consciousness and tactile processing in somatosensory cortex. *Scientific Reports, 8*(1), 9230. doi:0.1038/s41598-018-27698-2

Hill, E., Berthoz, S., & Frith, U. (2004). Brief report: Cognitive processing of own emotions in individuals with autistic spectrum disorder and in their relatives. *Journal of Autism and Developmental Disorders, 34*(2), 229-235. doi:JADD.0000022613.41399.14

Hogan, R. (1969). Development of an empathy scale. *Journal of Consulting and Clinical Psychology, 33*(3), 307-316. doi:10.1037/h0027580

Hogeveen, J., Bird, G., Chau, A., Krueger, F., & Grafman, J. (2016). Acquired alexithymia following damage to the anterior insula. *Neuropsychologia,* doi:10.1016/j.neuropsychologia.2016.01.021

Hölzl, R., Erasmus, L., & Möltner, A. (1996). Detection, discrimination and sensation of visceral stimuli. *Biological Psychology, 42*, 199-214. doi://dx.doi.org/10.1016/0301-0511(95)05155-4

Iarocci, G., & McDonald, J. (2006). *Sensory integration and the perceptual experience of persons with autism* Springer Netherlands. doi:10.1007/s10803-005-0044-3

Immordino-Yang, M. H., Yang, X., & Damasio, H. (2014). Correlations between social-emotional feelings and anterior insula activity are independent from visceral states but influenced by culture. *Frontiers in Human Neuroscience, 8* doi:10.3389/fnhum.2014.00728

Jabbi, M., Bastiaansen, J., & Keysers, C. (2008). A common anterior insula representation of disgust observation, experience and imagination shows divergent functional connectivity pathways. *PLoS ONE, 3*(8), e2939. doi:10.1371/journal.pone.0002939

Jacob, S., Brune, C. W., Carter, C. S., Leventhal, B. L., Lord, C., & Cook Jr, E. H. (2007). Association of the oxytocin receptor gene (OXTR) in caucasian children and adolescents with autism. *Neuroscience Letters, 417*(1), 6-9.

James, W. (1894). Discussion: The physical basis of emotion. *Psychological Review, 1*, 516-529. doi:10.1037/h0065078

Jerath, R., & Crawford, M. W. (2015). Layers of human brain activity: A functional model based on the default mode network and slow oscillations. *Frontiers in Human Neuroscience, 9*, 248.

Johnson, S. A., Filliter, J. H., & Murphy, R. R. (2009). Discrepancies between self- and parent-perceptions of autistic traits and empathy in high functioning children and adolescents on the autism spectrum. *Journal of Autism & Developmental Disorders, 39*(12), 1706-1714. doi:10.1007/s10803-009-0809-1

Johnson C. P., Myers S. M. (2007). Identification and evaluation of children with autism spectrum disorders. *Pediatrics 120,* 1183-1215.

Jones, A. P., Happé, F. G., Gilbert, F., Burnett, S., & Viding, E. (2010). Feeling, caring, knowing: Different types of empathy deficit in boys with psychopathic tendencies and autism spectrum disorder. *Journal of Child Psychology and Psychiatry, 51*(11), 1188-1197. doi:10.1111/j.1469-7610.2010.02280.x

Jones, G. E. (1994). Perception of visceral sensations: A review of recent findings, methodologies, and future directions.

Jones, G. E., Jones, K. R., Rouse, C. H., Scott, D. M., & Caldwell, J. A. (1987). The effect of body position on the perception of cardiac sensations: An experimental and theoretical implications. *Psychophysiology, 24*(3), 300-311. Retrieved from <http://search.ebscohost.com/login.aspx?direct=true&db=s3h&AN=12321170&site=ehost-live>

Jones, W. A., & Klin, A. (2009). Heterogeneity and homogeneity across the autism spectrum: The role of development. *Academic Academy of Child and Adolescent Psychiatry, 48,* 471-473. doi: 10.1097/CHI.0b013e31819f6c0d

Judah, M. R., Shurkova, E. Y., Hager, N. M., White, E. J., Taylor, D. L., & Grant, D. M. (2018b). The relationship between social anxiety and heartbeat evoked potential amplitude. *Biological Psychology,*

Kandasamy, N., Garfinkel, S. N., Page, L., Hardy, B., Critchley, H. D., Gurnell, M., & Coates, J. M. (2016). Interoceptive ability predicts survival on a london trading floor. *Scientific Reports, 6*, 32986. doi:10.1038/srep32986 [doi]

Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child, 2*(3), 217-250.

Kern, J. K., Trivedi, M. H., Grannemann, B. D., Garver, C. R., Johnson, D. G., Andrews, A. A., . . . Schroeder, J. L. (2007). Sensory correlations in autism. *Autism : The International Journal of Research and Practice, 11*(2), 123-134. doi:10.1177/1362361307075702

Kern, M., Aertsen, A., Schulze-Bonhage, A., & Ball, T. (2013). Heart cycle-related effects on event-related potentials, spectral power changes, and connectivity patterns in the human ECoG. *NeuroImage, 81*, 178-190.

Kessler, K., & Thomson, L. A. (2010). The embodied nature of spatial perspective taking: Embodied transformation versus sensorimotor interference. *Cognition, 114*(1), 72-88.

Keysers, C., & Gazzola, V. (2009). Expanding the mirror: Vicarious activity for actions, emotions, and sensations. *Current Opinion in Neurobiology, 19*(6), 666-671. doi:10.1016/j.conb.2009.10.006

Khalsa, S. S., Rudrauf, D., Feinstein, J. S., & Tranel, D. (2009). The pathways of interoceptive awareness. *Nature Neuroscience, 12*, 1494-1496. doi:10.1038/nn.2411

Khalsa, S. S., Adolphs, R., Cameron, O. G., Critchley, H. D., Davenport, P. W., Feinstein, J. S., . . . Mehling, W. E. (2018). Interoception and mental health: A roadmap. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging, 3*(6), 501-513.

