# Individual Differences in Behavioural & Physiological Responses to Affective Touch.

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#### Abstract

This thesis examines how individual differences in social traits relate to behavioural and physiological responses to affective touch. Over the last few decades the functionality of C-Tactile afferents (CTs) have been investigated, with researchers positing that CTs function to signal the rewarding value of social tactile interactions. Here, by exploring the relationship between trait sociability and affective touch perception this social touch hypothesis is explored. In the first three studies, the role of sociability on the vicarious experience of affective touch was investigated. In study one; the aim was to determine how trait sociability affected an individual's vicarious experience of affective and discriminative touch. Here, individuals with the lowest number of autistic traits and theoretically the highest sociability were found to show the greatest sensitivity in their affective ratings of different velocities of touch, resulting in a significant quadratic relationship between non-CT-optimal and CToptimal stimuli at CT-innervated locations. In study two the aim was investigate the vicarious experience of touch in young children. Children both with a diagnosis of ASD (here theorised to be one extremity of trait sociability) and without ASD observed the same videos depicting social touch. It was found that young children (aged 7-12) did not show the typically observed vicarious preference for CT-optimal velocity touch. Furthermore, there was no difference between children with an autism spectrum disorder (ASD) and typically developing children in their affective ratings of the observed touch. Study three again took the same sample of videos and used facial EMG to see whether the explicitly rated vicarious preference for CT-optimal over non-CT-optimal touch could be detected implicitly. It was found that observation of CT-optimal social tactile interactions did not elicit the same affective responses that have previously been reported in response to directly felt touch. This finding is perhaps consistent with the rather weak affective response elicited by touch in comparison to pain, for example. The fact that self-reported levels of empathetic concern

correlated negatively with corrugator muscle activity, indicative of negative affect, in response to touch on CT innervated sites suggests individual differences in implicit affective response to touch are present. In study four, the aim was to determine whether individual differences in trait sociability affected implicit affective responses to first-hand experience of touch. Consistently, participants will low levels of autistic traits (high trait sociability) showed greater zygomaticus activity, indicative of positive affect, during evaluation of the touch they received than those with high levels of autistic traits. Stroking touch elicited little activity in the Corrugator, indicative of negative affect, in either group. Finally, study 5 used EEG to determine how the cortical activity related to fast conducting Aβ stimulation compared to later activity in response to slow conducting CTs. Specifically an ultra-late potential (ULP) was measured for CT-optimal stimuli. Furthermore, 30cm/s, which generates greater A $\beta$  stimulation than 3cm/s, elicited a significantly greater p300 orienting response. Furthermore, there was a significant difference in the ULP peak amplitude between individuals with high and low levels of autistic traits suggesting differential patterns of activity. Taken together, these studies suggest that touch, including touch targeted to optimally activate CTs is indeed processed differently, both physiologically and behaviourally, by individuals with different levels of autistic traits, whether directly felt or vicariously experienced. It is hypothesised that these differences s reflect variation in sensitivity to the rewarding value of social stimuli. These studies provide some of the first evidence that individual differences in stable personality traits are associated with differential responses to social / affective touch.

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#### **<u>Chapter 1.</u>** General Introduction

#### 1.1. Primary Cutaneous Sensory Nerves & Receptors of Discriminative Touch

The sense of touch allows an individual to locate, interact with and distinguish between objects they come into contact with (McGlone, Wessberg, & Olausson, 2014). Anatomically, large myelinated A-type sensory fibres provide rapid information about stretch, pressure, slip and vibration.



**Figure 1**. Innervation of the hairy and glabrous skin (from McGlone et al., 2014). Shown here are the afferents responsible for different functions of Somatosensation, divided into A-type (1.1) and C-type (1.2) categories. These afferents are further subcategorised depending on their activation properties and the stimuli they respond most prominently to. For example,  $A\beta$  afferents that are rapidly adapting (for transient stimulation) are likely to be responsible for determining the texture of an object, and slow adapting afferents that provide a sustained response to skin contact, for detecting skin stretch and the continuous activation through static touch.  $A\delta$  afferents on the other hand are responsible for rapid detection of painful stimuli.

This discriminative aspect of touch is sub-served by four different receptors: 1. Meissner's corpuscles, 2. Pacinian corpuscles, 3. Merkel's disks & 4. Ruffini endings. Pacinian corpuscles are responsible for detecting rapid vibrations on the skin and Meissner's corpuscles detect slower vibrations likely to be responsible for texture detection. These are both served by rapidly adapting afferents, which provide transient responses to stimuli, thus providing frequent rapid inputs relating to the texture of a stimulus (*Figure* 1). Comparatively, Merkel's disks and Ruffini endings detect pressure and skin stretch respectively. These receptors are served by slow adapting afferents that produce sustained responses to stimulation (*Figure* 1).

In addition, thinly myelinated,  $A\delta$  fibres, with subtypes responding to mechanical, thermal and nociceptive stimuli, convey information to the brain at a medium velocity.  $A\delta$  nociceptors are the peripheral component of what is termed First pain, conveying rapidly perceived, discriminative information about potential skin damage (McGlone & Reilly 2011) (*Figure 1*).

#### 1.1.1. Central Projections of Myelinated Fibres

Discriminative somatosensory perception is sub served by myelinated afferents that ascend via the dorsal columns and dorsal column nuclei to the somatosensory cortex (SI) (Mountcastle, 2005). Further projections extend to the secondary somatosensory cortex (SII) which is theorised to integrate sensory input with motor input which may have a role in proprioception (Lin & Forss, 2002). S1 is divided into layers, each of which process input from different receptive fields on the cutaneous surface (Gardner, 1988). Each location on the skin is represented by a population of neurons in S1 meaning that somatosensory perception can be mapped onto the cortex (Nelson, Sur, Felleman, & Kaas, 1980). The cortical mapping in this region of the brain is represented by a sensory homunculus with more densely innervated body locations, resulting in higher tactile acuity, having greater cortical representation (Penfield & Rasmussen, 1953). This somatotopic organisation has been shown in infants as young as 7-months old (Saby, Meltzoff, & Marshall, 2015) where stimulation of the foot or hand activated distinctly different regions of S1.

The plasticity of this somatotopic representation of the body is demonstrated by the changes in cortical structure of S1 observed in individuals affected by neurological damage, which results in atypical sensory experience. For example, individuals with Carpal Tunnel Syndrome show altered somatotopic organisation in S1 as a result of continuous stimulation of the trapped median nerve (Tecchio, Padua, Aprile, & Rossini, 2002). Furthermore, in the motor disorder Dystonia there is some evidence that disturbances of the sensory system may underlie aspects of its symptomology. Consistent with this, in an fMRI study, fingertip stimulation revealed differences in the patients' cortical representation of these body sites compared to a healthy control group (Butterworth et al., 2003). In addition, in patients who have undergone limb amputation, changes in the cortical representation of the body are apparent. For example, in upper-limb amputees, the area of primary somatosensory cortex representing the face was found to shift several centimetres towards the area that previously received input from nerves supplying the absent limb (Elbert et al., 1994). This suggests somatosensory maps in S1 are dependent on regular activation of peripheral sensory afferents.

#### **1.2.** Primary Sensory Afferents and Receptors of Affective Touch

C-fibres are thin, unmyelinated, slowly conducting nerves typically recognised as encoding nociceptive and pruritic sensations. C-fibres are abundant in the hairy skin of the body. In fact, under electron microscopy 90% of nerve fibres found in the dermis were reported to be unmyelinated (Ebenezer et al., 2007). C-nociceptors are the peripheral component of what is termed Second pain. Their much slower conduction velocity means they have has little discriminative value but rather convey the negative emotional quality of the stimulus (McGlone & Reilly 2010; Bessou & Perl, 1969). The fact that, in addition to its discriminative function, there is also an emotional or affective dimension to touch has only relatively recently been recognised, with the identification and characterisation of a class of low threshold, mechanosensitive C-fibres, which in humans are named C-tactile afferents (CTs) (Vallbo, Olausson, Wessberg, & Norrsell, 1993)

C-low threshold mechanoreceptors (C-LTMs) were first identified in the cat; Zotterman (1939) recorded small amplitude impulses from the saphenous nerve during gentle stroking. He reasoned these were conveyed by small unmyelinated neurons due to their slow conduction velocity. Having now been identified in the hairy skin of a range of mammals (*see* Pitcher, Le Pichon, & Chesler, 2016), including humans (Nordin, 1990), their response characteristics have been mapped using the electrophysiological technique microneurography (MNG) (Vallbo and Hagbarth, 1968). MNG involves the insertion of a thin tungsten electrode (approximate tip diameter 5µm) percutaneously into individual cutaneous sensory nerve fascicles. These electrodes can then record the firing frequency of the nerve fibre in response to stimulation of its receptive field.

Using MNG, originally unexpected slow velocity activation was first measured directly from the supraorbital/infraorbital nerves of the face (Johansson, Trulsson, Olsson, & Westberg, 1988; Nordin & Hagbarth, 1989). CTs respond preferentially to slow, gentle stroking touch at between 1 and 10cm/sec (Vallbo et al., 1999), they have low mechanical thresholds of about 0.23g (Nordin, 1990). Recently, CTs have been found to be temperature sensitive, responding most prominently to a skin temperature stimulus (32 degrees) ( Ackerley, Backlund Wasling, et al., 2014). Anatomically, CT afferents are found solely in the hairy skin. In humans CTs have never been found innervating the glabrous skin on the palms of the hand or soles of the feet (Nordin, 1990; Vallbo, Olausson, Wessberg & Norrsell, 1993; Edin, 2001; Liu *et al*, 2007). Although one study reported C-LTMS were present in the skin of hind paw of rats (Djouhri, 2016).

Physiologically, CTs have different characteristics to the A $\beta$  sensory nerves most frequently measured on the palm (Löken, Wessberg, Morrison, McGlone, & Olausson, 2009). For instance, after activation CTs may produce spontaneous discharges that could last a number of seconds post stimulation (Nordin, 1990b), though the function of this after-discharge is not known. Conversely, A $\beta$  afferents' firing frequency is dependent upon a stimulus being in contact with the skin. That is, discharges stop as soon as stimulation ceases. Furthermore, CTs are highly fatigable; the first stimulation in a series results in a larger response and is perceived as more pleasant than subsequent stimuli (Nordin, 1990; Triscoli, Ackerley, & Sailer, 2014; Vallbo et al., 1999).

#### 1.2.1. Central Projections of CTs

While discriminative tactile sensations are processed in S1, a number of fMRI studies have reported activation in dorsal posterior insula cortex in response to CT targeted stimulation (Björnsdotter, Löken, Olausson, Vallbo, & Wessberg, 2009; McCabe, Rolls, Bilderbeck, & McGlone, 2008; Morrison, Björnsdotter, & Olausson, 2011; Olausson et al., 2002). From the receptors in the skin, unmyelinated afferents project to the laminae of the spinal cord, with C-type fibres projecting to lamina I & III in the dorsal horn. (*Figure 2*) (Sugiura, Lee, & Perl, 1984). From here CT and C-nociceptor afferents project to the dorsal posterior insula cortex (Craig, 2009; Lamm & Singer, 2010). Increased understanding of the central projection, physiological and perceptual consequences of CT activating touch has come from two individuals with a sensory ganglionopathy acquired through a viral infection, which destroyed sensory afferent cell bodies in the dorsal root ganglion. As a result, while these individuals have lost all innervation of large myelinated A-type afferents necessary for discriminative touch, their C-fibre innervation appears to be intact (*Figure 2*) (Ceko, Seminowicz, Catherine Bushnell, & Olausson, 2013; Sterman, Schaumburg, & Asbury, 1980)., These individuals, IW

activity in S1 during A $\beta$  targeted stimulation (Olausson et al 2008). Furthermore, the authors reported deactivation in S1 because of maladaptive supraspinal plasticity, an effect of spinal activity reported in individuals with phantom limb pain (Flor, Nikolajsen & Jensen, 2006). Here, in the absence of physical input individuals experience spontaneous sensations because of phantom activation in the spinal nerves.



**Figure 2.** The functional properties of  $A\beta$  and CT afferents and their central projections (from McGlone, Wessberg & Olausson, 2014). At the lowest level,  $A\beta$  and CT afferents respond differently to stimuli. Where  $A\beta$ afferents' discharge frequency increases linearly with stimulus velocity, CTs respond optimally to stimuli of between 1-10cm/sec with a lower discharge frequency to slower and faster stimuli. These afferents project to different lamina in the dorsal horn, while  $A\beta$ s project via the dorsal column to primary and secondary somatosensory cortices, CTs are believed to project via the spinothalamic tract to the posterior insula cortex.

Similarly to the somatotopic representation of discriminative tactile input in primary somatosensory cortex, there is some evidence there is also a somatotopically organised representation of the body in the posterior insula cortex (Björnsdotter et al., 2009). In an fMRI study, when individuals with sensory gaglionopathy and control participants experienced touch delivered at a velocity optimal for CT stimulation (CT-optimal touch, 1-10cm/s) (Löken et al., 2009) on their arm and thigh, location independent voxel clusters were identified within posterior insula cortex. This topographical organisation for affective somatosensory input has also been shown in response to noxious heat pain, whereby stimuli applied to the hand, foot and face elicited distinctly different voxel clusters within the posterior insula cortex (Brooks, Zambreanu, Godinez, Craig, & Tracey, 2005).

This topographical representation of body sites in the insula may affect the relative experience of CT-optimal touch at these locations. For example, in a psychophysical study, Essick et al (1999) reported that participants rated touch to the face more pleasant than touch to the arm, suggesting differences in the relative perception at these different locations. It is hypothesised that these differences in pleasantness and topographic representation of CTs reflect innervation densities in the periphery (Liu et al, 2009). Using a molecular genetic visualisation technique, Liu et al (2009) mapped the cutaneous innervation patterns of a MrgprB4+, gentle touch responsive C-fibre in mice. Their staining showed these fibres innervated the hairy but not glabrous skin and projected to lamina II of the spinal column. Furthermore, these fibres were more densely innervated on the dorsal than thoracic surface and more sparsely innervated in distal than proximal regions of the limbs. Maruyama et al (2012), reported that stroking to the back of rats resulted in a significantly larger release of dopamine within the nucleus accumbens than stroking to the front or hind limbs. Taken together, these studies indicate that touch at body sites densely innervated with C-LTMs may be more rewarding than at sparsely innervated sites. Consistent with these rodent studies, in humans

Walker, Trotter, Woods, and McGlone (2017) found that affective ratings of vicariously experienced touch match the hypothesised innervation density of CTs. That is, the highest ratings of perceived pleasantness were given for touch on the back and upper arm, in comparison to the distal regions of the limbs. It was hypothesised that these cutaneous innervation densities result in proportional representation in the insula cortex; typically, this relates to the S1 homunculus that shows cortical representation is proportional to peripheral innervation of A $\beta$  afferents resulting in greater tactile acuity and sensitivity.

The posterior insula cortex is typically associated with functions such as homeostasis, emotion and interoceptive experience (Craig, 2003; Moraga-Amaro & Stehberg, 2012), with increased arousal and autonomic pairing between individuals receiving gentle CT-optimal touch (Chatel-Goldman, Congedo, Jutten, & Schwartz, 2014). The anterior insula itself is responsible for processing personal subjective experiences of stimuli (Craig, 2002; 2009; Lamm & Singer, 2010). From here, information is transferred to the Anterior Cingulate Cortex (ACC), which is highly functionally and anatomically connected to the anterior insula cortex (Craig, 2009). The ACC is posited to be responsible for emotion processing, reward anticipation and decision-making (Bush, Luu, & Posner, 2000), thus supporting the role of CTstimulation in affect and motivational behaviour.

Strong functional connectivity between the insula and regions such as the amygdala and orbitofrontal cortex (OFC) link this region to processing information and underlying behaviour during social interactions and bonding (Uddin, 2014). It is therefore theorised that CT touch is a mediator for these social processes (Craig, 2009). Furthermore, these regions are associated with pain processing too, thus highlighting the social, motivational role that pain and pleasure have on behaviour. As well as fMRI evidence, recent EEG research found ultralate potential and theta power changes in the frontal cortex around two and a half seconds after initial CT-optimal stimulation (Ackerley, Eriksson, & Wessberg, 2013). The relative latency and theta synchronisation measured is purportedly the result of processing in the frontal regions of the brain where the ACC and OFC are located. Further, supporting the transfer of CToptimal stimuli processing from the posterior regions of the insula (Björnsdotter et al., 2009; Lucas et al., 2015; Olausson et al., 2008) to frontal regions of the brain (Lindgren et al., 2012; Rolls et al., 2003).

In conclusion, affective touch, signalled by CTs is tactile perception with valence, motivational and arousal context (Harmon-Jones, Gable, & Price, 2012) the purpose of which is hypothesised to encourage and elicit positive social interactions between individuals where pain sensations inhibit these interactions.

#### **1.3.** The Social Touch Hypothesis

As discussed, CTs respond optimally to stimuli moving at a slow velocity, with a gentle force and at a temperature similar to that of human skin (Ackerley, Backlund Wasling, et al., 2014; Rochelle Ackerley, Carlsson, Wester, Olausson, & Backlund Wasling, 2014). Such tactile stimulation is typical of that which occurs during comforting reciprocal interactions between individuals (Ackerley, Backlund Wasling, et al., 2014; Morrison, 2016; Schirmer et al., 2014). Given they project to brain regions associated with processing affect and reward it has been proposed that CTs form the first stage of a specialized pathway encoding socially relevant tactile information (Morrison, Loken & Olausson, 2010; Olausson et al., 2010). In a recent study, Croy et al (2016) observed participants whilst they touched: either an artificial arm, their partner's arm or held their baby. Participants were asked to stroke a region of skin marked out on each of these sites, for 30s with no other instructions relating to the stroking. For participants stroking their partner's arm or child, the velocity of stroking were consistently within a CT-optimal range with no participants stroking in a CT-suboptimal range. These findings demonstrate the social relevance of CT-optimal stroking, where participants spontaneously stroke at these velocities without any specific motivation to do so. Affective touch plays a fundamental role in non-verbal communication and bonding, a key component of prosocial behaviour (Kirsch et al., 2017). Furthermore touch is an effective way to project emotional state and intent (Hertenstein, Keltner, App, Bulleit, & Jaskolka, 2006). For example, in what has been referred to as the 'Midas touch' a brief touch between a waiter/waitress and their customer resulted in larger tipping, even though the customer didn't consciously rate the service as any better than individuals who were not touched (Crusco & Wetzel, 1984). This shows that the mere exposure to physical interactions can implicitly affect an individual's appraisal of an interaction.

Across a range of species, tactile interactions have been shown to benefit maturation. For example, touch sensitive development is observed in the nematode species *Caenorhabditis elegans* (Rose, Sangha, Rai, Norman, & Rankin, 2005). Individuals that were reared in isolation were significantly shorter and thinner compared with individuals reared in a colony. Isolated individuals also reacted to tactile stimuli less than grouped individuals did. Furthermore, Diamond, Krech and Rosenzweig (1964), found that enriching the environment of rats (i.e. incorporating miscellaneous objects into their environment) had a beneficial impact on chemical and physical development of the brain, highlighting the importance of sensory input to development. Further research has found that tactile input, such as handling, in early infancy decreases rats' levels of stress reactivity (Champagne & Meaney, 2007) and acts to mediate negative responses to stress in later life (Alvarez, Levine, & Green, 2015). A seminal study of primate social behaviour found that infant monkeys were more motivated to interact with soft surrogate models that resembled their mother's feel, as opposed to a wire mesh model which provided only food (Harlow & Zimmermann, 1959), thus showing the rewarding value that tactile comfort has in early life across species even at the expense of food.

In human infants too, a range of tactile interventions have been shown to have a beneficial effect on infant health, growth and development (Bystrova, 2009; Diego, Field, &

Hernandez-Reif, 2014; Feldman & Eidelman, 2003). For example, 'kangaroo care' skin-toskin contact between a parent and infant has been shown to increase the speed of maturation of preterm infants, with a larger increase in size and weight, and lower incidences of nosocomial infections, resulting in lower mortality rates than infants not receiving this contact intervention (Conde-Agudelo, Belizán, & Diaz-Rossello, 2011; Feldman & Eidelman, 2003). Furthermore, the autonomic stress responses of a preterm infants are reduced, helping to decrease the negative stress effects of preterm birth, including heart abnormalities and poor homeostatic control (McCain, Ludington-Hoe, Swinth, & Hadeed, 2007). Such early skin to skin interactions between an infant and primary caregiver do not only benefit the physical health of the infant (Hunt, 2008), but also the bonding between these dyads (Hunt, 2008; Tessier et al., 1998). Furthermore, massage therapy has been shown to improve the social, emotional behaviour and development of children with ASD, permanently changing undesirable behaviours (Escalona, Field, Singer-Strunck, Cullen, & Hartshorn, 2001).