Khalsa, S. S., Rudrauf, D., Damasio, A. R., Davidson, R. J., Lutz, A., & Tranel, D. (2008). Interoceptive awareness in experienced meditators. *Psychophysiology, 45*(4), 671-677. doi:10.1111/j.1469-8986.2008.00666.x

Kjelgaard, M. M., Tager-Flusberg, H. (2001) An investigation of language impairment in autism: implications for genetic subgroups. *Language and Cognitive Processes, 16,* 287-308. doi:[10.1080/01690960042000058](https://doi.org/10.1080/01690960042000058)

Klintwall, L., Holm, A., Eriksson, M., Carlsson, L. H., Olsson, M. B., Hedvall, Å, . . . Fernell, E. (2011). Sensory abnormalities in autism: A brief report. *Research in Developmental Disabilities, 32*(2), 795-800. doi://dx.doi.org/10.1016/j.ridd.2010.10.021

Knapp-Kline, K., & Kline, J. P. (2005). Heart rate, heart rate variability, and heartbeat detection with the method of constant stimuli: Slow and steady wins the race. *Biological Psychology, 69*(3), 387-396. doi://dx.doi.org/10.1016/j.biopsycho.2004.09.002

Knoll, J. F., & Hodapp, V. (1992). A comparison between two methods for assessing heartbeat perception. *Psychophysiology, 29*(2), 218-222. doi:10.1111/j.1469-8986.1992.tb01689.x

Koch, K. L., Hong, S., & Xu, L. (2000). Reproducibility of gastric myoelectrical activity and the water load test in patients with dysmotility-like dyspepsia symptoms and in control subjects. *Journal of Clinical Gastroenterology, 31*(2), 125-129.

Koroboki, E., Zakopoulos, N., Manios, E., Rotas, V., Papadimitriou, G., & Papageorgiou, C. (2010). Interoceptive awareness in essential hypertension. *International Journal of Psychophysiology, 78*(2), 158-162.

Kurth, F., Zilles, K., Fox, P. T., Laird, A. R., & Eickhoff, S. B. (2010). A link between the systems: Functional differentiation and integration within the human insula revealed by meta-analysis. *Brain Structure and Function, 214*, 519-534. doi:10.1007/s00429-010-0255-z

Kwakye, L. D., Foss-Feig, J. H., Cascio, C. J., Stone, W. L., & Wallace, M. T. (2011). Altered auditory and multisensory temporal processing in autism spectrum disorders. *Frontiers in Integrative Neuroscience, 4*, 129. doi:10.3389/fnint.2010.00129

Lackner, R. J., & Fresco, D. M. (2016). Interaction effect of brooding rumination and interoceptive awareness on depression and anxiety symptoms. *Behaviour Research and Therapy, 85*, 43-52.

Lambie, J. A., & Marcel, A. J. (2002). Consciousness and the varieties of emotion experience: A theoretical framework. *Psychological Review, 109*, 219-259. doi:10.1037/0033-295X.109.2.219

Lamm, C., Bukowski, H., & Silani, G. (2016). From shared to distinct self–other representations in empathy: Evidence from neurotypical function and socio-cognitive disorders. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1686), 20150083.

Lamm, C., Batson, C. d., & Decety, J. (2007). The neural substrate of human empathy: Effects of perspective-taking and cognitive appraisal. *Cognitive Neuroscience, Journal Of, 19*(1), 42-58. doi:10.1162/jocn.2007.19.1.42

Lamm, C., Decety, J., & Singer, T. (2011). Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *NeuroImage, 54*(3), 2492-2502. doi:10.1016/j.neuroimage.2010.10.014

Lamm, C., & Singer, T. (2010). The role of anterior insular cortex in social emotions. *Brain Structure and Function, 214*(5-6), 579-591. doi:10.1007/s00429-010-0251-3

Lawrence, E. J., Shaw, P., Baker, D., Baron-Cohen, S., & David, A. S. (2004). Measuring empathy: Reliability and validity of the empathy quotient. *Psychological Medicine, 34*(05), 911-920. doi:10.1017/S0033291703001624

Lawson, R. P., Mathys, C., & Rees, G. (2017). Adults with autism overestimate the volatility of the sensory environment. *Nature Neuroscience, 20*(9), 1293-1299. doi:10.1038/nn.4615

Lawson, R. P., Rees, G., & Friston, K. J. (2014). An aberrant precision account of autism. *Frontiers in Human Neuroscience, 8*, 302. doi:10.3389/fnhum.2014.00302

Lee, A., Hobson, R. P., & Chiat, S. (1994). I, you, me, and autism: An experimental study. *Journal of Autism and Developmental Disorders, 24*(2), 155-176. doi:10.1007/BF02172094

Leekam, S. R., Nieto, C., Libby, S. J., Wing, L., & Gould, J. (2007). Describing the sensory abnormalities of children and adults with autism. *Journal of Autism and Developmental Disorders, 37*(5), 894-910. doi:10.1007/s10803-006-0218-7

Lenggenhager, B., Tadi, T., Metzinger, T., & Blanke, O. (2007). Video ergo sum: Manipulating bodily self-consciousness. *Science, 317*(5841), 1096-1099. doi:10.1126/science.1143439

Leopold, C., & Schandry, R. (2001). The heartbeat-evoked brain potential in patients suffering from diabetic neuropathy and in healthy control persons. *Clinical Neurophysiology, 112*(4), 674-682.

Lind, S. E., & Bowler, D. M. (2009). Recognition memory, self-other source memory, and theory-of-mind in children with autism spectrum disorder. *Journal of Autism and Developmental Disorders, 39*(9), 1231.

Linden, W., Wen, F., & Paulhus, D. L. (1995). Measuring alexithymia: Reliability, validity, and prevalence. *Adv Pers Assess, 10*, 51-95. doi:10.1016/S0022-3999(96)00229-2

Lindner, J. L., & Rosén, L. A. (2006). Decoding of emotion through facial expression, prosody and verbal content in children and adolescents with asperger’s syndrome. *Journal of Autism and Developmental Disorders, 36*(6), 769-777.

Livingston, L. A., & Livingston, L. M. (2016). Commentary: Alexithymia, not autism, is associated with impaired interoception. *Frontiers in Psychology, 7*, 1103.

Lockwood, P. L. (2016). The anatomy of empathy: Vicarious experience and disorders of social cognition. *Behavioural Brain Research, 311*, 255-266.

Lockwood, P. L., Bird, G., Bridge, M., & Viding, E. (2013). Dissecting empathy: High levels of psychopathic and autistic traits are characterized by difficulties in different social information processing domains. *Frontiers in Human Neuroscience, 7* doi:10.3389/fnhum.2013.00760

Lombardo, M. V., Chakrabarti, B., Bullmore, E. T., Sadek, S. A., Pasco, G., Wheelwright, S. J., . . . Baron-Cohen, S. (2010). Atypical neural self-representation in autism. *Brain, 133*(2), 611-624. doi:10.1093/brain/awp306

Lombardo, M. V., Chakrabarti, B., Lai, M., & Baron-Cohen, S. (2012). Self-referential and social cognition in a case of autism and agenesis of the corpus callosum.(research)(report). *Molecular Autism, 3*, 14.

Lombardo, M. V., Barnes, J. L., Wheelwright, S. J., & Baron-Cohen, S. (2007). Self-referential cognition and empathy in autism. *PLoS One, 2*(9), e883. doi:10.1371/journal.pone.0000883

Lord, C., Risi, S., Lambrecht, L., Cook Jr, E. H., Leventhal, B. L., DiLavore, P. C., . . . Rutter, M. (2000). The autism diagnostic observation Schedule—Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders, 30*(3), 205-223.

Lord, C., Rutter, M., and Le Couteur, A. (1994). Autism diagnostic interview-revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*, 659–685. doi:10.1007/BF02172145

Loveland, K. A., Tunali–Kotoski, B., Chen, Y. R., Ortegon, J., Pearson, D. A., Brelsford, K. A., & Gibbs, M. C. (1997). Emotion recognition in autism: Verbal and nonverbal information. *Development and Psychopathology, 9*(3), 579-593.

Luft, C. D. B., & Bhattacharya, J. (2015). Aroused with heart: Modulation of heartbeat evoked potential by arousal induction and its oscillatory correlates. *Scientific Reports, 5*, 15717.

Lundqvist, D., Flykt, A., & Öhman, A. (1998). The Karolinska directed emotional faces (KDEF). *CD ROM from Department of Clinical Neuroscience, Psychology Section, Karolinska Institutet,* , 91-630.

Lyons, V., & Fitzgerald, M. (2007). Asperger (1906–1980) and kanner (1894–1981), the two pioneers of autism. *Journal of Autism and Developmental Disorders, 37*(10), 2022-2023.

Magnée, M. J., De Gelder, B., Van Engeland, H., & Kemner, C. (2007). Facial electromyographic responses to emotional information from faces and voices in individuals with pervasive developmental disorder. *Journal of Child Psychology and Psychiatry, 48*(11), 1122-1130. doi:10.1111/j.1469-7610.2007.01779.x

Mai, S., Georgiou, E., & Pollatos, O. (2016). Interoceptive accuracy and the heartbeat-evoked brain potential in adolescents. *European Health Psychologist, 18*(S), 321.

Mai, S., Wong, C. K., Georgiou, E., & Pollatos, O. (2018). Interoception is associated with heartbeat-evoked brain potentials (HEPs) in adolescents. *Biological Psychology, 137*, 24-33.

Maister, L., Cardini, F., Zamariola, G., Serino, A., & Tsakiris, M. (2015). Your place or mine: Shared sensory experiences elicit a remapping of peripersonal space. *Neuropsychologia, 70*, 455-461. doi:10.1016/j.neuropsychologia.2014.10.027

Marchesi, C., Brusamonti, E., & Maggini, C. (2000). Are alexithymia, depression, and anxiety distinct constructs in affective disorders? *Journal of Psychosomatic Research, 49*(1), 43-49. doi:10.1016/S0022-3999(00)00084-2

Marco, E. J., Hinkley, L. B., Hill, S. S., & Nagarajan, S. S. (2011). Sensory processing in autism: A review of neurophysiologic findings. *Pediatr Res, 69*(5 Pt 2), 54R.

Marshall, A. C., Gentsch, A., Jelinčić, V., & Schütz-Bosbach, S. (2017). Exteroceptive expectations modulate interoceptive processing: Repetition-suppression effects for visual and heartbeat evoked potentials. *Scientific Reports, 7*(1), 16525.

Marshall, A. C., Gentsch, A., Schröder, L., & Schütz-Bosbach, S. (2018). Cardiac interoceptive learning is modulated by emotional valence perceived from facial expressions. *Social Cognitive and Affective Neuroscience,*

Mash, L. E., Schauder, K. B., Cochran, C., Park, S., & Cascio, C. J. (2017). Associations between interoceptive cognition and age in autism spectrum disorder and typical development. *Journal of Cognitive Education and Psychology, 16*(1), 23-37.

Mathersul, D., McDonald, S., & Rushby, J. A. (2013a). Automatic facial responses to affective stimuli in high-functioning adults with autism spectrum disorder. *Physiology & Behavior, 109*, 14. doi://dx.doi.org/10.1016/j.physbeh.2012.10.008

Mathersul, D., McDonald, S., & Rushby, J. A. (2013b). Automatic facial responses to briefly presented emotional stimuli in autism spectrum disorder. *Biological Psychology, 94*(2), 397. doi:10.1016/j.biopsycho.2013.08.004

Matson, J. L., and Williams, L. W. (2013). Differential diagnosis and comorbidity: distinguishing autism from other mental health issues. *Neuropsychiatry* 3, 233–243. doi:10.2217/npy.13.1

McIntosh, D. N., Reichmann‐Decker, A., Winkielman, P., & Wilbarger, J. L. (2006). When the social mirror breaks: Deficits in automatic, but not voluntary, mimicry of emotional facial expressions in autism. *Developmental Science, 9*(3), 295-302. doi:10.1111/j.1467-7687.2006.00492.x

Medford, N., & Critchley, H. D. (2010). Conjoint activity of anterior insular and anterior cingulate cortex: Awareness and response. *Brain Structure and Function, 214*(5-6), 535-549.

Mehling, W. E., Price, C., Daubenmier, J. J., Acree, M., Bartmess, E., & Stewart, A. (2012). The multidimensional assessment of interoceptive awareness (MAIA). *PLoS ONE, 7*, e48230. doi:0.1371/journal.pone.0048230

Meissner, K., & Wittmann, M. (2011). Body signals, cardiac awareness, and the perception of time. *Biological Psychology, 86*(3), 289-297.

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: A network model of insula function. *Brain Structure and Function, 214*(5-6), 655-667.

Milosavljevic, B., Leno, V. C., Simonoff, E., Baird, G., Pickles, A., Jones, C. R., . . . Happé, F. (2015). Alexithymia in adolescents with autism spectrum disorder: Its relationship to internalising difficulties, sensory modulation and social cognition. *Journal of Autism and Developmental Disorders,* , 1-14.

Modahl, C., Green, L. A., Fein, D., Morris, M., Waterhouse, L., Feinstein, C., & Levin, H. (1998). Plasma oxytocin levels in autistic children. *Biological Psychiatry, 43*(4), 270-277.

Monk, C. S., Peltier, S. J., Wiggins, J. L., Weng, S., Carrasco, M., Risi, S., & Lord, C. (2009). Abnormalities of intrinsic functional connectivity in autism spectrum disorders. *NeuroImage, 47*(2), 764-772.