Recent evidence shows that touch for CT-optimal touch carries a positive motivational value (Berridge, Robinson, & Aldridge, 2009; Pawling, Trotter, McGlone, & Walker, 2017; Perini, Morrison, & Olausson, 2015; Triscoli et al., 2014) For example, Perini et al (2015) found that participants chose to repeat a CT-optimal stimulus more often than a non-CT-optimal one. Also, while desire to receive CT-optimal touch decreases over time when the stimulus is repeated, the decline in liking was less rapid than for non-CT optimal stimulation (Triscoli et al., 2014). Recently, in an evaluative conditioning study, Pawling, Trotter, *et al* (2017) found that neutral faces paired with CT-optimal touch were subsequently rated as more approachable than non-CT touch paired faces that were initially equally liked.

Fairhurst, Löken, and Grossmann (2014) conducted a study on nine-month-old children who were stroked at three speeds (0.3, 3 and 30cm/sec) whilst their pulse was measured and their attention towards a distractor video or the stroking brush was recorded. During touch

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delivered at 3cm/sec (CT-optimal speed), the children's pulse rate decreased significantly more than in response to faster or slower velocity stroking. Furthermore, during CT-optimal strokes their attention was on the brush for significantly longer than with faster or slower control trials. Recently in adults too, CT optimal velocity stimulation was found to decrease heart rate to a significantly greater degree than faster, non-CT optimal strokes (Pawling, Trotter *et al* (2017). However, further evidence suggests that this relaxation effect is not necessarily CT specific as a similar increase in inter-beat intervals was also reported for 3cm/sec stroking on the palm of the hand (Pawling, Cannon, McGlone, & Walker (2017). Also, in this study, facial electromyography was used to compare affective arousal responses to CT and Non-CT targeted stimuli. A location and velocity specific increase in Zygomaticus Major activity (the muscle responsible for smiling), was reported in response to CT optimal velocity touch on the forearm, suggesting that, consistent with other behavioural observations, touch which targets CTs carries an implicit positive affective value.

The cortical mechanisms and subsequent behavioural consequences of somatosensory perception are observed both during physical stimulation and vicarious observation of touch (Ebisch et al., 2008; Keysers, Kaas, & Gazzola, 2010; Lamm, Silani, & Singer, 2015; Morrison, Björnsdotter & Olausson, 2011). This effect is likely the result of the human ability to empathise with other's cognitive and emotional states (Kaplan & Iacoboni, 2006; Vachon-Presseau et al., 2012a). This is supported by the fact, vicarious experience of both pleasant and unpleasant somatosensory stimuli has been shown to activate regions of the cortex associated with imitation and socio-emotional behaviour, such as the anterior insula, anterior cingulate cortex and temporoparietal junction (Bufalari & Ionta, 2013; Gordon et al., 2013; Morelli & Lieberman, 2013). In two separate experiments Morrison et al., (2011) reported that both receiving and observing CT-optimal touch resulted in selective activation of the posterior insula cortex and not S1. Furthermore, participants rated the toucher more pleasant and likeable

after observing reciprocal interactions between a confederate and researcher (Schirmer et al., 2014). It was also reported that the toucher was attended to more often during subsequent viewing periods. Furthermore, the observation of images depicting social tactile interactions (bonding stimuli) has been reported to increase participant's subjective feelings of sociability and lower feelings of isolation and increase activity in comparison to controls who observed stimuli with no social interaction (non-bonding stimuli) (Campagnoli et al., 2015).

# **1.4.** Individual Differences in Touch Perception.

Individual differences in sensory fibre innervation density have been shown to affect not only an individual's direct experience of touch but also their vicarious ratings (Morrison et al, 2011). For example, HSAN-V patients, who experience a progressive loss of C-fibres as a result of a heritable mutation, do not experience pain in response to typically nociceptive input (Minde et al., 2004) and do not show the typically observed preference for CT optimal velocity stroking touch (Macefield et al 2014). Furthermore, providing evidence that direct sensory experience shapes vicarious ratings, HSAN-V patients also show flattened ratings of observed touch. Neurally, these blunted ratings are associated with reduced activation in posterior insula cortex in comparison to healthy controls (Morrison, Björnsdotter, et al., 2011).

Perceptions of somatosensory stimuli can also me modulated by contextual factors (Gazzola et al, 2012; McCabe et al, 2008). For example, Gazzola *et al* (2012) reported that when heterosexual males believed they were being stroked by a female experimenter they showed greater activation in S1 than when the same physical stimulus was believed to be delivered by a man. In fact, in trials where female touch was anticipated, S1 was active before the touch was applied. This effect was replicated by Scheele et al (2014), who also found that female delivered caress was deemed to be more pleasant and showed an increase in SI as a result of this female delivered touch. Similarly, McCabe et al (2008) found the label on a jar of moisturizing cream being applied to participants' arms modified their neural responses to

and explicit perceptual ratings of the sensation. Thus, when labelled "rich moisturizing cream" there was greater activation in the pregenual cingulate cortex and higher ratings of sensory pleasure than when the same cream was labelled "basic cream". Taken together, these findings indicate somatosensory perception is not just a result of peripheral stimulation but is affected by context dependent expectations.

Interestingly a number of top-down, social and cultural factors can affect how socially relevant touch is perceived. For example, in a large survey Suvilehto, Glerean, Dunbar, Hari and Nummenmaa (2017) found that the closer the social bond with an individual the more open respondents are to receiving touch from them. This included both family members, close friends and romantic partners. The areas perceived as most widely acceptable to touch were the extremities such as hands and arms, touch on more proximal areas was only acceptable between those with strong social bonds. Furthermore, affective ratings of touch pleasantness have been shown to be modulated by the social nature of the stimulation, with skin-to-skin contact rated as more pleasant than touch delivered by a velvet rod (Kress, Minati, Ferraro & Critchley, 2012). In addition, in a study investigating the impact of expectation on the experience of touch and pain, Ellingsen et al (2013) found that participant's experiences of pain were reduced and their ratings of touch pleasantness increased when they believed they were taking a pharmacological agent previously proven to have these effects. Demonstrating that prior expectations modulate perception of somatosensory sensations. Taken together this literature suggests that the context in which touch is experienced in has a significant impact on its affective and motivational appraisal. Individual differences are therefore posited to affect the experience of touch for individuals most likely through top-down manipulations of experience.

Beyond context dependent changes in cognitive state, individual differences in responses to both directly felt and vicariously experienced touch have also been shown to vary

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as a function of stable personality traits (Krahé, Drabek, Paloyelis, & Fotopoulou, 2016; Schaefer, Heinze, & Rotte, 2012). Of particular relevance to the work reported here, trait levels of sociability, as determined using the Autism Spectrum Quotient (AQ) (Baron-cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) have been found to be associated with variation in haemodynamic (Bennett, Bolling, Anderson, Pelphrey, & Kaiser, 2014; Scheele et al., 2014; Voos, Pelphrey, & Kaiser, 2013), psychophysiological (Peled-Avron & Shamay-Tsoory, 2017) and behavioural responses (Mayer, 2017; Robertson & Simmons, 2013) to touch. Furthermore, these differential responses have been reported in response to both physical touch (Bennett et al., 2014; Scheele et al., 2014; Voos et al., 2013) and observation of touch (Peled-Avron & Shamay-Tsoory., 2017) as well as self-reporting of touch preferences (Mayer, 2017; Robertson & Simmons, 2013). For example, in an fMRI study, higher scores on the AQ were associated with reduced activity in key brains areas involved in hedonic processing, such as the posterior superior temporal sulcus (pSTS) and OFC in response to CT-optimal stimuli (Voos et al., 2013). In an ERP study, Peled-Avron and Shamay-Tsoory (2017) reported a positive correlation between levels of autistic traits and the peak amplitude of the late positive potential elicited by observing social touch. Here, AQ scores were also positively correlated with self-reported social touch aversion. Furthermore, in a recent CT focused study, individuals with high levels of autistic traits rated CT-optimal touch as less pleasant and reported having fewer social tactile interactions than participants with low levels of autistic traits (Croy, Geide, Paulus, Weidner, & Olausson, 2016). The AQ is predominantly a measure of autistic traits however, theoretically this scale is a measure of sociability in autistic and otherwise typically developing individuals (Hoekstra et al, 2008) Taken together these results suggest variation in trait sociability affects both the perceived pleasantness for CT-optimal stimuli and how much an individual values social tactile interactions, providing further indirect support for CTs' putative social function.

At the extreme end of the AQ spectrum lies individuals diagnosed with Autism Spectrum Disorders (ASD). These represent individuals with the lowest trait sociability however some otherwise typically developing individuals also show these levels of AQ scores. Baron-Cohen et al (2001) reported that 80% of individuals diagnosed with ASD would achieve an score above 28 on the AQ scale however, it was also shown that a large number of otherwise typically developing individuals also fall within this range of scores, suggesting that the AQ it not simply a measure of autistic symptoms but of traits likely to be shared across individuals both with and without a diagnosis of ASD.

The DSM-V (American Psychological Society, 2013) categorises ASD as "deficits in social communication" and "restrictive, repetitive patterns of behaviour." There is a large body of literature which suggests that sensory abnormalities contribute to the development and maintenance of the behaviours and social difficulties that characterise ASD (Crane, Goddard, & Pring, 2009; Haigh, 2018; Leekam, Nieto, Libby, Wing, & Gould, 2007; Ornitz, 1973). Indeed, sensory deficits now form part of the DSM 5 diagnostic criteria for ASD. In ASD, sensory abnormalities vary across modalities as there is a great deal of heterogeneity within the condition (Marco, Hinkley, Hill, & Nagarajan, 2011). Both noxious and innocuous sensory stimuli are believed to be processed differently from control participants (Prescott, Ma, & De Koninck, 2014). While hyposensitivity can be dangerous due to blunted behavioural responses to painful and damaging inputs, hypersensitivity may result in overstimulation from typically innocuous stimuli leading to a negative valuation or allodynic type response. Such differential processing of sensory inputs results in abnormal experience of the world, including the social tactile interactions, which are prevalent between an infant and their biological mother or caregiver. It is possible that modulation of CTs could impact both the experience of pleasant touch and the experience of pain. Specifically recent animal studies have shown that hypersensitivity to touch is reduced in C-fibre knockout mice (Seal et al., 2009; Lou et al.,

2013). These studies further suggest that it is the processing of CT-stimuli that is responsible for the valuation of tactile input and thus a deficient system would result in differential experiences of the touch across individuals.

A number of studies have reported that individuals with ASD display differential patterns of cortical activity compared to typically developing controls in response to a range of tactile stimuli (e.g. Coben, Clarke, Hudspeth, & Barry, 2008; Delmonte et al., 2012; Kaiser et al., 2010; Lloyd-Fox et al., 2013; Oberman et al., 2005; Pelphrey & Carter, 2008), including videos of individuals interacting socially with the participant (Lloyd-Fox *et al*, 2013) and physical tactile stimulation (e.g. Kaiser et al., 2015; Miyazaki et al., 2007). Similar patterns of activity have been shown for individuals with high levels of autistic traits (e.g. Peeled-Avron et al., 2017; Voos et al., 2012). This further highlights the relationship between tactile autistic traits and individuals diagnosed with ASD.

Beyond purely discriminative functions, studies have reported relationships between tactile sensitivity and social functioning in ASD (Hilton et al., 2010; Lundqvist, 2015; Miguel et al., 2017). For example, self-report measures of tactile sensitivity and preference revealed social dysfunction in individuals with ASD was significantly mediated by altered responsivity to touch. In fact, Hilton et al (2010) found a strong significant negative relationship between touch sensitivity and social responsiveness. It could be that the individuals with ASD have fundamental cortical abnormalities affecting their social behaviour (e.g. Courchesne et al., 2011). For example, post-mortem analysis of the brains of individuals with ASD revealed greater neural density in the anterior and posterior insula cortices than in typically developing individuals (Courchesne *et al*, 2007). As these regions are targets of primary CT afferent projection, it is likely that abnormal innervation in these regions would result in atypical perception of CT-optimal stimuli.

#### **1.5.** Aims of this Thesis.

While evidence to date shows that typically developing individuals with high levels of autistic traits experience touch differently to individuals with low levels of autistic traits, there is a dearth of empirical evidence looking at how individual differences in trait sociability affect the processing of CT-optimal stimuli. In particular, how physiological and electrophysiological responses to CT stimulation differ according levels of social traits is not well understood. Thus the aims of this thesis are to address this gap as follows:

- A wealth of research has found similarities in the cortical and behavioural responses to both first hand and vicariously experienced affective touch. However, the impact of individual differences in trait sociability on vicarious responses to affective touch has not been widely researched. Thus the first aim is to investigate whether individual differences in trait sociability affect vicarious ratings of affective touch
- The vicarious experience of discriminative and affective touch will be measured in typically developing children and those with a diagnosis of ASD, to measure a theoretical range of high and low trait sociability. The aim is to add to existing literature that shows, children distinguish between affective and discriminative touch when felt first-hand.
- Recent evidence (Pawling, Cannon et al, 2017) shows differential activity between the Zygomaticus Major (smile muscle) and the Corrugator Supercilli (frown muscle) in response to affective and discriminative first hand touch. The third aim of this thesis is to explore the vicarious experience of affective touch by measuring physiological responses to the observation of touch.
- Following up from the work of Pawling, Cannon et al (2017), the fourth aim is to measure implicit affective responses to affective and discriminative touch and, to determine how trait sociability affects these responses.

• A final aim of this thesis is to research the ultra-late potential (ULP). This component of the ERP trace has been most prominently reported during C-nociceptor stimulation however, Ackerley et al (2013) also reported a ULP in response to CT stimulation. To add to this existing research, differential cortical responses to CT-optimal and non-CT-optimal stimuli will be recorded. In order to determine whether there are individual differences in the ULP or earlier ERP components in response to affective and discriminative touch.

#### Chapter 2. Methods for Studying Responses to Affective Touch.

# 2.1. Manual Stroking

Assessment of mechanoreceptive functioning has been commonplace since the 1800s however, Essick, James, McGlone (1999) were the first researchers to measure the relative valence of different somatosensory stimuli. Specifically, in this study participants rated the pleasantness of stimulation on the arm and face with different textured materials. From this study, somatosensory psychophysical methods were developed with researchers manipulating factors such as velocity, location, force and texture to differentially target different types of sensory nerves. In two studies presented here, participants received manual brush stroking to their arm and/or palm. These stimuli were delivered using a soft make up brush (No7 Make up Brush, The Boots Company). Many CT focused studies have used a rotary tactile stimulator (RTS) to ensure touch is delivered with a precise velocity and force optimal for CT stimulation (based on microneurography evidence Löken, Wessberg, Morrison, McGlone, & Olausson, 2009). This further allows social context to be removed from the stimulus. However, in the studies reported here a primary aim was to determine how trait differences in sociability affect the responses to touch, it was therefore decided that a social context was necessary. Although stroking participants with a brush has little external social validity, it allows for a social component to be included with the stimulus that is not present when touch is administered using a RTS. Manually administered brush strokes have been used effectively across a number of previous CT focused studies (Björnsdotter et al., 2009; Case et al., 2016; Gordon et al., 2013; Miguel, Lisboa, Gonçalves, & Sampaio, 2017; Pawling, Cannon, et al., 2017) and typically elicit pleasant sensations in comparison to other materials (Ackerley, Saar, McGlone, & Backlund Wasling (2014). Furthermore, using a brush, as opposed to a hand, ensures stimulus consistency without individual differences in skin texture and/or temperature affecting the

velocity or force of the stroking (Sivamani, Goodman, Gitis, & Maibach, 2003). Importantly, Triscoli, Olausson, Sailer, Ignell and Croy (2013) reported that touch delivered by an RTS was comparable in terms of perceived pleasantness and intensity to manually administered brush stroking. In the experiments reported here, participants had 10cm long apertures drawn on their forearm and palm (*Figure* 3). This ensured the stimuli were applied to a consistent area of skin.



*Figure 3*. The approximate location of the stroking areas on the palm and forearm used in study 4. In study 5, a 10cm long aperture was marked on the dorsal surface of participants' forearms.

At the beginning of each trial of a study, the velocity (Study 4 & 5) and location (Study 4) of the touch was signalled to the experimenter on a computer screen located behind the participant. This was followed by a three-second visual countdown before a visual metronome appeared to guide the experimenter in delivering the correct velocity of stroke. The countdown ensured the stroking began as close to the start of the metronome as possible. The visual metronome (*Figure* 4) was custom made for these studies to ensure accurate and consistent stroking velocities across trials. The metronome was designed in E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA), by first drawing a blank canvas figure. An empty rectangle

was then drawn on this representing the 10cm long stroking aperture on the participant's arm. The rectangle then filled at the velocity designated for the current trial. In Study 4, these stimulations lasted for the duration of the 5s stroking period. Strokes beginning proximal to distal were continuously administered to the area between the apertures drawn on participant's arms. In Study 5, a single proximal to distal stroke was administered.



*Figure 4.* A screen shot showing the metronome during one of its runs. In Study 4 this metronome ran back and forth for five seconds, stimuli were matched for contact time on the skin. The red metronome line represented a proximal to distal stroke whereas a white metronome represented distal to proximal strokes. Study 5 had only one colour metronome as participants received a single stroke per trial irrespective of velocity.

# 2.2. Touch Videos

Walker et al (2017) created a series of videos depicting touch delivered at CT-optimal and non-CT-optimal velocities. These videos were created to measure the vicarious affective responses to dynamic social touch, comparing ratings across sites hypothesised to have differing innervation densities of CTs. In three of the experiments presented, participants watched these videos depicting one actor touching the upper body of another actor. The actors, (one male and one female) were standing in front of a white screen. To minimise the effect of social context and top-down representation of the touch, only the touched location and the toucher's arm were visible in each shot (*Figure 5*). The videos lasted for five seconds showing constant stroking touch (or skin to skin contact in the static touch condition) The videos showed touch delivered to five locations (palm, ventral forearm, dorsal forearm, upper arm and back) at three different velocities (static touch, 3cm/sec and 30cm/sec). In Study 3 an extended selection of videos were used. These depicted touch at three velocities (static, 3cm/s and 30cm/s) across four locations (Palm, ventral forearm, upper arm and back). Analyses showed no difference in ratings between these two sets of videos so they were all included in further analyses (see **Chapter 5**, *Figure 20*).



*Figure 5.* Screen shots depicting stills of each body location being stroked. Only the location being touched and the toucher's arm are shown in these videos (from Walker et al 2017). These videos depicted touch at five locations: palm, ventral surface of the lower arm, dorsal surface of the lower arm, upper arm and back. At each of these locations, touch was delivered at three velocities: static, 3cm/s (optimal for CT stimulation) and 30cm/s (non-optimal for CT stimulation).

#### 2.3. Ratings Scales

In studies 1 to 4 participants rated how pleasant and /or intense the touch they received /viewed was perceived to be. In studies 1 and 3, adult participants were asked to rate "How pleasant was that action for the person being touched?" and "How much would you like to be touched like that?" These were answered on a seven-point Likert scale running from 1, very unpleasant/not at all to 7, very pleasant/very much so. These scales are the same as those used in Walker et al (2017).

Study 2 was conducted on young children aged between 7 and 12. Here, a "smiley face" scale which had previously been used successfully with children in this age group was employed (Cascio, Lorenzi, & Baranek., 2016; Croy et al 2017). Immediately after the children had watched each video they were asked "How nice do you think it was for the person being touched?" and "How much would you like to be touched like that?" They answered using the scale depicted in *Figure* 6.

			•		$\bigcirc$
How nice do you think it was for the person being touched?	0	0	0	0	0

*Figure 6.* In study two, the response scale used was one previously validated in sensory studies with children in this age group 7-12, (Cascio et al 2016; Croy et al., 2017).

As study 4 was an extension of the facial EMG study conducted by Pawling, Cannon, et al., (2017), the same response scale was used. Specifically, participants rated touch pleasantness on a 100-point visual analogue scale with anchors "not at all pleasant" and "very pleasant". The scale was coloured to represent a temperature like scale with the negative (not at all pleasant/not at all intense) appearing at the red end of the scale and the positive (very pleasant/very intense) appearing at the green end of the scale (*Figure* 7). Participants answered two questions "How pleasant was that touch?" and "How intense was that sensation?" after each stroke. To avoid confusion, the order of presentation of the two questions was counterbalanced between participants but not trials/blocks. While in previous CT focused studies participants are typically asked to rate how pleasant they perceived the touch they received to be, it has been less common to ask how intense the sensation was. The rationale for using the intensity scale came from a study conducted by Blakemore et al (2006) who reported that participant with Asperger's Syndrome rated vibrotactile stimuli as more intense than typically developing individuals.