Montoya, P., Schandry, R., & Müller, A. (1993). Heartbeat evoked potentials (HEP): Topography and influence of cardiac awareness and focus of attention. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section, 88*(3), 163-172.

Moriguchi, Y., Decety, J., Ohnishi, T., Maeda, M., Mori, T., Nemoto, K., . . . Komaki, G. (2007). Empathy and judging other's pain: An fMRI study of alexithymia. *Cerebral Cortex (New York, N.Y.: 1991), 17*(9), 2223-2234. doi:10.1093/cercor/bhl130

Moriguchi, Y., Ohnishi, T., Lane, R. D., Maeda, M., Mori, T., Nemoto, K., . . . Komaki, G. (2006). Impaired self-awareness and theory of mind: An fMRI study of mentalizing in alexithymia. *NeuroImage, 32*(3), 1472-1482. doi:10.1016/j.neuroimage.2006.04.186

Mukaddes, N. M., & Fateh, R. (2010). High rates of psychiatric co-morbidity in individuals with asperger's disorder. *The World Journal of Biological Psychiatry, 11*(2-2), 486-492.

Mul, C., Stagg, S. D., Herbelin, B., & Aspell, J. E. (2018). "The feeling of me feeling for you: Interoception, alexithymia and empathy in autism". *Journal of Autism and Developmental Disorders,* doi:10.1007/s10803-018-3564-3

Mundy, P. (2003). Annotation: The neural basis of social impairments in autism: The role of the dorsal medial‐frontal cortex and anterior cingulate system. *Journal of Child Psychology and Psychiatry, 44*(6), 793-809.

Mundy, P., Gwaltney, M., & Henderson, H. (2010). Self-referenced processing, neurodevelopment and joint attention in autism. *Autism, 14*, 408-429. doi:10.1177/1362361310366315

Murdaugh, D. L., Shinkareva, S. V., Deshpande, H. R., Wang, J., Pennick, M. R., & Kana, R. K. (2012). Differential deactivation during mentalizing and classification of autism based on default mode network connectivity. *PloS One, 7*(11), e50064.

Murphy, J., Brewer, R., Catmur, C., & Bird, G. (2017). Interoception and psychopathology: A developmental neuroscience perspective. *Developmental Cognitive Neuroscience, 23*, 45-56. doi:10.1016/j.dcn.2016.12.006

Murphy, J., Brewer, R., Hobson, H., Catmur, C., & Bird, G. (2018). Is alexithymia characterised by impaired interoception? further evidence, the importance of control variables, and the problems with the heartbeat counting task. *Biological Psychology, 136*, 189-197.

Murphy, J., Catmur, C., & Bird, G. (2018). Alexithymia is associated with a multidomain, multidimensional failure of interoception: Evidence from novel tests. *Journal of Experimental Psychology: General, 147*(3), 398-408. doi:10.1037/xge0000366

Nemiah, J. C. (1977). Alexithymia. *Psychotherapy and Psychosomatics, 28*(1-4), 199-206. doi:10.1159/000287064

Nguyen, V. T., Breakspear, M., Hu, X., & Guo, C. C. (2016). The integration of the internal and external milieu in the insula during dynamic emotional experiences. *NeuroImage, 124*, 455-463.

Niazy, R. K., Beckmann, C. F., Iannetti, G. D., Brady, J. M., & Smith, S. M. (2005). Removal of FMRI environment artifacts from EEG data using optimal basis sets. *NeuroImage, 28*(3), 720-737.

Noel, J. P., Cascio, C. J., Wallace, M. T., & Park, S. (2017). The spatial self in schizophrenia and autism spectrum disorder. *Schizophrenia Research, 179*, 8-12. doi:S0920-9964(16)30429-7 [pii]

Noel, J., Pfeiffer, C., Blanke, O., & Serino, A. (2015). Peripersonal space as the space of the bodily self. *Cognition, 144*, 49-57. doi:10.1016/j.cognition.2015.07.012

Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain—a meta-analysis of imaging studies on the self. *NeuroImage, 31*(1), 440-457. doi://dx.doi.org/10.1016/j.neuroimage.2005.12.002

Nuske, H. J., Vivanti, G., & Dissanayake, C. (2013). Are emotion impairments unique to, universal, or specific in autism spectrum disorder? A comprehensive review. *Cognition & Emotion, 27*(6), 1042-1061.

Oberman, L. M., Winkielman, P., & Ramachandran, V. S. (2007). Face to face: Blocking facial mimicry can selectively impair recognition of emotional expressions. *Social Neuroscience, 2*(3-4), 167-178. doi:10.1080/17470910701391943

Oberman, L. M., Winkielman, P., & Ramachandran, V. S. (2009). Slow echo: Facial EMG evidence for the delay of spontaneous, but not voluntary, emotional mimicry in children with autism spectrum disorders. *Developmental Science, 12*(4), 510-520. doi:10.1111/j.1467-7687.2008.00796.x

Ochsner, K. N., Zaki, J., Hanelin, J., Ludlow, D. H., Knierim, K., Ramachandran, T., . . . Mackey, S. C. (2008). Your pain or mine? common and distinct neural systems supporting the perception of pain in self and other. *Social Cognitive and Affective Neuroscience, 3*(2), 144-160. doi:10.1093/scan/nsn006; 10.1093/scan/nsn006

Ozonoff, S., Pennington, B. F., & Rogers, S. J. (1990). Are there emotion perception deficits in young autistic children? *Journal of Child Psychology and Psychiatry, 31*(3), 343-361.

Paakki, J., Rahko, J., Long, X., Moilanen, I., Tervonen, O., Nikkinen, J., . . . Haapsamo, H. (2010). Alterations in regional homogeneity of resting-state brain activity in autism spectrum disorders. *Brain Research, 1321*, 169-179. doi://dx.doi.org/10.1016/j.brainres.2009.12.081

Palma, J., & Benarroch, E. E. (2014). Neural control of the heart: Recent concepts and clinical correlations. *Neurology, 83*(3), 261-271.

Palmer, C. J., Lawson, R. P., & Hohwy, J. (2017). Bayesian approaches to autism: Towards volatility, action, and behavior. *Psychological Bulletin, 143*(5), 521.

Palser, E. R., Fotopoulou, A., Pellicano, E., & Kilner, J. M. (2018). The link between interoceptive processing and anxiety in children diagnosed with autism spectrum disorder: Extending adult findings into a developmental sample. *Biological Psychology, 136*, 13-21.