*Figure 7.* In Study 4 participants rated "How pleasant was that touch?" and "How intense was that sensation?" on a 100 point Visual Analogue Scale. The scale depicted a colour gradient between a red, negative and a green, positive anchor point. As with studies one to three, the lowest anchor point represented a negative sensation, or a lack of intensity and the highest anchor point a very positive or intense sensation.

# 2.4. Facial Electromyography (EMG)

In studies 3 and 4, facial Electromyography (EMG) was used to measure physiological responses to affective touch. Facial EMG measures electrical activity over facial muscles with increased activity reflecting greater contraction of the underlying muscle. In the experiments reported here, surface Ag-AgCl electrodes were used. To maximise signal quality, prior to the attachment of electrodes, the skin surface was cleansed with a facial wash then lightly abraded with a small scouring pad (Fridlund & Cacioppo, 1986). This process removed dead skin cells from the surface of the face, thus reducing electrical impedance. Finally, a small globule of conductive gel (SignaGel, Parker Laboratories, inc.) was placed in each of the cleansed locations to ensure close adherence of the electrodes to the skin.


*Figure 8.* Set up showing the location of electrodes for EMG measurements. Two on the cheek running from the corner of the mouth in line with the earlobe measure Zygomaticus Major activity. Two placed above the left brow measure activity of the Corrugator Supercilli and one electrode placed near the hairline acts as a reference electrode (based on van Boxtel, 2010).

## 2.4.1. Locations of interest

To minimise the effect of external electrical interference, each electrode was individually grounded. Location of the electrodes was approximate, based on individual participant's facial structure. The Corrugator Supercilli (CS) muscle runs above the participant's brow toward the nose and the Zygomaticus Major (ZM) muscle runs across the cheek from the corner of the mouth to the ear lobe (see *Figure* 8) (Fridlund and Cacioppo, 1986). To ensure electrodes had been placed in the correct locations, participants were asked to smile and frown to activate the ZM and CS respectively. However, to avoid any influence

of demand characteristics on task performance, participants were not asked to do this until after the experiment was over. At the start of the experiment, participants were informed these electrodes were measuring activity in their frontal lobe. This is the same cover story used by Pawling et al (2017). The aim of this initial deception was to ensure that the EMG activity recorded was the result of implicit affective responses to the touch as opposed to explicit responses due to demand characteristics.

A number of studies have shown that ZM activity is associated with the experience of positive affect and CS activity conveys negative affect (Epstein, 1990; Larsen, Norris, & Cacioppo, 2003; Tan et al., 2012). Furthermore it is typically shown that ZM and CS muscles have a differential relationship whereby increase in activity in one is associated with a decrease in the activity of the other (Larsen et al., 2003). Pawling, Cannon, et al (2017) has recently reported that touch that specifically targets CTs results in greater ZM activity than non-CT targeted touch.

### 2.4.2. Data Processing – EMG

The EMG data were collected on a laptop running LabChart Pro v.7 (ADInstruments, Oxford, UK), triggers relating to the start of the metronome countdown and the type of stimulus being delivered were sent via the computer displaying the metronome. Further triggers were sent to mark the start/end of the stroking period and the end of the subsequent post-stroking period. The EMG data were initially full wave rectified to allow for meaningful summation (van Boxtel, 2010). These data were then extracted using a custom-made macro in LabChart. Average peak amplitudes were taken in 100ms time bins across the 2000ms baseline. A further 50 time bins were taken from the stroking period (100ms bins x 5000ms period) and 30 time bins were taken from the post stroking period (100ms bins x 3000ms period). Data were then imported into SPSS where they were graphed. Separate graphs were created for each participant with individual lines representing each of the different trials in the study. The data

were eyeballed to determine the trials where baselines were contaminated by noise e.g. those that were deemed to have peak amplitudes far larger than the norm. These trials were then removed. Next percentage change scores were calculated for each data bin and in the first instance, any change score over 500% was removed. In a final step, a whole cohort average was taken and any data point  $\pm 3$ SD of this mean was removed.

### 2.5. Electroencephalography (EEG)

#### 2.5.1. Data Processing – EEG

A 64-channel active-electrode BioSemi v.7.07 (BioSemi, Amsterdam, NL) system was used. Data were collected using ActiView (BioSemi, Amsterdam, NL) then analysed using the EEGlab toolbox (Delorme & Mekeig, 2004) for Matlab. An online filter of 0.1Hz then an offline 0.1Hz-40Hz bandpass filter was applied to the data. In line with past research, data were collected online at 512Hz then offline down sampled to 256Hz (Ackerley et al., 2013). Data were average referenced across all electrodes. The data were epoched to remove between-trial data and excessively noisy trials were removed manually. The noisy trials were selected by scrolling through the epochs and choosing any with excessive interference from muscle activity or drift, not otherwise removed through filtering. All participants retained over 80% of trials (trials removed M=11.6, SD=6.2). Next, independent components analysis (ICA) was run on each data set, extracting 63 components. Noisy components were removed based on individual topographical heat maps (components removed M=3.59, SD=0.8). Data were averaged into categorical epochs representing CT-optimal and non-CT-optimal trials. These epochs were then grand averaged across participants.

To measure early responses, data were extracted from central electrodes Pz, Cz and Fz (blue, *Figure 9*). Peak amplitude measures were taken from 300-600ms after stimulus onset; this represented a region where the largest peak amplitude appeared in the ERP. These data were compared directly between CT-optimal and non-CT-optimal stimuli to compare the

differences in A $\beta$  input for these two velocities. As an additional control analysis, given the slower conduction velocity of CTs, measurements were also taken 700ms later in the signal, using the calculations for velocity x distance from the forearm to the cortex reported in Ackerley *et al* (2013). Thus, when 30cm/sec stimulation produced a maximal peak, 500ms after stimulus onset, data was extracted from 1200ms for CT-optimal stroking. Thus, activation due to the slower conduction velocity of CT afferents compared to fast conducting A $\beta$  afferents. For each participant, data were extracted from the point of maximal amplitude in the ULP (between 2800 and 3200ms), this data was compared to data from contralateral and ipsilateral somatosensory "arm" areas (electrodes CP3 and CP4 respectively, orange, *Figure 9*) in an ANOVA.

## 2.5.2. Components of interest.

EEG waveforms are time locked to particular events and averaged across many trials, in this way specific ERPs are drawn from the signal. ERPs consist of several specific components that together make up a standard waveform, individual components can tell us a lot, about how different types of stimuli are processed. For example, specific components have been found for face stimuli (N170), mismatched stimuli (N2) and salient stimuli (P3). Specifically, the P3 peak amplitude has been most commonly related to changes in arousal state and attentional processes relating to stimuli that are salient (Bradley, Keil, & Lang, 2012). The component is of interest here as previous studies have reported that Aβ targeted 30cm/sec stroking produces a greater increase in sympathetic arousal than CT targeted 3cm/sec strokes. (Pawling, Trotter, et al., 2017). A second ERP component of interest is the ultra-late potential (ULP). Initially this component was measured as a result of stimulating C-nociceptor fibres (Bromm & Treede, 1987; Bromm, Neitzel, Tecklenburg, & Detlef-Treede, 1983). This activity has subsequently been reported in response to CT-specific stroking touch (Ackerley et al., 2013). It is hypothesised that this ULP is a specific cortical signature of unmyelinated CT afferent activity both because these neurons have a slow conduction velocity and because they induce activation in the frontal regions where ULPs are measured. Specifically the ULP may represent activity in the OFC or ACC (Björnsdotter et al., 2009; Gordon et al., 2013; McCabe et al., 2008; McGlone et al., 2012; Morrison, Björnsdotter, et al., 2011). The ERPs in Study 5 were time locked to the breaking of a laser beam positioned over the participant's arm, to ensure the accuracy of stimulus onset. Furthermore, here participant's received one proximal to distal stroke from the laser beam to a drawn black line 10cm away (see **Figure 3**).



Figure 9. An image showing the standard 64-electrode layout based on the 10-20 system. The electrodes of interest are highlighted, blue represents electrodes used for early peak analysis and orange represents the electrodes used to characterise the ultra-late potential.

### 2.5.3. Strengths and Limitations of EEG Research.

There are a number of reasons why researchers choose to use EEG to measure evoked neural activity. One benefit is that EEG is cost effective with systems costing tens of thousands of pounds instead of millions of pounds for magnetic resonance imaging (MRI) and magnetoencephalography (MEG) systems. A further benefit of EEG is its superior temporal resolution over blood oxygenation level dependent measures such as fMRI. Typically, the brain processes information within milliseconds, so it is beneficial to be able to measure activity as it happens. *Figure* 10, shows that EEG provides the temporal resolution necessary for immediate measurement. However, its poor spatial resolution means the actual source of the signal cannot be accurately determined. In addition, it is important to consider that since EEG measures the direct activity of a firing neuron (or cluster of neurons) as opposed to haemodynamic response, it can therefore tell us more about the specific neural activity associated with different stimuli than slower cortical metrics like fMRI.



*Figure 10.* A comparison of the relative temporal and spatial resolution provided by a range of neuroscientific methodologies. The z-axis indicates how much each of these methods interfere with brain activity or indeed how closely what is measured correlates with underlying neural activity (from Walsh & Cowey, 2000).

### 2.6. Self-Report Measure of Trait Sociability.

## 2.6.1. Autism Spectrum Quotient

The Autism Spectrum Quotient (AQ) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) is a 50 item scale that measures autistic traits within a typical population. The scale is comprises five subscales: Social Skill (e.g. "I prefer to do things with other than on my own"), Communication (e.g. "I enjoy social chit-chat"), Attention Switching (e.g. "I prefer to do things the same way over and over again"), Imagination (e.g. "When I'm reading a story, I can easily imagine what the characters might look like") and Attention to Detail (e.g. "I often notice small sounds when others do not"). The internal validity of the subscales as determined by Cronbach's alphas were reported as follows: Social Skill = 0.77, Communication = 0.65, Attention Switching = 0.67 and Imagination = 0.65 and Attention to Detail = 0.63. However for the full scale a Cronbach's alpha of  $\alpha$  = 0.88, suggests use of the questionnaire as a single scale is more valid (Austin, 2005).

Although the scale was designed to measure these individual ASD relevant traits, it has been argued that four out of the five subscales (Social Skill, Communication, Attention Switching and Imagination) in fact measure social interaction skills (Hoekstra, Bartels, Cath, & Boomsma, 2008). In this study, 961 individuals were given a Dutch version of the AQ. The four aforementioned subscales were all highly correlated from each other, between r=.53 and r=.84. These four subscales, Social Skill, Communication, Attention Switching and Imagination, were analysed both independently (in a five factor model) and together compared to Attention to Detail as a hierarchical model using confirmatory factor analysis. Here, the hierarchical model was the most accurate fit for these scales suggesting that the two-factor model is the most appropriate use of this scale. Furthermore, two further factor-analytic models of the AQ found factors relating to Social Skills, Attention to Details and Communication/Misreading (Austin, 2005, Hurst, Mitchell, Kimbrel, Kwapil and Nelson-Gray, 2007). Even here the strongest factor related to Social Skills ( `~.85) and communication could also be deemed a factor of sociability.

Participants rate each of 50 questions on a four-point Likert scale, with the descriptors: "Definitely Agree", "Slightly Agree", "Slightly Disagree" and "Definitely Disagree". For half of the questions, answers "Definitely Agree" and "Slightly Agree" are scored with as 1 and "Definitely Disagree" and "Slightly Disagree" are scored as 0, half of the questions are reverse scored. Thus, scores on the scale can range from 0-50 with a typical population scoring 17 on average. It has been reported that that over 80% of individuals diagnosed with ASD score over 26 (Woodbury-Smith, Robinson, Wheelwright, & Baron-Cohen, 2005). In the latter study, individuals were tested using the AQ to determine whether the scale was appropriate for clinical diagnostic purposes. This is specifically as the original scale was mainly tested on typically developing individuals. The majority of individuals in this study with a prior diagnosis of Asperger's Syndrome or High Functioning Autism scored 26 or above on the scale indicating a suitable cut-off for clinically relevant autistic traits. Comparatively, a systematic review reported that mean AQ scores in a typical population should range from 11.6-20.0, this reduces the impact of the scale to a distribution not representative of the range of actual scores across the population (Ruzich et al., 2015), making it difficult to interpret how these scores represent autistic traits comparative to those diagnosed with ASD.

<u>Chapter 3.</u> High levels of Autistic Traits are not associated with reduced valuation of vicariously experienced social touch.

### 3.1. Introduction

Empathy is a function of social behaviour that allows and individual to understand the sensations and emotions experienced by others. Research suggests that empathic responses come from mirroring of another individual's emotional state (Decety & Jackson, 2004). Embodiment of another individual's somatosensory experience has most commonly been observed in vicarious responses to painful stimuli (Jackson, Rainville, & Decety, 2006; Morrison, Lloyd, di Pellegrino, & Roberts, 2004; Morrison, Tipper, Fenton-Adams, & Bach, 2013; Singer et al., 2004). In such studies, individuals experience the negative emotional components of touch (pain) without the accompanying peripheral input (Avenanti, Minio-Paluello, Bufalari, & Aglioti, 2009; Jackson et al., 2006; Singer et al., 2004). Specifically, Singer et al (2004) reported that observation of a romantic partner in pain resulted in similar activation in the 'pain matrix' i.e. regions of the brain responsible for pain processing, as seen when participants experienced the pain first hand. The one exception to this was that activation in S1 was not present, consistent with this primary sensory region's role in processing somatosensory sensations, further suggesting that the vicarious experience of pain is affective not sensory. In addition to mirrored neuronal activity, embodied responses to observing another in pain can also be behavioural. For example, Lamm, Porges, Cacioppo, and Decety (2008) reported increased muscle activity, indicative of negative affect, when participants were asked to imagine themselves in the place of a patient they watched undergoing a painful procedure.

Mirrored neuronal responses have also been reported during observation of emotionally neutral and indeed pleasant stimuli (Bufalari & Ionta, 2013; Chiesa, Liuzza, Macaluso, & Aglioti, 2017). In contrast to observing another's painful experience, a number of studies have

reported activation of S1 during observation of other's non-painful somatosensory experience (Bolognini, Rossetti, Fusaro, Vallar, & Miniussi, 2014; Keysers et al., 2010; Schaefer et al., 2012). For example, Schaefer et al (2012), reported activation in S1 during the observation of touch, specifically gentle stroking of the fingertip using a paintbrush. Activation of S1 has also been reported during observations of interpersonal touch, suggesting that the mirror-touch response is not stimulus specific (Bolognini et al 2014).

Several studies have reported mirrored neuronal responses to the observation of CTtargeted touch (Lucas et al., 2015; Morrison, Löken, et al., 2011). For example, Morrison et al 2011 reported significantly greater activation in the posterior insula cortex to observation of CT-optimal compared to non-CT optimal velocity touch. Furthermore, psychophysical ratings of observed touch have been reported to show the same relationship between stimulus velocity and perceived pleasantness as feeling that touch first hand (Morrison et al 2011 & Walker et al 2017).

Furthermore, Walker et al (2017) reported that touch was rated as most pleasant on skin sites posited to be more densely innervated with CT-afferents based on genetic molecular visualisation of C-LTMs in the mouse (Liu et al 2007) and epidermal nerve quantification in humans (Kennedy et al 2005). However, individual differences are observed in ratings of both directly felt and vicarious ratings of CT-optimal touch. For example, patients suffering from a rare congenital C-fibre deafferentation rate both directly felt and observed CT-optimal touch as less pleasant than control participants (Morrison et al 2011). Furthermore, their ratings of stroking touch do not show the usual velocity dependent pattern.

Variation in neural responses to and subjective ratings of directly felt touch have also been reported as a function trait sociability (Bennett et al., 2014; Croy, Sehlstedt, Wasling, Ackerley, & Olausson, 2017; Scheele et al., 2014; Voos et al., 2013). In the most recent of these studies, a negative correlation between autistic traits, as measured with the AQ, and sensitivity to the specific rewarding value of CT-optimal stroking touch was reported (Croy et al., 2016).

Thus, the aim of the present study was to determine whether, as previously reported for directly experienced touch, individuals with high levels of autistic traits show a reduced sensitivity to the specific rewarding value of CT-targeted touch. Given the hypothesised social function of CTs, it was predicted that, participants with high levels of autistic traits would show reduced ratings of touch delivered at CT optimal velocity to CT innervated locations, compared to those with low levels of autistic traits.

### 3.2. Method

#### 3.2.1. Participants

Participants were 96 healthy males aged between 18 and 30 (M=21.26, SD=2.49), recruited via staff and student email lists at Liverpool John Moores University. Previously, Baron-Cohen *et al*, (2001) reported that individuals from a science background scored higher on the AQ (Baron-cohen et al., 2001) than individuals from an arts background. Therefore, to recruit a broad a range of AQ scores, emails were sent out to subject lists relating to science, technology, performing arts and English. Furthermore, to maximise the range of potential AQ scores, only male participants were recruited in this instance, as males, on average, score higher on the AQ than females. All participants who completed the study were entered into a prize draw to win a £50 gift voucher. This study received ethical approval from Liverpool John Moores University research ethics committee.

#### 3.2.2 Measures & Procedure

The recruitment email contained a brief description of the study followed by the Participant Information Sheet. If after reading the information sheet, participants were willing to take part, they were asked to click on a hyperlink, which took them to the online study. The study was conducted using Qualtrics software, Version 60939 of the Qualtrics Research Suite. (Copyright © 2015 Qualtrics., Provo, UT, USA. http://www.qualtrics.com). Start and end time of survey completion was recorded. Mean time online was 11.7mins (± SD 3.19mins).

## 3.2.3. Participant Screening

An initial set of screening questions determined study eligibility. Participants were asked to answer "true" or "false" to indicate whether they had read the participant information sheet and agreed to take part. They were also asked whether they were male and aged between 18 and 30 years old. If a participant responded "false" to any of these questions, an "If Then"

function was implemented, so that these participants were thanked for their interest and then directed to the end of the study, thus excluding them from participating.

### 3.2.4. Demographic Information

If they fulfilled the study's inclusion criteria, participants were first asked demographic questions relating to their age and ethnic background. Participants were also asked to provide information about any current or past mental illnesses they have experienced, or treatments they might have received. In this study 22% (n=21) of participants had a current or past mental health condition these included three participants diagnosed with ASD, 11 with Depression, three with Bipolar, four with an Anxiety disorder. Using history/no history of mental health condition as a between subjects Factor, there was no significant effect of mental health on pleasantness ratings F(1,90)=7.41, p>.05.

### 3.2.5. Autism Spectrum Quotient

Participants then completed the AQ (see Chapter 2 for full description).

### 3.2.6. Touch Videos

Participants subsequently watched a series of 15 videos depicting touch between a male and female actor with minimal social context (see **Chapter 2** for full description), these videos were previously used in Walker, Trotter, Woods, et al (2017). The videos showed one actor being touched by another actor at five body locations (palm, dorsal forearm, ventral forearm, upper arm and back) these were delivered at three velocities (static touch, 3cm/sec and 30cm/sec. Videos were presented in a random order

Immediately after watching each video participants were asked two questions. The first question "How pleasant do you think that action was for the person being touched?" related to the empathic ability of participants to determine how the touch received in the video felt for the receiver. The second question "How much would you like to be touched like this?"

questioned participants' personal desire to receive the touch depicted. Thus, the two questions were hypothesised to measure different types of cognitive ability. The first question is specifically measuring the cognitive empathy necessary to understand how the individual in the video is feeling during the action. The second question relates to how participants can take the empathic response and understand how the touch would feel to them, an embodiment of the action. Questions were always presented in the same order.

#### **3.2.7.** Data Analysis

Data were analysed using SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

Participants were separated into three similar sized groups based on their scores on the AQ. The first group consisted of participants who scored 5-14 (n=31). The second group had scores deemed to be average for a typical population (15-20, n=33). The final group had scores associated with high level of autistic traits, scoring 21-39 (n=32). Three participants reported having a diagnosis of Autism Spectrum disorder (ASD), only two of these participants had an AQ score above 29, the typical boundary for individuals with clinical diagnosis, the third scored 18.

In previous studies touch applied to closely adjacent areas of the body areas of the body was rated as equally pleasant (Löken et al., 2009). Therefore, to increase power in the statistical analysis, rating scores for neighbouring locations were averaged together Thus, analysis was completed on three touch locations rather than five, i.e. dorsal and ventral forearms locations were averaged into a new variable, 'lower arm' and upper arm and back were averaged into the variable 'upper body'. The palm of the hand was the third location.

A repeated measures multivariate ANOVA with within subject factors of Question (2 levels), Velocity (3 levels) and Location (3 levels) was used to analyse the video ratings data.