Park, H., Bernasconi, F., Bello-Ruiz, J., Pfeiffer, C., Salomon, R., & Blanke, O. (2016). Transient modulations of neural responses to heartbeats covary with bodily self-consciousness. *Journal of Neuroscience, 36*(32), 8453-8460.

Park, H., Bernasconi, F., Salomon, R., Tallon-Baudry, C., Spinelli, L., Seeck, M., . . . Blanke, O. (2017). Neural sources and underlying mechanisms of neural responses to heartbeats, and their role in bodily self-consciousness: An intracranial EEG study. *Cerebral Cortex, 28*(7), 2351-2364.

Park, H., & Blanke, O. (2019). Coupling inner and outer body for self-consciousness. *Trends in Cognitive Sciences,*

Park, H., & Tallon-Baudry, C. (2014). The neural subjective frame: From bodily signals to perceptual consciousness. *Philosophical Transactions of the Royal Society B: Biological Sciences, 369*(1641), 20130208.

Parker, J. D., Taylor, G. J., & Bagby, R. M. (2003). The 20-item toronto alexithymia scale: III. reliability and factorial validity in a community population. *Journal of Psychosomatic Research, 55*(3), 269-275. doi:10.1016/0022-3999(94)90006-X

Paton, B., Hohwy, J., & Enticott, P. G. (2012). The rubber hand illusion reveals proprioceptive and sensorimotor differences in autism spectrum disorders. *Journal of Autism and Developmental Disorders, 42*, 1-14. doi:10.1007/s10803-011-1430-7

Paulus, M. P., & Stein, M. B. (2010). Interoception in anxiety and depression. *Brain Structure and Function, 214*, 451-463. doi:10.1007/s00429-010-0258-9

Pellicano, E., & Burr, D. (2012). When the world becomes ‘too real’: A bayesian explanation of autistic perception. *Trends in Cognitive Sciences, 16*(10), 504-510. doi:10.1016/j.tics.2012.08.009

Petzschner, F. H., Weber, L. A., Wellstein, K. V., Paolini, G., Do, C. T., & Stephan, K. E. (2018). Focus of attention modulates the heartbeat evoked potential. *bioRxiv,* 384305.

Pezzulo, G., Rigoli, F., & Friston, K. (2015). Active inference, homeostatic regulation and adaptive behavioural control. *Progress in Neurobiology, 134*, 17-35.

Philip, R., Whalley, H. C., Stanfield, A. C., Sprengelmeyer, R., Santos, I. M., Young, A. W., . . . Lawrie, S. M. (2010). Deficits in facial, body movement and vocal emotional processing in autism spectrum disorders. *Psychological Medicine, 40*(11), 1919-1929.

Phillips, G. C., Jones, G. E., Rieger, E. J., & Snell, J. B. (1999). Effects of the presentation of false heart‐rate feedback on the performance of two common heartbeat‐detection tasks. *Psychophysiology, 36*(4), 504-510. doi:10.1017/S0048577299980071

Phillips, M. L., Young, A. W., Scott, S., Calder, A. J., Andrew, C., Giampietro, V., . . . Gray, J. A. (1998). Neural responses to facial and vocal expressions of fear and disgust. *Proceedings of the Royal Society of London.Series B: Biological Sciences, 265*(1408), 1809-1817. doi:10.1098/rspb.1998.0506

Piech, R. M., Strelchuk, D., Knights, J., Hjälmheden, J. V., Olofsson, J. K., & Aspell, J. E. (2017). People with higher interoceptive sensitivity are more altruistic, but improving interoception does not increase altruism. *Scientific Reports, 7*(1), 15652.

Pollatos, O., & Ferentzi, E. (2018). Embodiment of emotion regulation. *Embodiment in psychotherapy* (pp. 43-55) Springer.

Pollatos, O., Herbert, B. M., Matthias, E., & Schandry, R. (2007). Heart rate response after emotional picture presentation is modulated by interoceptive awareness. *International Journal of Psychophysiology, 63*(1), 117-124.

Pollatos, O., Kirsch, W., & Schandry, R. (2005). Brain structures involved in interoceptive awareness and cardioafferent signal processing: A dipole source localization study. *Human Brain Mapping, 26*(1), 54-64.

Pollatos, O., & Schandry, R. (2004). Accuracy of heartbeat perception is reflected in the amplitude of the heartbeat-evoked potential. *Psychophysiology, 41*, 476-482. doi:10.1111/1469-8986.2004.00170.x

Pollatos, O., Traut‐Mattausch, E., & Schandry, R. (2009). Differential effects of anxiety and depression on interoceptive accuracy. *Depression and Anxiety, 26*(2), 167-173. doi:10.1002/da.20504

Pollatos, O., Traut-Mattausch, E., Schroeder, H., & Schandry, R. (2007). Interoceptive awareness mediates the relationship between anxiety and the intensity of unpleasant feelings. *Journal of Anxiety Disorders, 21*(7), 931-943.

Porges, S. (1993). Body perception questionnaire. *Laboratory of Developmental Assessment, University of Maryland,*

Preston, S. D., & De Waal, F. (2002). Empathy: Its ultimate and proximate bases. *Behavioral and Brain Sciences, 25*(01), 1-20. doi:10.1017/S0140525X02000018

Quadt, L., Critchley, H. D., & Garfinkel, S. N. (2018a). Interoception and emotion: Shared mechanisms and clinical implications. *The Interoceptive Mind: From Homeostasis to Awareness,* , 123.

Quadt, L., Critchley, H. D., & Garfinkel, S. N. (2018b). The neurobiology of interoception in health and disease. *Annals of the New York Academy of Sciences, 1428*(1), 112-128.

Quattrocki, E., & Friston, K. (2014). Autism, oxytocin and interoception. *Neuroscience & Biobehavioral Reviews, 47*, 410-430. doi:10.1016/j.neubiorev.2014.09.012

Reniers, R. L., Corcoran, R., Drake, R., Shryane, N. M., & Völlm, B. A. (2011). The QCAE: A questionnaire of cognitive and affective empathy. *Journal of Personality Assessment, 93*(1), 84-95. doi:10.1080/00223891.2010.528484

Rieffe, C., Oosterveld, P., Terwogt, M. M., Mootz, S., Van Leeuwen, E., & Stockmann, L. (2011). Emotion regulation and internalizing symptoms in children with autism spectrum disorders. *Autism, 15*(6), 655-670.

Ring, C., & Brener, J. (1996). Influence of beliefs about heart rate and actual heart rate on heartbeat counting. *Psychophysiology, 33*(5), 541-546.

Ring, C., & Brener, J. (2018). Heartbeat counting is unrelated to heartbeat detection: A comparison of methods to quantify interoception. *Psychophysiology,* e13084.

Ring, C., Brener, J., Knapp, K., & Mailloux, J. (2015). Effects of heartbeat feedback on beliefs about heart rate and heartbeat counting: A cautionary tale about interoceptive awareness. *Biological Psychology, 104*, 193-198.

Rizzolatti, G., & Craighero, L. (2004). The mirror-neuron system. *Annu.Rev.Neurosci., 27*, 169-192. doi:10.1146/annurev.neuro.27.070203.144230

Robertson, C. E., & Baron-Cohen, S. (2017). Sensory perception in autism. *Nature Reviews Neuroscience, 18*(11), 671.

Rogers, K., Dziobek, I., Hassenstab, J., Wolf, O. T., & Convit, A. (2007). Who cares? revisiting empathy in asperger syndrome. *Journal of Autism and Developmental Disorders, 37*(4), 709-715. doi:10.1007/s10803-006-0197-8

Rogers, C., Goddard, L., Hill, E. L., Henry, L. A., & Crane, L. (2016). Experiences of diagnosing autism spectrum disorder: A survey of professionals in the United Kingdom. *Autism: The International Journal of Research and Practice, 20*(7), 820–831.  [doi:10.1177/1362361315611109](https://doi.org/10.1177/1362361315611109)

Rouse, C. H., Jones, G. E., & Jones, K. R. (1988). The effect of body composition and gender on cardiac awareness. *Psychophysiology, 25*(4), 400-407. doi:10.1111/j.1469-8986.1988.tb01876.x

Rozga, A., King, T. Z., Vuduc, R. W., & Robins, D. L. (2013). Undifferentiated facial electromyography responses to dynamic, audio‐visual emotion displays in individuals with autism spectrum disorders. *Developmental Science, 16*(4), 499-514. doi:10.1111/desc.12062

Rueda, P., Fernández-Berrocal, P., & Baron-Cohen, S. (2014). Dissociation between cognitive and affective empathy in youth with asperger syndrome. *European Journal of Developmental Psychology,* (ahead-of-print), 1-14. doi:10.1080/17405629.2014.950221

Salomon, R., Lim, M., Pfeiffer, C., Gassert, R., & Blanke, O. (2013). Full body illusion is associated with widespread skin temperature reduction. *Frontiers in Behavioral Neuroscience, 7*, 65.

Salomon, R., Noel, J., Łukowska, M., Faivre, N., Metzinger, T., Serino, A., & Blanke, O. (2017). Unconscious integration of multisensory bodily inputs in the peripersonal space shapes bodily self-consciousness. *Cognition, 166*, 174-183. doi:10.1016/j.cognition.2017.05.028

Samson, A. C., Huber, O., & Gross, J. J. (2012). Emotion regulation in asperger's syndrome and high-functioning autism. *Emotion, 12*(4), 659-665. doi:10.1037/a0027975

Samson, A. C., Phillips, J. M., Parker, K. J., Shah, S., Gross, J. J., & Hardan, A. Y. (2014). Emotion dysregulation and the core features of autism spectrum disorder. *Journal of Autism and Developmental Disorders, 44*(7), 1766-1772.

Schachter, S., & Singer, J. E. (1962). Cognitive, social, and physiological determinants of an emotional state. *Psychological Review, 69*, 377-397. doi:10.1037/h0046234

Schaefer, M., Egloff, B., & WitthÃ¶ft, M. (2012). Is interoceptive awareness really altered in somatoform disorders? testing competing theories with two paradigms of heartbeat perception. *Journal of Abnormal Psychology, 121*, 719-724. doi:10.1037/a0028509

Schandry, R., Sparrer, B., & Weitkunat, R. (1986). From the heart to the brain: A study of heartbeat contingent scalp potentials. *International Journal of Neuroscience, 30*(4), 261-275.

Schandry, R. (1981). Heartbeat perception and emotional experience. *Psychophysiology, 18*, 483-488. doi:10.1111/j.1469-8986.1981.tb02486.x

Schandry, R., Bestler, M., & Montoya, P. (1993). On the relation between cardiodynamics and heartbeat perception. *Psychophysiology, 30*(5), 467-474.

Schandry, R., & Montoya, P. (1996). Event-related brain potentials and the processing of cardiac activity. *Biological Psychology, 42*(1-2), 75-85.

Schauder, K. B., Mash, L. E., Bryant, L. K., & Cascio, C. J. (2014). Interoceptive ability and body awareness in autism spectrum disorder. *Journal of Experimental Child Psychology, in press* doi:10.1016/j.jecp.2014.11.002

Schulz, A., Lass-Hennemann, J., Sütterlin, S., Schächinger, H., & Vögele, C. (2013). Cold pressor stress induces opposite effects on cardioceptive accuracy dependent on assessment paradigm. *Biological Psychology, 93*(1), 167-174. doi:10.1016/j.biopsycho.2013.01.007

Seth, A. K., Suzuki, K., & Critchley, H. D. (2012). An interoceptive predictive coding model of conscious presence. *Frontiers in Psychology, 2*, 395. doi:10.3389/fpsyg.2011.00395; 10.3389/fpsyg.2011.00395

Seth, A. K. (2013). Interoceptive inference, emotion, and the embodied self. *Trends in Cognitive Sciences, 17*(11), 565-573. doi:10.3389/fpsyg.2011.00395

Seth, A. K., & Critchley, H. D. (2013). Extending predictive processing to the body: Emotion as interoceptive inference. *Behavioral and Brain Sciences,* , 47-48. doi://dx.doi.org/10.1017/S0140525X12002270

Seth, A. K., & Friston, K. J. (2016). Active interoceptive inference and the emotional brain. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1708), 20160007.

Seth, A. K., & Tsakiris, M. (2018). Being a beast machine: The somatic basis of selfhood. *Trends in Cognitive Sciences,*

Shah, P., Catmur, C., & Bird, G. (2016a). Emotional decision-making in autism spectrum disorder: The roles of interoception and alexithymia. *Molecular Autism, 7*(1), 43.