AQ was included as a between subjects factor (3 levels). Inspection of model residuals indicated data were normally distributed. Finally, polynomial regression analyses were conducted to determine whether, consistent with previous findings, (Ackerley, Backlund Wasling, et al., 2014; Essick, James, & McGlone, 1999; Löken et al., 2009; Walker et al 2017) for ratings of touch on CT innervated body sites, a quadratic term accounted for significantly more of the velocity dependent variance in pleasantness ratings than a linear expression. Where assumptions of sphericity were violated, Greenhouse-Geisser correction was applied. To correct for multiple comparisons LSD posthoc tests were conducted on the data.

# 3.3. Results

**Table 1.** Descriptive statistics showing the number of participants in each group and the mean, standard

 deviation and range of their scores on the AQ.

Group	п	Mean	SD	Range
All	96	18.82	7.11	34
Low AQ	33	11.87	2.03	9
Average AQ	31	17.00	1.52	5
High AQ	32	27.52	4.53	18

As shown in Table 1, the average AQ score across the whole sample is representative of a typical population average (AQ~17, (Baron-Cohen et al., 2001).



**Figure 11.** Frequency of AQ scores in the sample. (n=96). Scores to the left of the first vertical cut off line represent the range of scores in the Low AQ group (M=11.87), between the first and second line are AQ scores represented in the Average AQ group (M=17) and scores to the right of the second vertical line represent the High AQ group (M=27.52).

Groups were split to ensure equal numbers of participants in each group however, as can be seen from Table 1, the range of scores in each group varies. Groups reliably represented below average, average and above average scores respectively (*Figure 11*).

# 3.3.1. Full model

A repeated measures ANOVA with the factors Question x Velocity x Location, revealed a significant main effects of Location F(2,186)=21.49, p<.001,  $\eta^2 = .25$  Velocity F(2,186)=21.61, p<.001,  $\eta^2 = .23$  and Question F(1,93)=26.07, p<.001,  $\eta^2 = .24$  individual analyses were therefore completed on each question separately.

### 3.3.2. Question one: "How pleasant was that action for the person being touched?"

A repeated measures ANOVA revealed a significant main effect of Location F(2,94)=13.123,  $p<.001 \ \eta^2 = .10$  and of Velocity F(2,94)=32.67,  $p<.001 \ \eta^2 = .19$  as well as a significant Velocity x Location interaction F(4,92)=6.82,  $p<.001 \ \eta^2 = .12$ . There was also a significant three-way interaction between Location x Velocity x AQ group,  $F(6.5, 303) \ 2.14$ , p<.05,  $\eta^2 = .04$ .

Simple main effects analyses of the two-way Location x Velocity interaction (*Figure 12*) revealed that 3cm/sec touch was perceived to be significantly more pleasant than both static and 30cm/sec touch (p < .001) at the two CT-innervated locations (lower arm and upper body). This was not the case on the palm, where CTs have not been found, here static touch and 3cm/sec touch were rated as equally pleasant (p > .05).



**Figure 12.** Mean ratings of all participants to the pleasantness of the touch (+/- SE bars). The Location x Velocity interaction revealed the typical inverted "U" ratings of touch pleasantness where CT-optimal touch is rated as most pleasant speed of touch, is shown.

To further explore the Location x Velocity x AQ interaction, individual repeated measures ANOVAs were used to explore ratings of touch Location and Velocity in each AQ group individually (*Figure 13*). In the Low AQ group there were significant main effects of Location F (2,60)=4.91, p<.05,  $\eta^2 = .14$  and Velocity F (2,60)=8.48, p<.01,  $\eta^2 = .22$ . There was also a significant Location x Velocity interaction F (2.88,86.50)=12.21, p<.001,  $\eta^2 = .29$  (*Figure 13a*). This group showed the greatest sensitivity to CT optimal stimuli with significant differences between CT-optimal 3cm/s at all locations, except the palm where it was rated as equally pleasant as static touch. Similarly, in the High AQ group, there were significant main effects of Location F(2,64)=4.27, p<.05,  $\eta^2 = .14$ , Velocity F(2,62)=8.87, p<.001,  $\eta^2 = .23$ 

and a significant Location x Velocity interaction F(3.04,94.28)=4.29, p<.01,  $\eta^2 =.12$  (*Figure 13c*). Individuals with the highest number of autistic traits still rated CT-optimal touch as significantly more pleasant than static or 30cm/sec touch at CT-innervated locations (Lower Arm and Upper Body). However, in the Average AQ group while there were significant main effects of Location F(2,64)=3.90, p<.05,  $\eta^2 =.11$  and Velocity F(1.46,46.81)=6.40, p<.01,  $\eta^2 =.17$  reflecting the preference of CT-optimal touch at CT-innervated locations , there was no significant Location x Velocity interaction F(4,128)=1.08 p=.36 (*Figure* 13b). To determine whether this was due to outliers, Mahalanobis scores were calculated for each variable and compared using chi squared. None of the Mahalanobis scores were significant at p<.001 suggesting scores all fell within a normal range.



**Figure 13**. Mean ratings of touch pleasantness for each of the AQ groups (SE bars). Figure 13a, shows the Low AQ group. Figure 13b, Average AQ group with AQs scores which are average of the general population.. Figure 13c, High AQ group with the highest number of autistic traits (\*\* denotes p<.01 and \* is p<.05).

To further investigate the Location x Velocity interactions, linear and quadratic polynomial regression models were used to define the velocity-pleasantness relationship for each AQ group individually. Only in the Low AQ group did a quadratic term provide a significant fit for ratings of touch on the Lower Arm (p < .01) and Upper Body (p < .01). In this group a linear term provided a significant for ratings of touch on the palm (p < .05) as static touch was more pleasant that other velocities. However, in the High AQ group neither quadratic nor linear terms explained a significant proportion of the variance in ratings (all p > .05). Overall, at CT innervated Locations, CT-optimal stroking touch was deemed to be the most pleasant.

### **3.3.2.1.** Question one: AQ group CT preference index

A preference index was calculated to determine whether degree of preference for CToptimal velocity touch differed between AQ groups (Table 2). This preference index was based on the *Affective Touch Index* developed by Croy et al (2017). Here the authors subtracted ratings of a non-CT-optimal 30cm/s away from CT-optimal 3cm/s then divided by the average rating from three velocities (0.3cm/s, 3cm/s and 30cm/s). Despite this being an affective touch index, the authors did not consider the 0.3cm non-CT-optimal stroking in comparison to 3cm/s whereas, here both non-CT-optimal velocities are considered in the calculation of CT preference. Here, average non-CT-optimal (0cm/sec and 30cm/sec) scores were taken away from CT-optimal (3cm/sec) scores then averaged themselves:

$$(3 \text{ cm/s} - \text{Static}) + (3 \text{ cm/s} - 30 \text{ cm/s})$$

2

A repeated measures ANOVA revealed a significant main effect of Location F(1.75,162.62)=10.43, p<.001,  $\eta^2 = .17$  reflecting the fact the hypothetically more densely CT

innervated the body site i.e. Upper Body > Lower Arm > Palm, the greater the preference for CT optimal over non-CT optimal velocities of touch. However, there was no significant effect of AQ group F(2,93)=.64, p=.53. Despite the previously described differences between AQ groups, this finding suggests these differences are not the result of an enhanced sensitivity to the CT targeted touch specifically. The main effect of Location is driven by greater pleasantness ratings in the Upper Body compared to the Lower Arm and Palm.

Table 2. Preference index for CT-optimal velocity touch at all locations separated by AQ group.

Group	Body Location	CT Preference Index
Low AQ	Palm	11
	Lower Arm	1.02
	Upper Body	1.19
Average AQ	Palm	.36
	Lower Arm	1.04
	Upper Body	.94
High AQ	Palm	.53
	Lower Arm	1.23
	Upper Body	1.25

### 3.3.3. Question two: "How much would you like to receive that touch?"

A repeated measures ANOVA revealed a significant main effect of Location, F(2, 94)= 26.79, p<.001,  $\eta^2 = .37$  and Velocity, F(2, 94)=25.27, p<.001,  $\eta^2 = .36$ . There was also a significant Location x Velocity interaction F(4,92)=36.74, p<.001,  $\eta^2 = .28$  (*Figure 14*) and a significant interaction between Location x Velocity x AQ group F(6,90)=14.35, p<.05,  $\eta^2 = .08$ . Simple main effects of the Location x Velocity interaction revealed that CT-optimal stroking was the most desired velocity of touch at CT-innervated Locations (ps<.05). Furthermore, as with ratings of perceived pleasantness, here for ratings of desire, CT-optimal and static touch did not differ at the Palm (p>.05).



**Figure 14.** Average ratings for Question 2 "How much would you like to be touched like that?" Here for CT innervated Locations (Lower Arm and Upper Body), CT-optimal 3cm/s is rated as the most desired velocity of touch. Consistent with the findings reported in Walker et al (2017) there is no significant difference between ratings of static and 3cm/sec touch on the Palm.

Individual repeated measures ANOVAs were used to explore the Location x Velocity x AQ group interaction. For the Low AQ group, significant main effects of Location F(2,60)=10.39, p<.001,  $\eta^2 = .17$  and Velocity F(2,60)=11.31, p<.001,  $\eta^2 = .23$  were found. Furthermore there was a significant Location x Velocity interaction F(2.89,86.54)=16.60,

p < .001,  $\eta^2 = .35$  (*Figure* 15a). Similarly, in the High AQ group, there were significant main effects of Location F(2,62)=17.02, p < .01,  $\eta^2 = .15$ , Velocity F(1.60,49.72)=7.04, p < .01,  $\eta^2 = .18$  and a significant Location x Velocity interaction F(2.79,86.47)=3.28, p < .05,  $\eta^2 = .09$ (*Figure* 15c). However, for the Average AQ group, while there were significant main effects of Location F(2,64)=5.65, p < .01,  $\eta^2 = .17$  and Velocity F(1.86,49.81)=3.75, p < .05,  $\eta^2 = .15$ there was no significant Location x Velocity interaction F(2.95,94.39)=1.22 p > .05 (*Figure* 15b).

Simple main effects analyses of the Location x Velocity interactions showed that, in the Low AQ group, 3cm/sec stroking was rated as more desired as significantly more desired than static or 30cm/sec stouch at both CT-innervated locations compared to non-CT-optimal velocities (all p<.001), furthermore there was no significant difference between static and CToptimal velocity stroking on the Palm (p>.05). In the High AQ group CT-optimal touch was only rated as the most pleasant for the Upper Body location, at the Lower Arm 3cm/s was not significantly different from non-CT-optimal 30cm/s.



Figure 15. Mean ratings of touch desire for each of the AQ groups (SE bars). Figure 15a, shows differences in touch desire ratings for Low AQ. Figure 15b, is ratings for Average AQ and Figure 15c, represents ratings in High AQ (\*\* denotes p < .01 and \* is p < .05).

To further investigate the Velocity x Location interactions, regression analyses were again conducted to investigate the velocity-desire relationship in each AQ group individually. In the Low AQ group, a linear term provided a significant fit for the ratings of touch on the palm (p<.01) and a quadratic term describes a significant amount of the variance in ratings of different velocities of touch on the lower arm and upper body (p<.01 & p<.05 respectively). However, in the High AQ group neither a quadratic nor a linear term provided a significant fit for ratings of touch on the lower arm, upper body or palm (all p>.05). Again, in line with ratings of perceived pleasantness, in all groups participants rated CT-optimal touch at CT-innervated locations as the most desired. In the Average and High AQ groups however, this was less consistent with fewer significant differences between velocities.

### 3.3.3.1. Question two: AQ group CT preference index.

A CT preference index was calculated for Question two (Table 3). A repeated measures ANOVA revealed a significant main effect of Location F(1.75,162.73)=8.28, p<.01,  $\eta^2 = .16$  but there was no significant effect of AQ group F(2,93)=.26, p>.05. This shows that, the significant differences between AQ groups did not reflect a specific preference for CT-optimal touch over non-CT-optimal touch. In terms of Location, the indices follow the predicted trend whereby the largest preference index for CT-optimal touch is measured where CTs are hypothetically most innervated (the Upper Body); further suggesting that innervation of CTs directly affects the desire to receive CT-optimal touch. Again, CT-optimal touch is most desired on the Upper Body where there is a greater innervation of CTs, at the Palm where no CTs are found there is less CT preference.

Group	Body Location	CT Preference Index
Low AQ	Palm	.08
	Lower arm	1.09
	Upper body	1.19
Average AQ	Palm	.22
	Lower arm	.77
	Upper body	.94
High AQ	Palm	.51
	Lower arm	.81
	Upper body	1.25

 Table 3. Preference index for CT-optimal speeds at all locations, by AQ group.

#### 3.4. Discussion

Consistent with previous findings (Walker et al 2017), in the present study, touch observed at CT optimal velocity, at CT innervated locations was rated as more pleasant than non-CT optimal touch. Furthermore, touch to the upper-body, was rated as more pleasant than touch on the lower arm and palm, a finding consistent with the greater innervation density of C-fibres here (Liu et al., 2007; Kennedy et al., 2005).

Consistent with previous reports of directly felt touch, in this study ratings of observed touch varied as a function of participants' trait sociability. Thus, the ratings of the group with the lowest scores on the AQ showed previously reported relationships between stimulus velocities and perceived pleasantness, with touch on CT innervated sites showing a quadratic relationship between velocity and pleasantness ratings, while touch on the non-CT innervated palm showed a linear relationship between the speed of touch and perceived pleasantness. That is, here static touch was rated higher than moving touch. In contrast, while average and high AQ groups did rate CT optimal touch on CT innervated skin sites as more pleasant than faster and slower speeds, the data were not described by a quadratic function. Additionally, in these groups, ratings of touch on the palm were not described by a linear function. These data suggest that there was less difference between the affective ratings of CT-optimal and non-CT-optimal velocities in the High AQ group, despite these differences being significant. The polynomial regression allows for a more direct measure of the relationship between these Velocities within each Location.

While preference for CT over non-CT velocity touch was greater on the upper-body than the lower arm and palm, levels of autistic traits did not affect this affective preference. Thus, in contrast to the study hypothesis, differential ratings in the high versus low AQ groups do not reflect a specific reduction in sensitivity to CT targeted touch. This finding contrasts with the previously reported negative relationship between autistic traits and preference for CT targeted touch (Croy et al 2016); though it should be noted that differing formulae were used to calculate CT preference in the present study. Furthermore, findings from Voos et al (2013) revealed significant negative relationship between autistic trait scores and activity in the posterior superior temporal sulcus (pSTS) during affective touch stimulation, suggesting an effect of trait sociability on the processing of CT stimuli.

It is noteworthy that individuals with the lowest number of autistic traits rated static touch on the palm as more pleasant and more desired than either 3cm/sec or 30cm/sec strokes. This contrasts with previous studies where static touch on the palm was not rated more pleasant than CT-optimal touch (Walker et al 2017). CT afferents have never been found in the glabrous skin of humans, yet one explanation for this finding is that static touch on the palm is typical of social interactions, whether as a form of non-verbal communication between individuals or a means of providing support to others (Coan, Schaefer, & Davidson, 2006; Fisher, Rytting, & Heslin, 1976; Johnson et al., 2013; Weekes, Kagan, James, & Seboni, 1993). It is interesting to note that, when directly experienced, CT-optimal touch on the palm is consistently rated as similarly pleasant to CT-optimal touch in CT-innervated locations (Morrison, Löken, et al., 2011), Taken together, these findings suggest that ratings in the present study may reflect the learned quality of prosocial interactions (McGlone et al., 2012). However, contribution of  $A\beta$ afferents to the emotional processing of touch have not been widely explored. It is hypothesised that gentle touch to an A $\beta$  innervated surface also result in a positive affective valence similar to CT-innervted sites. Furthermore, Ellingsen et al (2016) discussed how top-down context can modulate the perception of touch making past tactile interactions likely to affect future experiences.

The questions presented to participants in this study measure their ability to experience empathically the touch depicted in the videos. Theoretically, a good empathic ability would show the most similar ratings of pleasantness and desire that first hand CT-optimal touch elicits. However, a key limitation of this study is that participant's trait empathic ability was not measured. The empathic ability of participants has been shown to affect their ability during tasks of embodiment or vicarious experience (Kaplan & Iacoboni, 2006; Minio-Paluello, Baron-Cohen, Avenanti, Walsh, & Aglioti, 2009; Rueda, Fernández-Berrocal, & Baron-Cohen, 2014), therefore it would have been prudent to consider how this may have affected participants ratings of the videos. Furthermore, an important consideration in research with individuals with ASD is that many researchers have shown the ability to cognitively empathise is atypical while emotional empathy appears typical (Dziobek et al., 2008; Mazza et al., 2014). If individuals with the highest number of autistic traits were comparable to individuals with ASD then it would be expected that empathic ability would also be lower in this group. This would result in atypical vicarious experience and subsequent ratings of both pleasantness and desire for observed CT-optimal touch. However, it is important to note that individuals with average number of autistic traits were also not as sensitive to the specific value of CT-optimal velocities as individuals with the lowest number of autistic traits.

A caveat to these results is with the nature of self-report measures. It is not possible to ascertain how truthful participants are being when reporting their responses. This may be particularly likely in an on-line experiment as conducted here. Thus, caution should be taken when considering both the results of the ratings task and the subsequent information provided by participants in relation to their trait sociability and demographics.

Given vicarious responses have been shown to reflect direct tactile experience it seems likely that the rewarding value of CT targeted touch is learned (Morrison, Löken, et al., 2011). Thus, it would be of interest to determine when developmentally this preference is acquired, given the early identification of somatotopic maps (Marshall & Meltzoff, 2015; Saby, Meltzoff, & Marshall, 2013; Saby et al., 2015). In future research, it would be beneficial to determine to what extent the vicarious experience of affective touch is a learned behaviour and the age when this is acquired. Research shows that first-hand experience of CT-optimal stimuli elicits similar responses to adults in infants (Fairhurst et al., 2014; Kida & Shinohara, 2013), young children and adolescents (Björnsdotter, Gordon, Pelphrey, Olausson, & Kaiser, 2014; Croy et al., 2017). This suggests that children do indeed process CT-optimal stimuli and thus should experience the typically pleasant, rewarding benefits of these social tactile interactions.

<u>Chapter 4</u>. Childhood Experience of Vicarious Affective Touch in Typically Developing and Autistic Children.

### 4.1. Introduction

It is not clear how children vicariously experience CT-optimal stimuli given the paucity of evidence. Croy et al (2017) reported a positive correlation for an affective touch index (preference for CT-optimal touch over other velocities) and participant age, suggesting that the older a participant was the more they showed a preference for CT-optimal stimuli. However, the cortical representation of CT-optimal stimuli is present in children younger than a year old (Jönsson et al., 2018; Kida & Shinohara, 2013). Croy, Sehlstedt, et al, (2017) showed that children showed a preference for CT-optimal velocities of touch, whilst this is in line with what is reported in studies with adults, it is not clear whether children experience the vicarious touch as adults do.

Abnormal sensory responsivity has recently been added to the diagnostic criteria for ASD (American Psychiatric Association, 2013). In particular, reference is made to somatosensory experiences of pain, with studies suggesting that ~70% of individuals with ASD experience some form of sensory processing abnormality (Zwaigenbaum et al., 2007). These sensory deficits have been shown across all modalities however, there is a paucity of evidence looking at deficits associated specifically with affective touch processing in ASD (Cascio et al., 2012; Kaiser et al., 2015). These studies indicated that individuals with ASD displayed reduced cortical activity in regions such as the pSTS and Insula cortex in response to CT-optimal velocity. Furthermore, Cascio et al (2012) reported that, beyond the initial sensory integration of stimuli in S1 and SII, individuals with ASD showed little other activity in non-primary somatosensory areas in comparison to typically developing participants. These

findings suggest that, in addition to early sensory processing, later processing of the socioemotional value of this touch is also atypical in individuals with ASD.

As well as these deficits in social behaviour, individuals with ASD are also reported to have fundamental deficits in empathic ability (Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006; Hamilton, Brindley, & Frith, 2007; McIntosh, Reichmann-Decker, Winkielman, & Wilbarger, 2006). It has been hypothesised that this is the result of a broken mirror neuron system, however Minio-Paluello, Baron-Cohen, Avenanti, Walsh, and Aglioti, (2009) found that it was not the mirror neurons themselves but the inhibition of this system for selfpreservation that was deficient. Here the authors recorded the muscle activity in participant's hands whilst they observed another individual receiving pain to their same hand. It was expected that the observation of another individual receiving pain would typically cause cognitive but not physical empathic responses to the stimuli. This is due to individuals being able to inhibit sensorimotor responses when not receiving the stimulus themselves. However, individuals with ASD did not show any reduction in evoked sensorimotor response to observed painful stimuli suggesting a reduced capacity to inhibit affective embodiment of the pain.

On the other hand, Hadjikhani et al (2014) reported that individuals with ASD are able to empathically experience pain stimuli but have atypical levels of cognitive reappraisal suggesting on whole abnormal empathic responses to others in pain. This suggests that these painful stimuli require an empathic ability not related to the aforementioned deficits. As discussed by Singer et al (2004) the empathic responses to pain are typically related to affective empathy. Specifically this suggests the difference in empathic ability between individuals with ASD and typically developing individuals is the result of fundamental differences in emotional and cognitive empathy. Conversely, Mazza et al (2014) reported that individuals with ASD showed significant impairments in cognitive empathy but not affective empathy, however these results were based on self-reported empathic ability. Here cognitive empathy is described as an individual's ability to understand what others are thinking or feeling. Emotional empathy on the other-hand is the ability to resonate with other's emotional state. It is clear that these atypical empathic responses to stimuli vary between individuals and stimulus type; however the ability to vicariously experience pleasant touch has not yet been researched.

The aim of the current study was to compare how children with ASD and age matched typically developing peers rate vicariously experienced affective touch. Typically developing adults show a quadratic relationship between different velocities of touch, with CT-optimal (~3cm/sec) being rated consistently as the most pleasant in both first hand (e.g. Ackerley et al., 2014; Pawling, Cannon, McGlone, & Walker, 2017) and vicarious experience of the touch (Walker et al., 2017). It is hypothesised that preference for CT-optimal touch is present from early childhood and therefore typically developing children will vicariously rate CT-optimal stimuli as the most pleasant and most desired. However, due to disturbances in the central processing of touch and empathic ability reported in ASD, it is hypothesised that children with an ASD diagnosis will rate touch as less pleasant and be less sensitive to the specific rewarding value of CT-targeted touch than their typically developing peers. In children with ASD it is hypothesised ratings of touch pleasantness will be negatively correlated with parental reports of tactile hypersensitivity.

### 4.2. Method

#### 4.2.1. Participants

Fourteen participants diagnosed with ASD aged 7-12 (males = 12, M=9.14, SD= 1.70), were recruited through a child support group (ASC-Inclusion, Speke, Liverpool), specialising in LEGO based therapy. To ensure an official diagnosis had been made, parents were asked to provide the name of their child's diagnosing physician. Each child attended a laboratory session at Liverpool John Moores University, which lasted approximately half an hour. All children in the ASD group attended the session with a parent who provided informed consent for their child's participation in the study. Each child also provided informed assent individually before beginning the research. These children received a LEGO toy for taking part in the study.

A further 25 typically developing participants (males = 10, M=8.4, SD= 0.6) were recruited from a year four class (typical age 8-9) at Westhead Lathom St James, Primary School, Ormskirk. None of them had a diagnosis of ASD. Consent was given in loco parentis by the class teacher. Each child also provided informed assent individually before beginning the research. Liverpool John Moores University Research Ethics Council approved the study prior to recruitment.

#### 4.2.2. Measures

#### 4.2.2.1. British Picture Vocabulary Scale.

To ensure groups were matched for receptive vocabulary, participants completed the British Picture Vocabulary Scale (BPVS, Dunn, Dunn, Whetton, & Burley, 1997) one-on-one with the researcher. During the test, the researcher read out a word, and the child indicated which of four pictures shown represented that word. All participants began the test at the receptive vocabulary level expected for their age. The test progressed until the child scored 8/10 incorrect answers in a single age-related block. Their receptive vocabulary was defined by the level of the preceding block.
#### 4.2.2.2. Sensory Profile

Parents of children in the ASD group were given the Sensory Profile (Dunn, 1999) to complete. The scale consists of 60 questions asking how the child responds to sensory experiences at home. Parents completed this by hand whilst their child completed the touch rating task. Individual questions refer to a single sensory modality. For this study, responses to questions relating to the sense of touch were extracted. For example, "reacts emotionally or aggressively to touch" and "touches people and objects". Touch sensation scores ranged from 18 to 90 with sensitivity "definitely different from others" scored 18-64.

#### 4.2.2.3. Touch Videos

Next, the children watched a series of short (5s) video clips showing touch delivered from one individual to another (as described in **Chapter** 2 and **Chapter** 3) (Walker et al, 2017). After each video the children were asked, "How nice do you think that was for the person being touched?" and "How much would you like to be touched like that?"

The response scale used was one previously designed and validated for use with young children (Cascio, Lorenzi, and Baranek, 2016; Croy et al 2017) (*Figure 16*). To ensure the children could use the scale effectively, before rating the videos participants completed a series of six practice trials. Here they were shown a randomised series of pictures each depicting a food that children typically find pleasant (sweets, fries and chocolate) or unpleasant (mushrooms, Brussels sprouts and tomatoes). Children were asked to use the smiley face scale to rate how much they personally liked or did not like each food. Additionally, on half of the practice trials children were also asked to rate how much a member of their family liked that food. This ensured that they understood both how to use the scale and that others might have different preferences to them.



*Figure 16. Example of the smiley face scale used to make answering the questions more accessible to children (adapted from Cascio et al, 2016 & Croy et al, 2017).* 

## 4.2.3. Procedure

The test procedure differed slightly for the two groups. For the ASD group, testing took place in psychology laboratory at Liverpool John Moores University. A parent was present in the test room throughout the session. During the testing, parents were asked to complete the Sensory Profile. Participants in the ASD group completed the entire procedure on a one-on-one basis with the experimenter. First, they completed the BPVS, and then they received training on the use of the rating scale (*Figure 16*). To do this a series of typically, pleasant and unpleasant foods were shown to the participants one at a time and asked to rate how pleasant or unpleasant they found these foods. It was expected that there would be some variation in how the children would rate these food items, so they were asked to say why they were choosing that particular face on the scale so the researcher could determine that the child understood the scale. Participants then watched the touch videos in a random order, immediately after viewing each one they rated how pleasant they perceived the touch to be for the person receiving it and how much they would like to be touched like that.

For the control group, testing took place at school. Participants first completed the BPVS on a 1:1 basis with the experimenter in a quiet room. Due to unresolved issues with the school firewall, it was not possible to get the YouTube hosted videos working on the individual

tablets computers children were supposed to use to complete the task. Thus, the videos were shown via a projector to the whole class, each participant watched the videos in the same order and rated them on their individual tablet immediately after watching.

## 4.2.4. Analysis

Three children did not complete questions for all of the videos, thus their responses could not be matched to a specific stimulus and their data was removed prior to analysis. Additionally, four children gave the same response for every question regardless of the Velocity or Location shown in the videos, they too were excluded prior to analysis. Therefore, final participant numbers were n=13 for the ASD group (males = 11, M = 8.32 years) and n=19 for the control group (males = 8, M = 9.31 years). First a repeated measures ANOVA was completed on the data with diagnosis set as a between subject variable and within-subjects variables of Location (Palm x Lower Arm x Upper Body) and Velocity (Static x 3cm/s x 30cm/s). Secondly, a polynomial regression was used to determine how well quadratic and linear terms describe the relationship between perceived pleasantness and touch velocity at each of the three body sites. Independently, a repeated measures ANCOVA was completed on ASD group data to assess the relationship between that parent reported sensory experiences and the child's ratings of touch pleasantness.

#### 4.3. Results

Initially independent samples T-Tests were run on the data to determine whether the groups were matched for Age and receptive vocabulary. There was no significant difference between Control and ASD participants in terms of Age t(14.1)=2.08, p > .05 (M=8.36,

M=9.14 respectively) or BPVS score t(30)= -1.96, *p*>.05 (M=9.95, M=10.85 respectively).







*Figure* 17 shows the frequency of scores for individuals in the ASD group for the touch processing subsection of the Sensory Profile (Dunn, 1999). Low scores on this scale reflect atypical responses to tactile stimuli whereas a score of 64 or above reflects typical responses to touch. Three individuals in this group scored above 64, suggesting typical touch processing.

# 4.3.2. Question one: "How pleasant was that action for the person being touched?"

As described in **Chapter** 2, data were condensed into three Locations. A repeated measures ANOVA with the factors Group (Control vs ASD) x Location (Palm x Lower Arm x

Upper Body) x Velocity (Static x 3cm/s x 30cm/s), revealed no significant main effect of Location F(2,60)=.709, p=.496 or Velocity F(2,60)=2.09, p=.132. Furthermore there was no significant interaction between Location x Velocity F(4,120)=.435, p=.783 and no significant main effect of Group F(1,30)=1.56, p=.222. Also, Group didn't interact with any other factor (all p>.05) (*Figure 18*).



*Figure 18.* Mean ratings of touch pleasantness for the question "How nice was that for the person being touched?" for 18a) Control participants 18b) ASD participants (+/- SE bars).

First, Touch Processing score was correlated with individual ratings to determine whether there was a relationship between touch sensitivity and perceived pleasantness of touch. Here, only Static Palm and Static Upper Body videos significantly correlated with Touch Processing score r=.555, n=13, p<.05 and r=.608, n=13, p<.05 respectively suggesting the highest ratings of pleasantness for individuals with the most typical responses to touch. However, Touch Processing score did not correlate with affective ratings at any other Location or Velocity (ps>.05). An ANCOVA was conducted to test the effect of the ASD group's sensory profile score on their touch ratings. There was no significant interaction between Location x Touch Processing Score F(2,22)=2.35, p=.121 nor Velocity x Touch Processing Score F(2,22)=.299, p=.745. Furthermore there was no significant main effect of Touch Processing score F(1,11)= 2.47, p>.05.

Polynomial regression analyses were then conducted to determine whether a quadratic term would provide a significant fit for ratings of touch on CT-innervated Locations as shown in previous studies (e.g. Walker, Trotter, Woods, & McGlone, 2017). In neither control group nor the ASD group did a quadratic term provide a significant fit for the data. (Lower Arm p=.212 & p=.324, Upper Body p=.982 & p=.534 respectively). Furthermore, a linear model did not provide a significant fit for either group's ratings of the different velocities of touch at any of the Locations (all p>.05). Here, neither typically developing children nor those with ASD rated CT-optimal touch as any more pleasant than non-CT-optimal or static touch.

# 4.3.2.1. CT preference index: "How pleasant was that action for the person being touched?"

As with Study 1, a CT preference index was calculated for each Group and each Location using the following equation:

2

Table 4, shows the CT- preference index scores for question one. A repeated measures ANOVA with a between subject factor Group and within subject factor of Location was run on the data to determine whether CT-optimal stroking was preferred at CT-optimal Locations. There was no main effect of Location in either the control F(2,17)=.1304, p=.297 or ASD group F(2,11)=.718, p=.509 suggesting that, unlike previous reports with adults, touch location had not effect on children's ratings of touch pleasantness.

Table 4. CT preference index for CT optimal velocities at all Locations, separated by group

Group	Location	CT Preference Index
Control	Palm	.24
	Lower arm	.58
	Upper body	05
ASD	Palm	08.
	Lower arm	.44
	Upper body	.48

# 4.3.3. Question two: "How much would you like to be touched like that?"

Again, a repeated measures ANOVA revealed no significant main effect of Location F(2,60)=.325, p=.724 or Velocity F(2,60)=.466, p=.630. Also there was no significant interaction between Location x Velocity F(4,120)=.133, p=.970 and no significant effect of Group F(1,30)=.094, p=.762 (*Figure 19*).



*Figure 19.* Mean ratings for of touch desire for the question "How much would you like to be touched like that? for 19a) Control participants (9b) ASD participants (SE bars).

Initially, Touch Processing score was correlated with individuals' ratings to determine whether there was a relationship between touch sensitivity and desire for touch. Here there were no significant correlations for any desire rating at any Location or Velocity (all ps>.05). As with question one, for the ASD group, sensory profile score was added to the model as a covariate. The ANCOVA revealed no significant interaction between touch processing score and Location F(2,22)=.739, p>.05 or Velocity F(2,22)=.126, p>.05. Again there was no significant main effect of Touch Processing score F(1,11)=.98, p>.05. Indicating that differences in parent reported touch experience are not related to children's ratings of touch desire for the touch shown in the videos.

Polynomial regression was conducted to determine whether there was a preference for CT-optimal Velocity touch at CT-innervated Locations. However, neither quadratic nor linear terms provided a significant fit for the data, at any of the Locations, in either group (all p>.05).

# 4.3.3.1. CT preference index: "How much would you like to be touched like that?"

Table 5 shows the preference index scores for participants. Again, a repeated measures ANOVA with between subject factor of Group (Control & ASD) and within subject factor of Location (Palm x Lower Arm x Upper Body) was run. There was no significant main effect of Location for either the control F(2,11)=1.255, p=.323 or ASD group F(2,17)=1.635, p=.224 suggesting that, unlike adults, ratings did not differ depending on the location of the observed touch in either group.

Group	Location	CT Preference Index
Control	Palm	.66
	Lower arm	.59
	Upper body	11
ASD	Palm	23
	Lower arm	.04
	Upper body	.40

Table 5. CT preference index for CT optimal velocities at all Locations, separated by group type.

#### 4.4. Discussion

In contrast to previous reports of directly felt touch (Croy et al 2016), here young children did not show the previously reported relationship between velocity and perceived pleasantness for vicariously experienced touch. That is, ratings on CT innervated skin sites were not described by a quadratic term and touch on the palm was not described by a linear term. In addition, children's ratings of touch pleasantness were not location specific; they did not rate touch applied to skin sites where CTs are hypothesised to be most densely innervated as any more pleasant than touch applied to sparsely innervated and non-CT innervated locations. Taken together these results suggest that young children have not learned the specific value of CT-optimal touch or the cognitive system responsible for determining the rewarding properties of stimuli is not functional at this age.

In addition, in contrast to the main study hypothesis, children with a diagnosis of ASD did not show blunted ratings of CT optimal touch in comparison to their typically developing peers. Indeed, there was no effect of diagnosis on any aspect of touch ratings. Furthermore, parent reports of children with ASD's sensitivity to tactile stimuli were not related to the children's own ratings of touch pleasantness. In Chapter 3, the impact of using self-report measures as opposed to more objective measures were considered. Again, here the sensitivity of a child to tactile input is influenced by their parent's own experiences with their child so this makes the reported sensitivity less accurate than a psychophysical test of sensitivity. A further consideration is that the participants with ASD had their parents in the experiment room with them whereas the typically developing children had their peers. This would fundamentally result in a different atmosphere for the child and may cause them to act differently in order to behave as the accompanying individual would expect.

Data from this behavioural ratings study contrasts with physiological and neurological studies, which indicate affective touch elicits the same responses in children as in adults (e.g.

Björnsdotter et al., 2014; Croy et al., 2017; Fairhurst et al., 2014). For example, 9-month old infants were reportedly more engaged in attending to the stroking touch delivered at a CT-optimal than non-CT optimal velocity. Children's heart rate reduced more in response to CT-optimal stroking than to faster or slower velocities (Fairhurst et al., 2014). A caveat to this is that these published studies all used physical first-hand touch and not observation of CT-optimal stimuli.

Further, an fMRI study reported activation in the insula cortex in response to CT optimal touch in typically developing 12-year-old children, which was significantly blunted in children of the same age with an ASD diagnosis (Kaiser et al 2015). Thus, it appears children do not experience these vicarious stimuli in the same way as adults. While differences in neural responses to touch are commonly reported between those with ASD (high traits) and control participants, these processing differences are not always reflected in explicit affective ratings (Voos et al., 2013).

Here unlike other studies, the tactile experience of children with ASD were comparable to the control participants. Furthermore, the novel use of touch videos with this population show that both the control and ASD participants show similar levels of empathic ability for the emotional components of touch processing (despite being different to adult studies). Conversely however, pain research suggests differently, whereby typically developing children show activation in the regions of the brain responsible for pain empathy in adults (Decety, Michalska, & Akitsuki, 2008). Furthermore, this research showed that activation for pain regions was present regardless of whether the individuals depicted in the stimuli hurt themselves by accident or whether they were hurt by another individual present, suggesting that these empathic responses do not rely on social context. Furthermore emotional contagion for pain is also intact in ASD populations (Hadjikhani et al., 2014). One possible explanation of these null results is the ability of the child to empathise with the individuals being touched. Specifically the videos depict touch between two adults, whereas these children are more likely to experience peer-to-peer touch or parent/caregiver delivered touch (adult-to-child). Future studies should consider this as a variable and show videos matched to the age group being tested.

To date, the vicarious experience of children observing CT-optimal touch has not been studied so the hypotheses for this study were based on evidence of vicarious touch in adults (Walker et al., 2017) and evidence from studies using physical tactile sensations as the stimuli (Croy et al., 2017; Kida & Shinohara, 2013). It is therefore possible that the children at this young age do not experience the same empathic responses to CT-optimal touch as adults do. This therefore suggests that vicarious experience of CT-optimal touch may well be present in children but self-report measures are not sensitive enough to measure this capacity.

Furthermore, the differences between children and adults in vicarious CT-optimal touch processing is potentially due to a continued optimisation of the regions of the brain responsible for processing affective touch. Specifically, children show larger neural responses to affective touch than adolescents and adults (Björnsdotter et al., 2014), ultimately connections that are not used regularly are repurposed for other functions. If the brain networks responsible for processing CT touch become optimised over development then it is likely that the children will learn the function and benefit of affective touch through this neuronal streamlining. As described previously, affective touch preferences are likely to be the result of conditioned response to these tactile interactions with others (Morrison Löken et al, 2011). However, this is not supported by first-hand processing of CT-optimal stimuli, where children rate first-hand CT-optimal touch as more pleasant than other velocities (Croy et al 2017) as with adults (McGlone et al., 2012; Pawling, Cannon, et al., 2017). It is important to consider that in this study the participants who rated stimuli at the highest levels of pleasantness consistently were removed from analyses as this suggested that they did not perceive differences between the

touch types in terms of pleasantness or desire. In Croy et al (2017) this was not the case, here the authors retained participants who rated all velocities at the same maximum pleasantness.

A further limitation of this study came from the running of the stimuli for the control participants. The study was due to be completed in one visit to the school but it was not anticipated that the presentation software would not operate with the school's IT system. The participants in this group observing all the videos as a social group together may well have affected their subsequent ratings of pleasantness and desire. Despite the fact participants were required to answer themselves without discussing the answers with their peers, it must be taken into consideration that they were sat with their peers during the experiment. In future research it would be better to have children complete this study one-on-one so they do not feel the need to comply with others around them.

In conclusion, despite previous research suggesting that typically developing individuals appear to show a preference for CT-optimal stroking when it is felt directly, here young children do not show the expected preference for CT-optimal touch when it was experienced vicariously. Furthermore, no significant differences were found between ratings of typically developing children and those with ASD, despite literature showing that cortically individuals with ASD do not process touch in the same way as typically developing individuals. However, it is important to note that the most prominent differences in past research are from measures of cortical activation suggesting that behavioural ratings are not sensitive enough to reveal trait differences in vicarious experience of children with ASD or typically developing controls.

<u>Chapter 5.</u> The vicarious experience of social touch does not convey affective context.

# 5.1. Introduction

One way to measure an objective affective response to stimuli is using facial electromyography (EMG). This has been shown to be a reliable measure of affective state (Boxtel, 2010; Lamm, Porges, Cacioppo, & Decety, 2008; Larsen, Norris, & Cacioppo, 2003; Tan et al., 2012). In these studies, activity from the muscles of the face associated with explicit affective arousal, such as smiling and frowning are measured. These affective states are usually measured for highly salient stimuli, such as images selected from the International Affective Picture System (IAPS) (Lang, Bradley, & Cuthbert, 1997), with increase in positive affect resulting in a decrease in negative affect (Larsen et al., 2003). This has been shown across all sensory modalities with physiological affective state changes reported in response to emotional videos (Cacioppo, Petty, Losch, & Kim, 1986), affective vocal tones (Hietanen, Surakka, & Linnankoski, 1998), positively and negatively valenced odours (de Groot et al., 2015), sweet, bitter, and neutral tastes (Chapman, Kim, Susskind, & Anderson, 2009) and empathic pain sensation (Lamm et al., 2008).

Such affective responses have been shown to vary depending on individual experience with the stimuli used (Kirsch, Snagg, Heerey & Cross, 2016). Thus, in a study where participants viewed short videos of ballet dance moves, only in experienced dancers were affective responses predictive of subjective ratings of how much the observed move was liked. A recent facial EMG study reported positive affective responses, as indicated by increased zygomaticus activity, to CT targeted touch (Pawling, Cannon, et al., 2017). Here, activity in the Zygomaticus Major (ZM, smile muscle) increased more in response to a -CT-optimal stimulus than to non-CT-optimal stimulus, while activity in the Corrugator Supercilli (CS, frown muscle) was not affected by stimulus type. Autistic traits have been shown to correlate negatively with CT-optimal touch awareness (Croy et al., 2016). Furthermore, individuals with Autism Spectrum Disorders (ASD) do not experience emotional empathic responses as typically developing individuals do (Mathersul, McDonald, & Rushby, 2013; Oberman et al., 2009). These studies both suggest that individuals with ASD have delayed affective responses to visual stimuli, it is not known how individuals with ASD or indeed, high level of autistic traits will respond to affective touch. However, it is noteworthy that the differences reported in these studies are latent mimicry rather than physiological differences in EMG amplitude, suggesting the responses are typical but delayed.