Shah, P., Hall, R., Catmur, C., & Bird, G. (2016). Alexithymia, not autism, is associated with impaired interoception. *Cortex, 81*, 215-220. doi:10.1016/j.cortex.2016.03.021

Shalom, D. B., Mostofsky, S. H., Hazlett, R. L., Goldberg, M. C., Landa, R. J., Faran, Y., . . . Hoehn-Saric, R. (2006). Normal physiological emotions but differences in expression of conscious feelings in children with high-functioning autism. *Journal of Autism and Developmental Disorders, 36*(3), 395-400. doi:10.1007/s10803-006-0077-2

Shamay-Tsoory, S. G., Shur, S., Barcai-Goodman, L., Medlovich, S., Harari, H., & Levkovitz, Y. (2007). Dissociation of cognitive from affective components of theory of mind in schizophrenia. *Psychiatry Research, 149*, 11-23. doi://dx.doi.org/10.1016/j.psychres.2005.10.018

Sherrington, C. S. (1966). *The integrative action of the nervous system*. Cambridge, England: Cambridge University Press Archive.

Shields, S. A., Mallory, M. E., & Simon, A. (1989). The body awareness questionnaire: Reliability and validity. *Journal of Personality Assessment, 53*(4), 802-815.

Silani, G., Bird, G., Brindley, R., Singer, T., Frith, C., & Frith, U. (2008). Levels of emotional awareness and autism: An fMRI study. *Social Neuroscience, 3*, 97-112. doi:10.1080/17470910701577020

Simmons, W. K., Avery, J. A., Barcalow, J. C., Bodurka, J., Drevets, W. C., & Bellgowan, P. (2012). Keeping the body in mind: Insula functional organization and functional connectivity integrate interoceptive, exteroceptive, and emotional awareness. *Human Brain Mapping, 34*, 2944-2958. doi:10.1002/hbm.22113

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., and Baird, G. (2008). Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child and Adolescent Psychiatry,*  *47,* 921–929. doi:10.1097/CHI.0b013e318179964f

Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R. J., & Frith, C. D. (2004). Empathy for pain involves the affective but not sensory components of pain. *Science (New York, N.Y.), 303*(5661), 1157-1162. doi:10.1126/science.1093535 [doi]

Singer, T. (2009). Understanding others: Brain mechanisms of theory of mind and empathy. *Neuroeconomics: Decision Making and the Brain,* , 251-268.

Singer, T., Critchley, H. D., & Preuschoff, K. (2009). A common role of insula in feelings, empathy and uncertainty. *Trends in Cognitive Sciences, 13*(8), 334-340. doi://dx.doi.org/10.1016/j.tics.2009.05.001

Skokauskas, N., & Gallagher, L. (2010). Psychosis, affective disorders and anxiety in autistic spectrum disorder: Prevalence and nosological considerations. *Psychopathology, 43*(1), 8-16. doi:10.1159/000255958 [doi]

Sridharan, D., Levitin, D. J., & Menon, V. (2008). A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proceedings of the National Academy of Sciences, 105*(34), 12569-12574.

Stevenson, R. A., Siemann, J. K., Schneider, B. C., Eberly, H. E., Woynaroski, T. G., Camarata, S. M., & Wallace, M. T. (2014). Multisensory temporal integration in autism spectrum disorders. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 34*(3), 691-697. doi:10.1523/JNEUROSCI.3615-13.2014 [doi]

Stewart, M. E., McAdam, C., Ota, M., Peppé, S., & Cleland, J. (2013). Emotional recognition in autism spectrum conditions from voices and faces. *Autism, 17*(1), 6-14.

Summerfield, C., Trittschuh, E. H., Monti, J. M., Mesulam, M., & Egner, T. (2008). Neural repetition suppression reflects fulfilled perceptual expectations. *Nature Neuroscience, 11*(9), 1004.

Summerfield, C., Wyart, V., Mareike Johnen, V., & De Gardelle, V. (2011). Human scalp electroencephalography reveals that repetition suppression varies with expectation. *Frontiers in Human Neuroscience, 5*, 67.

Suzuki, K., Garfinkel, S. N., Critchley, H. D., & Seth, A. K. (2013). Multisensory integration across exteroceptive and interoceptive domains modulates self-experience in the rubber-hand illusion. *Neuropsychologia, 51*(13), 2909-2917. doi://dx.doi.org/10.1016/j.neuropsychologia.2013.08.014

Swart, M., Kortekaas, R., & Aleman, A. (2009). Dealing with feelings: Characterization of trait alexithymia on emotion regulation strategies and cognitive-emotional processing. *PloS One, 4*(6), e5751. doi:10.1371/journal.pone.0005751

Tager-Flusberg, H. (2000). Understanding the language and communicative impairments in autism. In L. M. Glidden (Ed.), *Autism* (pp. 185-205). San Diego: Academic Press.

Tallon-Baudry, C., & Bertrand, O. (1999). Oscillatory gamma activity in humans and its role in object representation. *Trends in Cognitive Sciences, 3*(4), 151-162.

Tani, P., Lindberg, N., Joukamaa, M., Nieminen-von Wendt, T., von Wendt, L., Appelberg, B., . . . Porkka-Heiskanen, T. (2004). Asperger syndrome, alexithymia and perception of sleep. *Neuropsychobiology, 49*(2), 64-70.

Teneggi, C., Canzoneri, E., di Pellegrino, G., & Serino, A. (2013). Social modulation of peripersonal space boundaries. *Current Biology, 23*(5), 406-411. doi:10.1016/j.cub.2013.01.043

Terasawa, Y., Moriguchi, Y., Tochizawa, S., & Umeda, S. (2014). Interoceptive sensitivity predicts sensitivity to the emotions of others. *Cognition & Emotion,* (ahead-of-print), 1-14. doi:10.1080/02699931.2014.888988

Terhaar, J., Viola, F. C., Bär, K., & Debener, S. (2012). Heartbeat evoked potentials mirror altered body perception in depressed patients. *Clinical Neurophysiology, 123*(10), 1950-1957.

Todorovic, A., & de Lange, F. P. (2012). Repetition suppression and expectation suppression are dissociable in time in early auditory evoked fields. *Journal of Neuroscience, 32*(39), 13389-13395.

Tordjman, S., Celume, M. P., Denis, L., Motillon, T., & Keromnes, G. (2019). Reframing schizophrenia and autism as self-consciousness disorders associating a deficit of theory of mind and empathy with social communication impairments. *Neuroscience & Biobehavioral Reviews,*

Tracy, J. L., Robins, R. W., Schriber, R. A., & Solomon, M. (2011). Is emotion recognition impaired in individuals with autism spectrum disorders? *Journal of Autism and Developmental Disorders, 41*(1), 102-109.