The aim of the present study was to determine whether observation of CT-optimal stimuli results in the same affective responses that first-hand CT-touch does. Given the evidence that observation of CT-optimal stimuli elicits the same cortical and behavioural responses as with first-hand touch it is hypothesised that observation of CT-optimal stimuli will result in the same affective facial responses reported by Pawling et al (2017) in response to directly felt touch. Additionally, it is hypothesised that participant's self-reported level of trait sociability (autistic traits) will affect their subsequent vicarious experience of CT-optimal touch, with levels of EMG activity associated with positive affect reduced in participants with the highest levels of autistic traits.

#### 5.2. Method

#### 5.2.1. Participants

Participants were 38 (Females = 29, M = 19.9 years, SD = 2.7) undergraduate psychology students from Liverpool John Moores University who were recruited using an online participant recruitment tool (SONA) and took part in exchange for course credit. Participants were aged 18-30, with no history of mental health condition and no neurological disorder that affected their perception of touch. It was also required that participants had not completed any previous studies on affective touch. The study was approved by Liverpool John Moores University Research Ethics Committee.

## 5.2.2. Materials

#### 5.2.2.1. EMG

Participants' skin was prepared in line with the guidelines laid out in chapter 2. Bipolar placement of the shielded 4mm Ag-AgCl electrodes were positioned along the Zygomaticus Major and Corrugator Supercilli muscles of the face, (*Figure* 8) as activity in these muscles has been associated with positive and negative affective arousal respectively (Larsen et al., 2003). A grounded electrode was placed by the participant's hairline in the centre of their forehead. The EMG data were filtered online between 0.1 and 5000Hz and an offline 50Hz notch filter was then applied. A further offline bandpass filter was applied between 20-400Hz as laid out in Pawling, Cannon, McGlone and Walker (2017). Prior to further analysis the data were full-wave rectified.

# 5.2.2.2. Video Stimuli

The experiment was programmed in E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA). Participants watched a series of 27 videos depicting touch between two actors with minimal social context (e.g. *see Figure* 20). The videos showed one actor being touched by another actor at five body locations (palm, dorsal forearm, ventral forearm, upper arm and

back) at three velocities (static touch, 3cm/sec and 30cm/sec). Fifteen of these videos were those used in Walker et al (2017), Study 1, and 2. A second set of 12 videos were also added, these depicted touch at the same three velocities but only at 4 locations as they did not include any touch delivered to the ventral surface of the forearm. These videos had previously been validated in a pilot study and elicited the same relationship between velocity, location and perceived pleasantness as the previously published set (Walker et al 2013 unpublished observation). These videos depict two male actors (*Figure 20*) compared with the previously used videos that showed female-on-male touch. These extra videos were used to increase the power of the data. Furthermore, analyses revealed no significant main effect or interaction with video type.



*Figure 20.* Additional videos to those used in studies 1 & 2 were included here. In these, touch occurred between two Asian male actors. The videos depicted touch at the same three velocities as previously used videos however, touch was only delivered at four locations: Palm, Dorsal Forearm, Upper Arm and Back.

The 27 videos were shown twice each. First, participants passively viewed each of the videos once in a random order. Then, after a short break, they watched all the videos once more in a random order but this time, immediately after each one they were prompted to rate: "How pleasant do you think that action was for the person being touched?"

To ensure participants remained focussed on the videos during the task they were required to complete a simple attentional task five times, presented randomly between videos during both the passive and active phases of the experiment. This attentional task was chosen as it required minimum effort and was free from any affective context (e.g. Hommel, 1993). Here the letters "R, P, L, K, J, G, F, D, S, C, B" were presented on the screen in random locations. On each trial one of the letters was flipped 180° on their vertical-axis. These letters were chosen as they are all clearly different when mirrored in this way. Participants' task was to search for the letter that was in the incorrect orientation and use their mouse to click on it. Participants did not progress to the next trial until they had chosen the correct letter.

## 5.2.2.3. Questionnaires

Upon completing the video task, participants were asked to complete a series of questionnaires presented on the laptop in front of them. Questionnaires were delivered using custom made scripts running in PsychoPy (Pierce, 2007). In this study participants completed a series of questionnaires aiming to measure self-reported levels of sociability and empathy. First the participants completed the AQ (Baron-cohen et al., 2001) (detailed description in **Chapter** 2). They then completed the Interpersonal Reactivity Index (IRI) (Davis, 1980). This questionnaire measures different functions of empathic ability using 4 subscales: Fantasy, Perspective-Taking, Empathic Concern and Personal Distress. Each of the four, subscales consist of seven questions rated from 0, "does not describe me very well" to 4, "describes me very well". The four subscales display poor inter-scale correlation and are thus treated separately (ranging from r = -.29-0.33).

#### 5.2.3. Procedure

Upon arriving at the laboratory, participants were presented with the participant information sheet. Participants provided written consent with the understanding they were completing a study that was measuring frontal lobe responses to the videos they would be shown. Participants were not informed at this stage that in the second half of the study they would be expected to rate the same videos they had already seen to ensure passive viewing of the videos without specific priming. This was revealed after the first passive viewing phase had been completed. To reduce the electrical interference the experiment took place in a Faraday cage. During EMG set up, participants were talked through each procedure so they were comfortable with the process. The researcher remained outside the Faraday cage whilst participants watched the videos only going in to explain the active phase of the study (*Figure 21*).



*Figure 21.* Set up of the study, showing participants sat in the Faraday cage watching videos on a monitor set in the wall of the cage. The researcher sat outside the cage for the duration of the experiment monitoring the EMG output.

Each trial (*Figure 22*) began with a cue asking participants to relax. Participants made a mouse click when they were ready to watch the following video. The videos were presented in a random order and all lasted for 5000ms, immediately after each video, participants observed a blank screen for a further 2000ms. In the active phase, the rating question was presented immediately after the 2000ms post video screen. In the passive phase, after the blank screen, the trial was complete and the next one commenced. The visual search task appeared randomly between trials five times during each phase. Once the video task was complete, participants were asked to complete the questionnaires presented in PsychoPy (Pierce, 2007).



*Figure 22.* The procedure for each of the trials. In the passive phase (black boxes), participants observed the videos without making any response. In the active phase, participants answered the question "How pleasant was that action for the person being touched?" (Blue box).

# 5.2.4. Analysis

The EMG data were extracted using a custom-made macro in LabChart (ADI). Average peak amplitudes were taken in 20, 100ms time bins across the 2000ms baseline. A further 50,

100ms time bins were taken from the video period of the trial and 20, 100ms time bins were taken from the post video 'evaluation' period. Data were then imported into SPSS where they were graphed. Separate graphs were created for each participant with individual lines representing the 54 trials in the study. The data were eyeballed to determine the trials where baselines were contaminated by noise. Percentage change scores were calculated for each data bin and initially any change score over 500% was removed. Next, a whole cohort average was taken and data points +-3SD of this mean were removed. Trials remaining M=49, SD=1.84. These processing steps were based on those incorporated in Pawling, Cannon et al (2017).

All data were analysed in SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Similarly, to **Chapters** 3 & 4, ratings data were analysed as a 3x3 ANOVA condensing ratings across equally densely innervated locations. As in Pawling et al (2017) EMG data were analysed separately for each muscle in a 2x2 ANOVAs. These were all run with Time (stroking period x post stroking period), Location (Palm x Forearm) and Velocity (3cm/s, CT-optimal x 30cm/s, non-CT-optimal) factors to determine the difference in activity for CT-optimal vs non-CT-optimal (Pawling et al., 2017). These Locations typically produce the largest velocity dependent differences in pleasantness ratings and are those most regularly used in CT research, representing a CT-innervated (Arm) and a non-CT-innervated (Palm) body site.

#### 5.3. Results



Figure 23. Frequencies of AQ scores in the study sample. Participants mostly scored around the typically developing average (17) (Baron-Cohen et al., 2001). The sample population range was 6-39 with an average AQ score of 19 (SD= 8.08).

AQ scores were calculated and graphed (*Figure 23*) to determine how this data would be included in further analysis. In previous studies, groups have been divided based on AQ score however here, due to the small range of scores particularly clustered around the typical population average, these scores were added as a covariate. Also in analysis of the IRI, scores on relevant subscales were added to the analysis as a continuous variable (*Table 6*).

To determine how these scales related to each other, a Pearson's correlation was run on the data. AQ as a measure of autistic traits in the typical population was significantly negatively correlated with Perspective Taking r=-.65, n=36, p<.001 and Empathic Concern r=-.56, n=36,

p<.001 for the IRI subscales. Therefore, in further analysis these two IRI subscales were the ones selected.

**Table 6.** Individual subscale scores for the IRI of empathic ability. Here the Mean, SD, Min and Max scores forall participants are presented.

IRI Sub-Scale	Mean	SD	Min	Max
Fantasy	17.50	4.28	6	24
Perspective Taking	14.89	4.76	3	22
Empathic Concern	18.86	4.20	8	27
Personal Distress	14.53	6.01	0	28

#### 5.3.1. Pleasantness Ratings

Initially a 3x3 repeated measures ANOVA with the factors Location (Palm x Lower Arm x Upper Body) and Velocity (Static x 3cm/s x 30cm/s) was run on the video ratings data. Consistent with previous findings in adults, this revealed a significant main effect of Location F(2,68) = 5.50, p < .01,  $\eta^2 = .14$ , Velocity F(2,68) = 40.28, p < .001,  $\eta^2 = .44$  and a Location x Velocity interaction F(4,136) = 25.44, p < .001,  $\eta^2 = .43$ . Simple main effect analyses revealed 3cm/s (CT-optimal) touch was rated as significantly more pleasant than Static and 30cm/s (non-CT-optimal) touch at CT-innervated locations (all p < .001, *Figure* 24). This was not the case for the Palm, where CTs are not found, here there was no significant difference between ratings of Static and 3cm/s touch (p > .05).



*Figure 24.* Average pleasantness ratings across locations for each velocity. Significant differences are found between all velocities at the Lower Arm and Upper Body locations with CT-optimal 3cm/s being rated as the most pleasant (\* = p < .05, \*\* = p < .001).

# 5.3.2. EMG – Zygomaticus Major

Data from active and passive stages of the study were combined in these analyses and to further maximise power in the analysis of the EMG data, consistent with previous studies, only responses to trials depicting 3 and 30cm/sec touch to the arm and palm were compared ass ratings data show significant velocity dependent differences in pleasantness ratings at these body sites. Initially an ANOVA with the factors Time (Video x Post-Video), Location (Palm x Lower Arm), Velocity (3cm/s x 30cm/s) was conducted (*Figure 25*). Here there was a significant main effect of Time F(1,35)= 7.82, p < .001,  $\eta^2 = .19$ , but no significant main effect of Location F(1,35)=.015, p > .05 of Velocity F(1,35)= .1, p > .05. There were also no



# significant interactions between these factors (ps>.05).

*Figure 25.* Average (across participants and trials) percentage change in the Zygomaticus Major activity for the Palm (25a) and Lower arm (25b). Data on the x-axis reflects 100ms time bins, the initial 50 bins represent

the 5000ms video period followed by 20 bins in the 2000ms post-video period. These Time periods are separated by a black line.

To further look at the significant main effect of Time, data were collapsed across Locations and Velocities. Using a one sample T-Test a significant difference was found between Video (M= .22, SD= 12.33) and Post-Video (M= 11.91, SD= 15.49) sections of the trial t (35)= 4.23, p>.001 (*Figure 26*). This reflects that fact that there was significantly greater activity in the zygomaticus muscle during the 2000msec post video period, even if they were not actively evaluating it in preparation for making an explicit rating in the second block.



*Figure 26.* There was a significant main effect of Time, reflecting a significant increase in ZM activity in the post-video period (S.E. bars).

Additional analyses were run to determine the impact of AQ and IRI scored on ZM activity. An ANCOVA with the factors Time x Location x Velocity x AQ revealed there were no significant main effects of Location F(1,34)=.02, p>.05, or Velocity F(1,34)=1.18, p>.05, however there was a significant main effect of Time F(1,33)=32.62, p<.001,  $\eta^2=.50$ . Time did not interact with Location F(1,34)=.01, p>.05 or Velocity F(1,34)=.47, p>.05. Furthermore AQ did not interact with any other factor (ps>.05). Secondly, the ANCOVA was run with the Empathic Concern subscale of the IRI as a covariate. In this analysis there were no significant main effects at all, the aforementioned main effect of time was no longer significant when adding this subscale to the analysis F(1,34)=.78, p>.05. Finally, an ANCOVA with Perspective taking as a covariate was included in the analysis. Here, again there were no significant interactions between Perspective taking and any of the other variables (ps>.05).

#### 5.3.3. EMG – Corrugator Supercilli

Again, the CT-optimal (3cm/s), non-CT-optimal (30cm/s), Palm and Lower Arm data were extracted from the CS activity. An initial ANOVA with the factors Time (Stroking x Post-Stroking), Location (Palm x Lower Arm) and Velocity (3cm/s x 30cm/s) was run on the data (*Figure 27*). Here there was a significant main effect of Time F(1,34)= 5.53, p<.05,  $\eta^2=.14$ , again reflecting greater muscle activity in the post video period. There was also a significant Time x Location x Velocity interaction F(1,35)= 7.51, p=.01,  $\eta^2=.18$ . However, there was no significant main effect of Location F(1,35)= 3.15, p>.05 or Velocity F(1,35)= .36, p>.05 however.



Figure 27. Average (across participants and trials) percentage change in the Corrugator Supercilli muscle activity for the Palm (27a) and Lower arm (27b). Data on the x-axis represents 100ms time bins, the initial 50 represent the 5000ms video period followed by 20 time bins for the 2000ms post-video, these Time periods are separated by a black line.

To determine where the Time x Location x Velocity interaction was being driven, ANOVAs were run on Locations individually. In response to videos depicting touch on the Palm there was a significant interaction between Time and Velocity F(1,35)= 6.04, p<.05,  $\eta^2=.15$ , however, there were no significant main effects of Time F(1,35)= 2.65, p>.05or Velocity F(1,35)= 1.50, p>.05 individually (*Figure 28*). Simple main effect analysis revealed that for Video period there was a significant difference in CS activity between Velocities (p<.01), with greater activity to 3cm/sec than 30cm/sec touch. However, in the Post-Video period there was no significant difference between these velocities (p>.05) (*Figure 28*). Furthermore, there was no significant difference between video and post-video periods for either 3cm/s or 30cm/s stimuli, despite 30cm/s stimuli suggesting a strong trend (all p>.05). For data from the Lower Arm there were no significant interaction between these factors F(1,35)=.52, p>.05. Again, there were no significant difference between Time period for either Velocity (p>.05).



**Figure 28**. Average percentage change in the Corrugator Supercilli muscle activity for Palm and Lower Arm Locations. The analyses show that only at the Palm (28a) was there a significant difference between velocities for the Video period with 3cm/s resulting in an increase of CS activity and 30cm/s resulting in a decrease in CS activity (S.E bars). There were no significant differences between Velocities for the Lower Arm (28b).

Next, an ANCOVA with the factors Time x Location x Velocity x AQ was run on the CS data. As with the previous ANOVA, there were no significant main effects of Time F(1,34)=1.53, p>.05 or Location F(1,34)=.05, p>.05 however, there was a significant main effect of Velocity F(1,34)=4.06, p<.05,  $\eta^2=.11$ . Also, there was also a significant Time x

Location x Velocity interaction F(1,34) = 4.39, p < .05,  $\eta^2 = .11$ , (*Figure 27*). Again AQ score did not interact with any of the other factors (all p>.05).

Finally, two ANCOVAs were run on CS data with the Empathic Concern and Perspective Taking subscales of the IRI. Here, there was a significant main effect of Location F(1,34)=5.05, p<.05,  $\eta^2=.14$ , but no significant main effect of Time F(1,34)=.44, p>.05 or Velocity F(1,34)=.06, p>.05. However, Location also interacted with the Empathic Concern subscale of the IRI F(1,33)=3.98, p<.05,  $\eta^2=.11$ , (*Figure 29*). Here the larger Empathic Concern score was related to an increase in CS activity for non-CT-innervated touch and a decrease in CS activity for CT-innervated touch. The Perspective Taking subscale of the IRI did not interact with any other variables (ps>.05).



*Figure 29*. The relationship between Empathic Concern and CS activity collapsed across Velocities and Time for each location. A larger score for Empathic Concern suggests a greater ability to feel emotionally concerned for another individual in a difficult situation.

#### 5.4. Discussion

Here, facial EMG has been used to determine whether observation of CT-optimal touch elicits similar patterns of affective response as first-hand touch (Pawling et al., 2017). However, in contrast to directly felt touch, here activity in neither the ZM nor the CS differentiated between different velocities of touch or between touch on CT and non-CT innervated locations. In contrast, subjective ratings of touch pleasantness were consistent with previous studies. That is, touch delivered at CT optimal velocity to the Upper Body was rated as most pleasant.

The increase in activity for the ZM in the post-video period could be the result of many factors. Here, it is hypothesised that this increase is the result of an evaluation and subsequent affective output consistent with the slower activity associated with CT input processing. However, other factors could be that the participants chose this time to blink, after the video before the next trial (or rating). Furthermore, participants may have moved, or readjusted during this period. Although these are plausible explanations, the initial cleaning and eventual grand averaging of the data would reduce/remove any of these potential threats to the signal.

Research into the effects of affective touch observation consistently show patterns of behavioural and neurological data comparable with first-hand touch experience (Keysers et al., 2010; Morrison, Björnsdotter, et al., 2011; Morrison, Löken, et al., 2011; Schirmer et al., 2014; Walker et al., 2017). These studies all show that observation of CT-optimal or socially relevant touch is processed in a similar way to first-hand experience of the touch. However, the current study shows that the vicarious experience of CT-optimal touch does not result in a positive affective response. In fact, this draws into consideration what the benefit and function of vicarious experience is. As psychophysical, but not physiological, affective responses to CToptimal touch observation match responses to first-hand touch, this suggests vicarious responses reflect the learned value not embodied experience. This interpretation is supported by the reported enhancement of affective responses to observed actions through experience and expertise (Kirsch et al., 2016).

A wealth of evidence suggests that the observation of another individual in pain produces empathic experience of this pain (Jackson, Meltzoff, & Decety, 2005; Mailhot, Vachon-Presseau, Jackson, & Rainville, 2012; Vachon-Presseau et al., 2012b). However, with pleasant stimuli (such as CT-optimal touch) the effect may be subtler. In fact Baumeister, Bratslavsky, Finkenauer, and Vohs, (2001) discussed that humans are more motivated to avoid negative situations than to pursue positive ones. Thus, observing an individual in pain results in large affective EMG or physiological responses than observing an individual receiving CToptimal pleasant touch. The empathic experience of pain has obvious advantages as it allows an individual to know when a particular event is painful and when someone else requires assistance. Furthermore, empathy for pain, is reliant on other social factors., For example, Decety, Echols and Correll (2010) found that the means by which an individual contracted AIDS affected the way others empathised with their suffering, with accidental contraction eliciting greater empathetic concern than drug related contraction. Cheng, Chen, Lin, Chou and Decety (2010) also found that empathic brain mechanisms were more active when a participant witnessed a loved one in pain compared to observing a stranger in the same pain. The benefits of vicariously experiencing CT-optimal touch are unclear however, as it does not signal the need for either avoidant or affiliative behaviour.

In this study, levels of CS activity varied in relation to participants' levels of Empathic Concern (EC) as well as the touched location. The EC subscale of the IRI assesses the feelings of concern for others. CS activity is representative of negative affect, so when empathically concerned for another individual this activity would theoretically increase. However, here there was a negative relationship between EC and CS activity for touch on the Lower Arm, suggesting that the greater empathic concern an individual has is related to a decrease in CS

activity for CT-innervated location. These data suggest that seeing someone receive touch to a CT-innervated location results in a reduction of negative affect the more empathic an individual is.

As shown in chapter 3 showed that individuals with the fewest number of autistic traits showed a greater sensitivity to the velocity and location specific value of vicariously experienced touch, than individuals with average or high levels of autistic traits. It was therefore hypothesised that a similar pattern of responses would be seen in the present facial EMG study. Specifically, it was anticipated that ZM (smile muscle) in particular would show distinguishable differences in activity between individuals with high or low levels of autistic traits. However, here there was a narrower range of AQ scores in the study sample, with fewer individuals exhibiting high levels of autistic traits than in the behavioural study. In fact, most participants scored around the typical population average (17) making it less likely that individual differences in affective response would be apparent.