Tsakiris, M., Tajadura-Jimenez, A., & Costantini, M. (2011). Just a heartbeat away from one's body: Interoceptive sensitivity predicts malleability of body-representations. *Proceedings.Biological Sciences / the Royal Society, 278*(1717), 2470-2476. doi:10.1098/rspb.2010.2547; 10.1098/rspb.2010.2547

Tsakiris, M. (2008). Looking for myself: Current multisensory input alters self-face recognition. *PloS One, 3*(12), e4040. doi:10.1371/journal.pone.0004040

Uddin, L. Q., & Menon, V. (2009). The anterior insula in autism: Under-connected and under-examined. *Neuroscience & Biobehavioral Reviews, 33*(8), 1198-1203. doi://dx.doi.org/10.1016/j.neubiorev.2009.06.002

Uddin, L. Q., Supekar, K., Lynch, C. J., Khouzam, A., Phillips, J., Feinstein, C., . . . Menon, V. (2013). Salience network–based classification and prediction of symptom severity in children with autism. *JAMA Psychiatry, 70*(8), 869-879.

Uljarevic, M., & Hamilton, A. (2013). Recognition of emotions in autism: A formal meta-analysis. *Journal of Autism and Developmental Disorders, 43*(7), 1517-1526. doi:10.1007/s10803-012-1695-5

Vaitl, D. (1996). Interoception. *Biological Psychology, 42*(1), 1-27. doi:10.1016/0301-0511(95)05144-9

Van Boxtel, J. J., & Lu, H. (2013). A predictive coding perspective on autism spectrum disorders. *Frontiers in Psychology, 4*, 19. doi:10.3389/fpsyg.2013.00019

Van de Cruys, S., Evers, K., Van der Hallen, R., Van Eylen, L., Boets, B., de-Wit, L., & Wagemans, J. (2014). Precise minds in uncertain worlds: Predictive coding in autism. *Psychological Review, 121*(4), 649.

Volkmar, F., Chawarska, K., & Klin, A. (2005). Autism in infancy and early childhood. *Annual Review of Psychology, 56,* 315-336.

Wechsler, D. (2011). *Wechsler abrreviated scale of intelligence second edition - WASI-II.* London: Pearson.

Weineck, F., Messner, M., Hauke, G., & Pollatos, O. (2019). Improving interoceptive ability through the practice of power posing: A pilot study. *PloS One, 14*(2), e0211453.

Weng, S., Wiggins, J. L., Peltier, S. J., Carrasco, M., Risi, S., Lord, C., & Monk, C. S. (2010). Alterations of resting state functional connectivity in the default network in adolescents with autism spectrum disorders. *Brain Research, 1313*, 202-214.

Werner, N. S., Jung, K., Duschek, S., & Schandry, R. (2009). Enhanced cardiac perception is associated with benefits in decision‐making. *Psychophysiology, 46*(6), 1123-1129.

Werner, N. S., Peres, I., Duschek, S., & Schandry, R. (2010). Implicit memory for emotional words is modulated by cardiac perception. *Biological Psychology, 85*(3), 370-376.

Whitehead, W. E., Drescher, V. M., Heiman, P., & Blackwell, B. (1977). Relation of heart rate control to heartbeat perception. *Biofeedback and Self-Regulation, 2*, 371-392. doi:10.1007/BF00998623

Wicker, B., Keysers, C., Plailly, J., Royet, J., Gallese, V., & Rizzolatti, G. (2003). Both of us disgusted in< i> my insula: The common neural basis of seeing and feeling disgust. *Neuron, 40*(3), 655-664. doi:10.1016/S0896-6273(03)00679-2

Wiebking, C., Duncan, N. W., Tiret, B., Hayes, D. J., Marjaǹska, M., Doyon, J., . . . Northoff, G. (2014). GABA in the insula—a predictor of the neural response to interoceptive awareness. *NeuroImage, 86*, 10-18.

Wiens, S. (2005). Interoception in emotional experience. *Current Opinion in Neurology, 18*, 442-447.

Wiens, S., Mezzacappa, E. S., & Katkin, E. S. (2000). Heartbeat detection and the experience of emotions. *Cognition & Emotion, 14*(3), 417-427. doi:10.1080/026999300378905

Wing, L. (1997). The autistic spectrum. *The Lancet, 350*, 1761-1766. doi:10.1016/S0140-6736(97)09218-0

Wittmann, M. (2013). The inner sense of time: How the brain creates a representation of duration. *Nature Reviews Neuroscience, 14*(3), 217.

Woodbury-Smith, M. R., Robinson, J., Wheelwright, S., & Baron-Cohen, S. (2005). Screening adults for asperger syndrome using the AQ: A preliminary study of its diagnostic validity in clinical practice. *Journal of Autism and Developmental Disorders, 35*(3), 331-335.

Yoris, A., García, A. M., Traiber, L., Santamaría-García, H., Martorell, M., Alifano, F., . . . Manes, F. (2017). The inner world of overactive monitoring: Neural markers of interoception in obsessive–compulsive disorder. *Psychological Medicine, 47*(11), 1957-1970.

Yuan, H., Yan, H., Xu, X., Han, F., & Yan, Q. (2007). Effect of heartbeat perception on heartbeat evoked potential waves. *Neuroscience Bulletin, 23*(6), 357-362.

Zaki, J., Davis, J. I., & Ochsner, K. N. (2012). Overlapping activity in anterior insula during interoception and emotional experience. *NeuroImage, 62*(1), 493-499. doi://dx.doi.org/10.1016/j.neuroimage.2012.05.012

Zamariola, G., Frost, N., Van Oost, A., Corneille, O., & Luminet, O. (2019). Relationship between interoception and emotion regulation: New evidence from mixed methods. *Journal of Affective Disorders, 246*, 480-485.

Zamariola, G., Maurage, P., Luminet, O., & Corneille, O. (2018). Interoceptive accuracy scores from the heartbeat counting task are problematic: Evidence from simple bivariate correlations. *Biological Psychology, 137*, 12-17.

# Appendix 1



 The Self To Other Model (SOME) – Bird & Viding (2014).

1. A shorter version of this chapter, reporting study 3, was published: Mul, C., Stagg, S. D., Herbelin, B. & Aspell, J. E. (2018). The feeling of me feeling for you: Interoception, alexithymia and empathy in autism. *Journal of Autism and Developmental Disorders, 48,* 2953-2967. doi: 10.1007/s10803-018-3564-3 [↑](#footnote-ref-1)
2. A shorter version of this chapter was published: Mul, C., Cardini, F., Stagg, S. D., Sadeghi Esfahlani, S., Kiourtoglou, D., & Aspell, J. E. (2019). Altered bodily self-consciousness and peripersonal space in autism. *Autism,* doi:10.1177/1362361319838950. [↑](#footnote-ref-2)