In future studies it would be important to consider how autistic traits may affect the activity of ZM and CS muscles as well as the subsequent pleasantness ratings particularly with salient first-hand stroking. Evidence shows that individuals with ASD experience touch differently, and concurrently chapter 3 showed that these differences are even present with high numbers of autistic traits. Furthermore despite the deficits in somatosensory processing, another common symptom of ASD is abnormal emotion regulation (Bachevalier & Loveland, 2006; Mazefsky et al., 2013; Samson, Huber, & Gross, 2012; Samson, Wells, Phillips, Hardan, & Gross, 2014). This further determines that activity in these muscles associated with positive and negative affect should show different responses in individuals with ASD.

In recent studies, researchers directed their analysis of facial EMG data around the ratings that participants gave (Kirsch et al 2016). Specifically, Kirsch et al (2016) looked at the

highest and lowest rated dance videos that individual participants chose and used just those trials to examine EMG responses. . In the present study all trials were used regardless of whether they were in the passive or active phase of testing, furthermore it would have been interesting to consider how explicit ratings related to the EMG responses as previous studies have shown greater effects of EMG activity because of selective analysis based on individual differences in ratings data.

In conclusion, this study shows that simply observing touch at a CT-optimal or non-CT-optimal velocity is not salient enough to elicit physical affective responses in ZM and CS activity. Furthermore, the effect of individual differences in sociability and empathy do not appear to affect the development of ZM activity. However, there was a significant effect of EC, an empathic trait commonly associated with negative situations. Here, greater EC was associated with reduced CS activity (indicative of reduced negative affect) when viewing touch at a CT innervated location, and increased CS activity (indicative of increased negative affect) when viewing touch on a non-CT innervated site. This suggests the individual differences in vicarious response to affective touch can be measured implicitly.
# <u>Chapter 6.</u> How Does That Make You Feel? The Effect of Trait Sociability on Implicit Emotional Responses to Affective Touch.

## 6.1. Introduction

The behavioural and cortical responses to CT stimulation have been widely researched, however evidence for the physiological responses to this stimulation is lacking. The continuous regulation of autonomic functioning in the body is by homeostasis, whereby the internal systems are kept at a neutral state to ensure the health and wellbeing of an organism (Craig, 2003). Within homeostatic functioning comes the ability to recognise the state of the body, through this interoceptive capacity, an organism is able to perceive somatic sensations such as temperature, pain, itch and pleasant sensations. These individual sensations result in physiological and behavioural responses, such as vasoconstriction/vasodilation in response to temperature changes or the compulsion to scratch an itch (McMahon & Koltzenburg, 1992).

As with other slowly conducting C-fibres, CTs are hypothesised to carry interoceptive information via the lamina I spinothalamic tract to the dorsal posterior insula cortex (Björnsdotter, Morrison, & Olausson, 2010). Consistent with an interoceptive function, CT targeted touch has clear physiological effects, such as decreased heart rate and reduced sympathetic arousal (Björnsdotter et al., 2010; Etzi, Carta, & Gallace, 2018; Olausson, Cole, Rylander, Mcglone, et al., 2008; Pawling, Cannon et al 2017; Pawling Trotter et a 2017). Further, support for a homeostatic function comes from the recent report that activation of CTs carries a positive affective value that can be measured implicitly (Pawling, Cannon, et al., 2017). This is an important homeostatic consequence of social interaction as from an evolutionary prospective, the reduction in heart calms an animal and thus reduces stress furthermore, it allows for an evaluation of the current situation. Pawling et al (2017) in fact reported that reduction in heart rate was not specific to CT-optimal stimuli, where the relaxation effect was present for CT-optimal velocity stroking on both the Arm and Palm,

despite no CTs being present in the palm. This suggests that the action of interacting with someone in a way that is deemed pleasant such as stroking someone at a CT-optimal velocity, has some benefits not specific to the stimulation of CT afferents. Furthermore, the reduction is heart rate has been shown in other interpersonal interactions that may not necessarily be optimal for CT-stimulation such as hugging (Morrison, 2016).

Comparatively, individuals with ASD have been reported to display atypical autonomic arousal to a variety of stimuli including odours (Legisa, Messinger, Kermol, & Marlier, 2013), various sensory stressors, including negative tastes, loud noises and physical exertion (Goodwin et al., 2006) and social stress (Trier Social Stress Test) (Levine et al., 2012). Limited evidence suggests atypical responses to CT-optimal stimuli in individuals with ASD (Cascio et al, 2008; Cascio, Lorenzi, & Baranek, 2016; Kaiser et al., 2015). Specifically, individuals with ASD report lower ratings of perceived pleasantness (Cascio et al 2008; Cascio et al 2016) and show lower activation in the pSTS and insula cortex compared to control participants for CT-optimal stimuli (Kaiser et al 2015). Taken together these results suggest that the central processing of CT-optimal stimuli is atypical for individuals with ASD.

Furthermore, enhanced sensitivity to tactile stimuli has been observed in individuals with high levels of autistic traits but who are otherwise typically developing (Bennett et al., 2014; Croy et al., 2016; Peled-Avron & Shamay-Tsoory, 2017; Voos et al., 2013). For example, participants with high level of autistic traits show significantly diminished neural responses in the pSTS compared to participants with low level of autistic traits during CT-optimal stimuli (Voos et al, 2013), comparable to individuals diagnosed with ASD (Kaiser et al, 2015). The authors also reported a significant negative relationship between autistic traits and OFC activity, a result that has been linked to deficits in reward processing for individuals with ASD (Zeeland, Dapretto, Ghahremani, Poldrack, & Bookheimer, 2011). Furthermore, autistic traits were positively correlated with scores on the Social Touch Questionnaire (Wilhelm, Kochar, Roth,

& Gross, 2001), this suggests that individuals with reduced cortical activity (and subsequently higher levels of autistic traits) also report lower preference for social tactile interactions and greater anxiety for social touch. Behaviourally, Croy *et al* (2016) reported that preference for CT-optimal affective touch was negatively correlated with autistic traits, as well as reported frequency of social tactile interactions.

The aim of the current study was to use objective physiological measurements of affect (EMG) to determine whether these responses to CT stimulation differ between individuals with high and low levels of autistic traits. It was hypothesised that individuals with high levels of autistic traits would show a blunted physiological and affective response to CT stimulation because of finding CT-optimal touch less pleasant and less rewarding than participants with low levels of autistic traits.

## 6.2. Method

#### 6.2.1. Participants

Participants were 23 individuals (females= 18, M=26.29, SD=5.83), recruited through the Liverpool John Moores University research participation panel. Additionally, 13 participants diagnosed with ASD (females=4, M=26.7, SD=6.3) were recruited through the Liverpool Asperger's Team, which specialises in the diagnosis and regular support of individuals with ASD in order to increase the range of AQ scores in the study population. The study received ethical approval from the Liverpool East NHS research ethics committee and the health research authority. Participants were compensated for their time with a £15 shopping voucher. Individuals who travelled over five miles to get to the university received a further £5 voucher.

## 6.2.2. Materials

## 6.2.2.1. Tactile stimuli

The researcher delivered tactile stimuli manually, using a soft cosmetic brush (Boots No. 7). Participants sat with their left arm resting comfortably on a cushion with the ventral surface of the forearm and palm of the hand facing upwards. Two lines, 10cm apart, were drawn on the palm and ventral surface of participant's left forearm; which was closest to the researcher (*Figure 30*). At the start of each trial, a screen located behind the participant indicated to the researcher the velocity and location (arm or palm) of touch to be delivered. The researcher then clicked a mouse in their right hand to initiate a three-second countdown before a visual metronome appeared. Irrespective of touch location or velocity, tactile stimuli we delivered for 5 seconds per trial.

The study consisted of three blocks of 12 trials (36 trials total). The order of trials was randomised between blocks. Before the start of the first experimental block, participants experienced three practice trials so they understood the format of the experiment. Participants

closed their eyes for the duration of each experimental trial, opening them again when they heard a tone, which signalled they should rate the touch they had just received on two factors: "how pleasant was that touch" and "how intense was the sensation from that touch". The order of presentation of these questions was counter balanced between participants but not between trials to avoid confusion. The questions were answered on a temperature VAS scale with negative ratings coloured red, leading to positive ratings coloured green (see **Chapter** 2). Participants selected any point between the positive and negative anchor points on this scale.



Figure 30. Set up of the lab showing how participants were sat receiving the stroking stimuli. Participants rested both of their arms on a pillow with their left hand on the mouse required for the post-stroking questions. During trials, their left arm rested ventral surface up however, they were allowed to adjust its position between trials a screen located behind the participant showed the researcher the location and velocity of the touch required for the following trial. Participants were asked to close their eyes, which signalled the researcher to begin the

metronome countdown. After the five-second stroking stimulus, participants were asked to keep their eyes closed until they heard a tone (coded into the metronome program) at which time they rated how pleasant and intense they perceived the touch they had just received to be.

#### 6.2.2.2. Questionnaires

Upon completing the stroking task, participants were asked to complete a series of questionnaires presented using custom made scripts running in PsychoPy (Pierce, 2007) on the laptop in front of them. In this study participants completed a series of questionnaires designed to measure self-reported levels of sociability (AQ, Baron-cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), touch preference (STQ, Wilhelm et al., 2001) and anxiety experience (STAI, Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983).

## **Social Touch Questionnaire**

The Social Touch Questionnaire (STQ) (Wilhelm, Kochar, Roth, & Gross, 2001) is designed to measure an individual's preferences for receiving touch in different social situations. Typical questions such as "I consider myself a 'touchy-feely' person" aim to determine an individual's preference for touch and particularly interpersonal touch. Participants answer these 20 questions on a five point Likert scale from 0, not at all to 4, extremely. This scale was initially designed as part of a research study but has since been used successfully by other authors (Fairhurst et al., 2014; Vieira et al., 2016). In a test of internal consistency the scale in this study had a Cronbach's  $\alpha = 0.9$ . Possible scores can range from 0 (lowest touch avoidance) to 80 (highest touch avoidance).

## **State/Trait Anxiety Index**

The State-Trait Anxiety Index (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) consists of two scales, each containing 20 questions. One measures how anxious an individual is feeling right now (STATE anxiety) and the other, how anxious an individual is in

general (TRAIT anxiety). Participants rate these questions on a four point Likert scale with individual anchors for each scale. For state anxiety questions, participants rated their responses from 1, not at all to 4, very much so, whereas for trait anxiety questions participants rated from 1, almost never to 4, almost always. The scales have high internal consistency with a Cronbach's alpha score of  $\alpha = 0.86$ . Possible scores for each scale range from 20 (lowest level of anxiety) to 80 (highest level of anxiety).

#### 6.2.2.3. EMG

As discussed in **Chapter 5**, here facial EMG was used to measure the implicit affective responses to CT-optimal stimuli in both groups. Bipolar placement of the shielded 4mm AgCl electrodes were positioned along the ZM and CS muscles of the face (*Figure 8*) as these are the locations associated with affective arousal (Larsen et al., 2003). First, the area was cleaned using a facial wash on a cotton pad and then each area was lightly exfoliated using a small piece of scouring pad. For placement of the EMG electrodes in these locations, two small drops of gel were syringed over the ZM and CS muscles, similar guidelines for EMG preparation were set out in Fridlund and Cacioppo (1986). A grounded electrode was placed by the participant's hairline in the centre of their forehead. The EMG data were filtered online between 0.1 and 5000Hz and an offline 50Hz notch filter was then applied. A further offline bandpass filter was applied between 20-400Hz as described in Pawling, Cannon, et al (2017).

## 6.2.3. Procedure

Prior to giving informed consent, participants were shown the layout of the lab and the procedure was fully explained. Next, the EMG electrodes were attached. Whilst EMG electrodes were attached, the researcher described each of the cleaning stages to the participants. To avoid movement of the electrodes, the cables were taped to the top of the participant's chair. The participants were asked whether they felt comfortable before the cables were fixed. To

ensure resting state measurements, participants were required to watch a nature documentary for relaxation over a five-minute period prior to beginning the stroking procedure.

Participants then experienced three practice strokes two on the arm and one on the palm. Two of these were delivered at 3cm/s and the other at 30cm/s. During the first practice trial, participants were able to keep their eyes open so they could see how the study ran. During each subsequent trial (*Figure 31*) participants remained with their eyes closed until they heard a tone signalling the end of the trial (played from the metronome computer). Participants then completed three, 12 trial, blocks of the stroking procedure, after each block there was a minimum break of 30 seconds to allow the participants to move their arm/hand and to relax.

Once the stroking procedure was over, participants completed the four questionnaires on the participant computer in front of them (*Figure 31*). Finally, participants received a full debrief explaining the aim of the experiment and how their affective responses to the stimuli were being measured by the EMG electrodes.



Figure 31. Typical experimental trial for the participant's computer. The "Please close your eyes" section of the trial consisted of the countdown (3000ms), stroking period (5000ms) and the post-stroking period (3000ms). The order of the questions was counterbalanced between participants so that half the participants received the question about pleasantness first and the other half received the intensity question first.



Figure 32. Typical experimental trial for the researcher's computer. Once participants have closed their eyes, the researcher can begin the three-second countdown. This then leads into the metronome, which lasts 5000ms. Once this is finished there is a period of 3000ms where participants wait, then a tone sounds and the participants rate the pleasantness and intensity of the stimuli on the computer in front of them.

## 6.2.4 Analysis

The EMG data were extracted using a custom-made macro in LabChart (ADI). Average peak amplitudes were taken in 20, 100ms time bins across 2000ms baseline. A further 50, 100ms time bins were taken from the 5000ms stroking period of the trial and 30, 100ms time bins were taken from the 3000ms post stroking 'evaluation' period. Data were then imported into SPSS where they were graphed. Separate graphs were created for each participant with individual lines representing each trial in the study. The data were visually inspected to determine the trials where baselines were contaminated by noise (trials retained M=89%).

Percentage change scores were calculated for each data bin and initially any change score over 500% from baseline was removed. These data were again graphed and large differences were seen between participants with a diagnosis of ASD and control participants. This is likely due to the large facial responses observed by the researcher during some trials in the ASD participants. As the study aimed to measure the implicit responses to touch, a whole cohort average was taken and data points +-3SD of this mean were removed as explicit affective responses to the stimuli. Four participants (3 with ASD, 1 Typically Developing control) were removed from analysis due to an excessive number of nosy trials (threshold 50%).

All data were analysed in SPSS. ANOVAS for the EMG data were all run with Time (stroking period x post stroking period), Location (Palm x Forearm) and Velocity (3cm/s, CT-optimal x 30cm/s, non-CT-optimal) variables. Behavioural data had the factors of Location (Palm vs Arm) and Velocity (3cm/s vs 30cm/s). Participants were divided into groups based on their Autistic Spectrum Quotient scores (AQ) (Baron-Cohen *et al.*, 2001). The median score for the AQ (20) determined the boundary for the two groups, these were then Low AQ group (n=17, M= 14, SD=4.7) and High AQ group (n=15, M=31, SD=7.3). AQ was used to form these groups as they represent individuals with high and low levels of sociability.

# 6.3. Results

Participants were divided into two groups to test the effect of autistic traits on responses to affective touch. Median AQ score was 20 (*Figure 33*). These groups represented participants with the lowest number of autistic traits, Low AQ group (M= 14.4, SD= 4.7) and those with the highest number of autistic traits, High AQ (M= 30.8, SD= 7.3). All participants diagnosed with ASD were also in the High AQ groups. As anticipated high AQ group, showed greater anxiety (Table 8) and reduced liking of touch (Table 7).



*Figure 33*. The frequency of AQ scores in the participant sample. All participants diagnosed with ASD scored in the high AQ group. The median score of 20 is shown by the black line.

*Table 7.* Here are presented the STQ data for participants in Low and High AQ groups, participants with the lowest number of autistic traits also had the lowest mean score for STQ suggesting more touch preference.

Group	STQ				
	Mean	SD	Range		
Low AQ	29.59	13.2	11-57		
High AQ	43.87	7.25	32-58		

*Table 8.* Here the data for STAI are presented for Low and High AQ groups. Individuals with the lowest number of autistic traits also showed the lowest levels of both state and trait anxiety.

Group	STAI-TRAIT			STAI-STATE		
	Mean	SD	Range	Mean	SD	Range
Low AQ	41.59	10.49	23-59	29.94	9.70	20-60
High AQ	55.20	11.57	40-77	35.73	7.14	28-55

# **6.3.1.** Pleasantness Ratings

A Location (Arm vs. Palm) x Velocity (3cm/s vs. 30cm/s) x Group (Low AQ vs. High AQ) ANOVA was performed on the data. For pleasantness ratings, there was no significant main effect of Location F(1,30)=1.34, p>.05 or of Velocity F(1,30)=.29, p>.05. There were also no significant interactions (Fs<1) Thus, while on average 3cm/sec strokes were rated as more pleasant than 30cm/sec by both groups, these differences were not significant (*Figure 34*).



*Figure 34.* Shows mean ratings of perceived pleasantness of touch (+/- SE) across groups, velocities and locations. There were no significant main effects of interactions.

# 6.3.2. Intensity Ratings

For ratings of intensity there was no significant main effect of Velocity F(1,30)=.24, p>.05 or Location F(1,30)=.3.23, p=.08. Nor was there a Location x Velocity interaction F(1,30)=1.41, p>.05 There was however a significant interaction between Velocity and AQ group, F(1,30)=5.30, p<.05, which reflected the fact that the low AQ group rated 3cm/sec strokes as more intense, while the high AQ group rated 30cm/sec strokes as more intense, irrespective of location (*Figure* 35).



*Figure 35.* Shows mean intensity ratings (+/- SE) for touch across groups, velocities and locations. There was a significant Group x Velocity interaction (p<0.005).

To explore this interaction further, data were collapsed across locations. For stimuli delivered at CT-optimal 3cm/s there was no significant difference between AQ groups t(30)= 1.05, *p*>.05, however there was a significant difference between groups for non-CT-optimal 30cm/s touch t(30)= -2.04, *p*<.05 (*Figure 36*), with the high AQ group rating the touch as more intense (M=61.59, SD=16.28) than the low AQ group (M=47.35, SD=22.33). There were however, no significant differences between velocities within AQ groups (ps>.05).



Figure 36. Intensity ratings were collapsed across Locations to investigate the Velocity x AQ group interaction (+/- SE). Here there was a significant difference between High and Low AQ groups for stimuli delivered at 30cm/s but not 3cm/s. This shows that individuals with High autistic trait scores find 30cm/s touch more intense than participants with few autistic traits.

## 6.3.3. Zygomaticus Major

A repeated measures ANOVA with the variables Time x Location x Velocity x Group was calculated. There was a significant main effect of Time F(1,30)= 12.58, p<.001,  $\eta^2 = .30$  and Velocity F(1,30)=6.59, p<.05,  $\eta^2 = .18$  as well as a Time x AQ group interaction F(1,30)= 8.07, p<.01,  $\eta^2 = .21$  (*Figure 37*).



Figure 37. Here, percentage change from baseline for ZM activity is shown.. These data show that for CT-optimal velocity stimuli there is an initial relaxation effect in the first 50 time blocks (stroking period) followed by an increase in ZM activity for the post-stroking period. Furthermore, ZM activity was not specific to CT-innervated locations and showed similar patterns of activity for the Palm and Arm.

When data were collapsed across Locations and Velocities to look at this interaction further, the low AQ group showed a significant increase in zygomaticus activity in the post-stroking period that was not present in the high AQ group (*Figure 38*).



*Figure 38.* This shows the percentage change in ZM activity between the High AQ and Low AQ collapsed across the different and locations and velocities to measure the Time x AQ group interaction. Despite there being a trend suggesting more activity in the Post-Stroking period for participants in the Low AQ group, this difference was not significant.

## 6.3.4. Corrugator Supercilli

There was a significant main effect of Time F(1,30)=9.85, p<.05,  $\eta^2 = .25$  and a significant four way interaction Time x Location x Velocity x AQ group F(1,30)=5.68, p<.05,  $\eta^2 = .16$  (*Figure 39*).



*Figure 39*. Shown are the mean change from baseline at each 100ms time bin for data collected at the CS muscle. *These are presented individuals for CT-innervated (solid lines) and non-CT-innervated (dotted lines) and, for each Velocity (3cm/s, blue line and 30cm/s, red line).* 

To measure this interaction further, individual Location x Velocity x AQ group ANOVAs were run on Time periods separately. For the stroking period there were no significant main effects of Location F(1,30)=.003, p>.05 or Velocity F(1,30)=.10, p>.05 and no significant main effect of AQ group F(1,30)=.54, p>.05. There were also no significant interactions. For the Post-Stroking period there were again no significant main effects of Location F(1,30)=.003, p>.05 or Velocity F(1,30)=.10, p>.05 and no significant main effects of AQ group F(1,30)=.10, p>.05 and no significant main effect of AQ group F(1,30)=.10, p>.05 and no significant main effect of AQ group F(1,30)=.10, p>.05 and no significant main effect of AQ group F(1,30)=.10, p>.05 and no significant main effect of AQ group F(1,30)=.54, p>.05 and no significant interactions.

## 6.4. Discussion

The aim of this study was to determine whether there was a difference in the physiological arousal to CT-optimal and non-CT-optimal stimuli between in individuals with High and Low levels of trait sociability (autistic traits). It was hypothesised that individuals with High levels of autistic traits would show a blunted response to CT-optimal stimuli finding the touch less pleasant in both behavioural ratings and affective state arousal.

#### 6.4.1. Ratings – Pleasantness and Intensity

Here both the ratings of pleasantness and intensity were not as predicted. A wealth of research has regularly shown that CT-optimal touch is rated as more pleasant than non-CToptimal velocities, however here there was no significant difference in pleasantness ratings between velocities. Ratings at the same Velocity but different Locations were all positively correlated suggesting that participants rated velocities similarly regardless of the location. Furthermore, there were no effects of individual differences on ratings of touch. This is interesting in light of EMG data that shows differences in affective arousal between Low and High AQ groups. Typically pleasantness ratings between CT-optimal and non-CT-optimal Velocities/Locaitons are consistently different regardless of whether there are two velocities (Pawling, Cannon et al., 2017), three velocities (Croy et al., 2017) or more (Ackerley et al., 2014). An explanation for these null results is that participants were consistently rating velocities the same regardless of the location of the touch, suggesting that individuals were not perceiving a difference between locations. Furthermore, here for ease of use, a temperature themed VAS scale was used. This may not have been as clear to participants as a typical sliding scale. Also, the ends of the scale were anchored by highly negative and positive statements which may have made participants more inclined to rate closer to the middle of the scale.

For ratings of intensity, there was a significant main effect of Location. This was driven by a higher rating of intensity for 30cm/s (non-CT-optimal) touch. As the velocity of non-CT- optimal touch is so different to those within the optimal range for CT stimulation is it likely this intensity is the result of A $\beta$  afferent activity. In a key paper, Edin, Essick, Trulsson and Olsson (1995) showed that A $\beta$  afferents increase in firing frequency as stroking velocity increases. This means that a large amount of activity is being processed in the brain across the five-second period of 30cm/s. It is therefore possible that participants find this more intense than slow gentle CT-optimal stroking that results in much less A $\beta$  activity.

Furthermore, the significantly higher rating of intensity for 30cm/s stimuli was only found in the High AQ group. Past research shows that individuals with ASD may be hypersensitive to tactile stimuli (Blakemore et al., 2006; Cascio et al., 2008; O'Riordan & Passetti, 2006; Tommerdahl, Tannan, Cascio, Baranek, & Whitsel, 2007) and therefore stimulus intensity may be a measure of this sensitivity to tactile stimulation.

## 6.4.2. EMG data

Activity in the ZM and CS were treated separately as it is not clear how these different affective states relate to each other when both are active. Past evidence has shown an increase in the ZM (positive affect) muscle during CT-optimal stroking (Pawling *et al.*, 2017). Interestingly here this increase in activity only occurred once participants were preparing to rate how pleasant and intense the sensation was. Similarly Cannon et al., (2009) found that participants mimicked affective state more when focusing on the facial expressions shown in an image as opposed to when they were focusing on the colour of a mask over the face. These data suggest that when attending to affect, such as in the evaluation stage prior to rating the touch, participants have heightened affective arousal.

Here there was a significant difference between ZM activity in the Stroking period and Post-Stroking period. For the group with low levels of autistic traits this showed an initial reduction in ZM activity from baseline followed by an increase during the evaluation (PostStroking period). Despite this differing from the previously observed increase in activity, there is strong evidence to suggest that CTs result in a relaxation effect, particularly observed in autonomic activity (Fairhurst et al., 2014; Pawling, Cannon, et al., 2017). Conversely, this increase in ZM activity may be the result of noise from participants such as them being tickled by the brush (and thus smiling explicitly) or other active facial expressions suggesting embarrassment or disdain as a result of the unusual situation they are in. It is important to consider that the output from each trial is observed to determine how it matches other trials within the same Velocity/Location, this should therefore have removed any excessively noisy trials that would have arisen from such explicit facial movements by participants. Furthermore, these data support the increase in activity reported in chapter 5, suggesting that this activity represents an effect from the CT-optimal/non-CT-optimal stimuli regardless of whether the touch was first hand or observed.

It is noteworthy, despite the differences between groups being non-significant, there is a strong trend showing that individuals with low levels of autistic traits do in fact elicit stronger ZM positive affective responses to CT optimal touch. Furthermore, all participants diagnosed with ASD were also in the high AQ group so it makes sense that increasing the number of participants with ASD or high level of autistic traits would increase the magnitude of this group difference. Again, the largest differences between groups were in the Post-Stroking evaluation period where individuals with low levels of autistic traits elicit a large increase in ZM activity. A common symptom of ASD is abnormality in emotion regulation, this is particularly deemed to be associated with anatomical abnormalities in the orbitofrontal-amygdala circuit (Bachevalier & Loveland, 2006; Loveland, Bachevalier, Pearson, & Lane, 2008). This particularly important as the orbitofrontal cortex (OFC) plays an important role in reward and affective value of CT-optimal stimuli (McGlone, Wessberg, & Olausson, 2014). Though it is not clear from this data whether this affects the perception of CT-optimal velocity touch, it is important to consider that these effects be clearer with a larger sample size. Pawing, Cannon et al., (2017), reported significant main effects across 29 participants, however, in this study there were just over half as many participants in each group. If these implicit affective state changes are indeed weak positive arousal changes then it may take larger numbers of participant in each group for these differences to become significant.

On the other hand, there were no clear changes in activity in the CS. While there was a significant interaction between all factors, when analysed further there were no significant differences between AQ groups or Location/Velocity factors. Overall, activity changes elicited in the CS by the stroking stimuli were small. Again as with ZM there were differential patterns of activity between high and low AQ groups suggesting that these individuals are experiencing touch differently, however, these differences were non-significant. One interesting finding is that for the Post-Stroking period there was a decrease in CS activity for 3cm/s the opposite for ZM activity. This is important in terms of the positive and negative affect that ZM and CS represent respectively. In response to CT-optimal stimuli there appears to be an increase in positive affective state (ZM) and a subsequent decrease in negative affective state (CS) however, as these effects were not significant the suggested effects remain hypothetical until further research is conducted with larger groups.

Taken together these data suggest that individuals with a high number of autistic traits fail to regulate their affective state as effectively as individuals with low levels. It has been hypothesised that the AQ is most reliably a measure of social interaction and attention to detail as opposed to the initially five factors proposed by the authors (Hoekstra et al., 2008). As the differences here are observed mainly in a CT-optimal velocity, this further supports the role of social traits on CT processing. It has previously been hypothesised that the bottom up mechanism of CT dysfunction could affect trait sociability; however here we show this is also the case for trait sociability affecting the perception of CT-optimal stimuli.

## 6.4.3. Conclusions

Together this data suggest that individuals with high levels of autistic traits do experience affective touch differently to typically developing individuals. Although it is unclear why subjective measures of pleasantness and intensity recorded with the experimental protocols here did not reflect past research, the objective measures of affective arousal showed differences between Low and High AQ groups. This brings into question whether individuals with high levels of autistic traits and thus poor sociability have not learned the value of CToptimal touch or whether they do not find the touch as rewarding as individuals with high sociability (low levels of autistic traits). Future research should strengthen the sample size in terms of individuals diagnosed with ASD to determine whether differences can be further separated from individuals with high number of autistic traits.

## Chapter 7. Early and Late Cortical Responses to Affective Touch

# 7.1. Introduction

The cortical mechanisms of CT processing have been well established with activation reliably reported in affective brain regions, including the dorsal posterior insula, ACC and OFC, in response to CT optimal in contrast to non-CT-optimal touch (McGlone et al., 2012; Morrison, Björnsdotter, et al., 2011). In contrast to fMRI studies, there is a dearth of research looking at the electrophysiological cortical correlates of CT-optimal stimulation. On one hand, this is understandable given that CTs have a 10 times slower conduction velocity than A $\beta$  afferents (responsible for discriminative touch), thus temporal resolution is not a specific priority of this research. On the other hand, the superior temporal resolution of EEG allows neural responses to CT and A $\beta$  targeted stimulation to be separated.

Early in the ERP signature, a reliable measure of stimulus salience has been identified. This P300 peak is most prominent at the central electrodes for novel stimuli or other salient stimuli, such as those with a clear positive or negative value. (Gray, Ambady, Lowenthal, & Deldin, 2004; Linden, 2005; Rule, Shimamura, & Knight, 2002). Furthermore, Gray et al (2004) highlighted that the P300 amplitude can be used as a marker of individual perceptions of stimulus salience. Thus, autobiographical words, such as the name of a participant's school or hometown, resulted in a larger P300 peak amplitude than non-selfrelevant words. Indeed, in this study the P300 peak was comparable to that elicited by rare novel stimuli in an oddball task.

Salient stimuli also elicit valence specific patterns of physiological arousal. Bradley, Keil, and Lang, (2012) reported that the enhanced P300 response to strongly valenced images, is accompanied by heightened cardiac deceleration and electrodermal reactivity, both

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established indices of attentional orienting (Balconi, Vanutelli, & Finocchiaro, 2014; Spapé, Harjunen, & Ravaja, 2017).

To date, physiological investigation of responses to CT targeted touch have shown that while CT-optimal touch produces greater heart-rate deceleration than non-CT optimal touch (Pawling, Cannon et al 2017; Pawling, Trotter et al., 2017) this effect was velocity rather than CT dependent as the increase in inter-beat intervals was reported in response to touch on both the CT-innervated forearm and the non-CT innervated palm (Pawling, Cannon et al., 2017). Furthermore, while CT optimal velocity strokes elicit significant sympathetic skin responses in both healthy participants and ganglionopathy patients lacking myelinated fibres (Olausson et al., 2008; Pawling, Trotter, McGlone, & Walker, 2017), consistent with their weaker perceptual impact (Olausson et al 2008), the magnitude of GSR to CT-optimal strokes was significantly lower than to A $\beta$  targeted 30cm/sec stroking (Pawling et al 2017). Together this highlights that CT-optimal stroking touch results in a relaxation effect suggested by both the slowing of the heart rate and the mild increase in GSR activity compared to A $\beta$  activity.

Later in the ERP waveform, a component specific to input from unmyelinated afferents has been identified. This ultra-late potential (ULP) has been measured in response to laser stimuli specifically targeting C-nociceptive fibres (Bromm & Treede, 1987; Bromm, Neitzel, Tecklenburg, & Detlef-Treede, 1983). In contrast to innocuous somatosensory stimuli, these ULPs are recorded in the frontal region of the brain, as opposed to parietal S1 region. It has been reported that ULPs were only observed when input from A-delta pain afferents was reduced through a nerve block and CO<sub>2</sub> laser stimulation (Bromm & Treede, 1987; Bromm, Neitzel, Tecklenburg, & Detlef-Treede, 1983). Specifically, Bromm *et al* (1983) showed that when a nerve block was applied, the neural activity evoked by CO<sub>2</sub> laser stimulation appeared later, around 1800ms after stimulus onset. This ULP was therefore a specific response to C-nociceptor stimulation resulting from a slow conducting unmyelinated afferent.

To date, only one study has reported a ULP evoked by CT targeted touch (Ackerley et al., 2013). Using a RTS, over two hundred individual brush strokes were delivered to the ventral surface of participant's forearms at CT-optimal 3cm/s. Here the authors reported a ULP, which peaked around 2500ms after stimulus onset. As CTs have a conduction velocity of <1m/s, it is probable that the ULP is the cortical response associated with processing CT specific stimulation. Furthermore, the activity recorded at electrode Fz (where the ULP was located) was significantly greater than that recorded over somatosensory areas typically associated with discriminative tactile perception. This further suggests the ULP is a C-fibre specific component. This ULP appeared over frontal electrodes suggesting that the underlying activity is in the frontal lobe, it was therefore hypothesised that this ultra-late activity is indicative of activity in regions such as the OFC and ACC, responsible for the affective valuation of these stimuli (Ackerley et al., 2013; Francis et al., 1999; Rolls et al., 2003). Furthermore, in a study comparing MEG and EEG responses to Aδ and C-nociceptor stimulation, Kakigi et al (2004) found that myelinated and unmyelinated pathways were similar in that they both projected initially to regions in SII and the insula. However, Cnociceptor responses were larger than the A $\delta$  responses in the anterior cingulate, amygdala and hippocampus, suggesting activity in these regions reflects the emotional and cognitive rather than purely discriminative.

Recently, a negative correlation was reported between levels of autistic traits and selfreported preference for CT over non-CT optimal touch, as well as frequency of social tactile interactions (Croy et al., 2016). Further evidence also suggests that individual differences in trait sociability affect cortical responses to social tactile images. Thus, in comparison to individuals with low levels of autistic traits, participants scoring high on the AQ showed

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enhanced early and stronger late ERP responses to images depicting social but not object touch (Peled-Avron & Shamay-Tsoory, 2017). While in an fMRI study, levels of autistic traits were negatively correlated with OFC and pSTS responses to CT-optimal touch (Voos et al 2013), individual differences in electrophysiological cortical responses remain untested.

The aim of the present study is to determine whether an ULP can be identified in response to manually delivered CT-targeted stroking touch. Furthermore, the specificity of neural responses to CT versus A $\beta$  touch will be examined by comparing the P300 elicited by 3cm/s versus 30cm/s strokes. It is hypothesised that a higher P300 amplitude response will be seen in response to A $\beta$  targeted 30cm/sec versus CT-targeted 3cm/sec stimulation; as the latter would not activate fast conducting myelinated fibres as intensely. Furthermore, A $\beta$  activation is perceived more strongly than CT stimulation (Olausson et al., 2008). It is hypothesised that individual differences in trait sociability will modulate the amplitude of both responses to CT-optimal and non-CT-optimal touch and its subsequent cortical functioning, therefore showing differential patterns of neural activity between individuals with different numbers of autistic traits.

## 7.2. Method

#### 7.2.1. Participants

Twenty-two participants (Females=18, M=23.7, SD=6.8) were recruited through Liverpool John Moores university. They were either undergraduates who took part in exchange for course credit, or members of the psychology research participant panel, who were compensated for their time with a shopping voucher. Participants were required to be over 18, healthy, with no history of a neurological condition or Autism Spectrum Disorders. The Liverpool John Moores University research ethics committee approved the study prior to recruitment.

## 7.2.2. Materials

# 7.2.2.1. Tactile stimuli

During the experiment, participants received manual brush strokes to the dorsal surface of their right forearm using a soft cosmetic brush (No7 cosmetic brush, Boots UK). The participant's right arm rested on a rectangular piece of foam and their right hand rested on a computer mouse. Two lines, 10 centimetres apart, were drawn on the dorsal surface of their right forearm and a laser light (Dancer Design, UK) was shone over the arm between the emitter and a vertical piece of white plastic placed the other side of their arm, for laser deflection. The laser allowed the precise time locking of the manual brush strokes to the EEG signal. The laser deflection screen both minimised the distance the laser travelled, optimising timing accuracy, and occluded the participant's view of the stroked area.

A visual metronome presented on a computer screen behind the participant, guided the researcher in delivering the brush strokes at each of the three velocities used: CT-optimal (3cm/s), non-CT-optimal (30cm/s) and a midrange oddball (15cm/s). The metronome was created using a custom E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) script, which provided a three second countdown then showed a rectangle filling at the stroking

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velocity required for each trial (see chapter 2). Specifically, for stimuli delivered at 3cm/s the box filled over around three seconds (10cm stroking area x 3cm/s), for stimuli delivered at 30cm/s the metronome box filled in ~300ms (10cm stroking area x 30cm/s). A single proximal-to-distal stroke was run from the laser to a line 10cm down the arm. A wireless mouse in the researcher's right hand controlled the progression of the metronome computer through the experiment to ensure participants were ready before the start of each trial. In comparison to Ackerley et al (2013), these single strokes were continuous over 3s and at a constant pressure, whereas the RTS sweeps are shorter and have gradually increasing pressure over the stroke distance.

Participants sat facing a laptop computer controlled by the mouse in their right hand. This ran a separate E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) programme unconnected to the other computers in the experiment. They used the mouse to make responses to the oddball task, which was completed as a means of maintaining attention to the stroking stimuli they received in an otherwise passive task. Within each 5-trial block, the task involved comparing each subsequent stroke delivered to the first. Thus, immediately after the  $2^{nd} - 5^{th}$  trials of each block participants were asked, "Was that touch the same as the first". Blocks contained between 0 & 2 oddball strokes. The layout of the Faraday cage, where participants were seated during the experiment is shown in *Figure* 40.



**Figure 40**. A diagram depicting the layout of the Faraday cage during the experiment. Participants were seated facing a computer running the E-prime (Psychology Software Tools, Pittsburgh, PA) program, described in Figure 44. Their right arm is rested on a foam pad with their hand holding a mouse. The setup was adjusted to ensure neck and shoulder muscles were not strained, and thus avoid muscle artifacts in the EEG trace. The researcher sat on the participant's right side stroking with their left hand and controlling the metronome computer with a wireless mouse in their right hand. The metronome computer can be seen through a window built into the Faraday cage.

#### 7.2.2.2. EEG

A 64-channel active-electrode BioSemi (BioSemi, Amsterdam) system was used. Data were collected using ActiView (BioSemi, Amsterdam). An online filter of 0.1Hz then an offline 0.1Hz-40Hz bandpass filter was applied to the data. A custom-made cable (from Cortech Solutions, Wilmington, NC) was used to send trial triggers from the PC displaying the visual metronome and the laser. Triggers from the E-Prime computer were coded to ensure that the velocity of the stroking was recorded with the EEG and then the laser trigger allowed for the start of the event-related potential to be recorded. Data were imported into EEGLab (Delorme & Mekeig, 2004) for further processing. Offline, data were down sampled to 256Hz (Ackerley et al., 2013). Data were then re-referenced to the left temporal P9 electrode. The data were epoched to remove between-trial signal and excessively noisy trials were removed manually, over 80% of trials were retained from all participants (trials removed M=11.6, SD=6.2). Next, independent components analysis (ICA) was run on each data set, extracting 63 components, noisy data were then removed based on individual topographical heat maps (M=3.59, SD=0.8). Data were averaged into categorical epochs representing CT-optimal and non-CT-optimal trials. These epochs were then grand averaged across participants.

## 7.2.2.3. Questionnaires

Upon completing the EEG task, participants were asked to complete a series of questionnaires presented using custom scripts running in PsychoPy (Pierce, 2007) on the laptop in front of them. In this study participants completed the AQ (Baron-cohen et al., 2001), Social Touch Questionnaire (Wilhelm et al., 2001) and the State/Trait Anxiety Index (Spielberger et al., 1983) these measure self-reported levels of sociability, touch preference and anxiety respectively (described in Chapter 6). Here STATE anxiety did not correlate with AQ scores r(17)=.087, p>.05 however, TRAIT anxiety scores were strongly positively correlated with AQ scores r(17)=.67, p>.01, suggesting participants with lower levels of trait sociability (high AQ scores) also had the highest levels of trait anxiety.

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## 7.2.3. Procedure

Participants were first provided with an explanation of the EEG setup and shown the Faraday cage where the experiment would take place. Once participants were satisfied with the procedure they provided written informed consent and the setup of the EEG system began. Initially, the circumference of the participant's head was taken to ensure the correct size cap was used. A loose cap would result in excessively noisy data. To ensure the cap was placed centrally on the participant's head, measurement of the central Cz electrode was taken from nasion to inion and left to right mastoid.

Next, a small amount of conductive gel (SignaGel, Parker Laboratories, Fairfield, NJ) was applied to each electrode site before the electrodes were connected to the appropriate locations based the 10-20 international system (Jasper, 1958). Participants were then brought into the Faraday cage where they were asked to sit in a comfortable chair. The foam cushioning on the desk was adjusted so participants did not have to reach for the mouse in their right hand, reducing the effect of muscle activity on the EEG measurement.

The task consisted of 20 blocks of five trials. In each block participants received either CT-optimal (3cm/sec) or non-CT-optimal (30cm/sec). To focus participant's attention on the sensation of the stroking, during each block they were asked to complete and oddball task. They were informed within each block there could be between 0-2 oddballs in each block of 5 strokes. Oddballs were delivered at 15cm/sec. Across twenty blocks participants experienced 43 CT-optimal strokes, 43 non-CT-optimal strokes and 14 oddballs strokes, split evenly between CT-optimal and non-CT-optimal blocks. The first trial in each block was always CT-optimal or non-CT-optimal stroke, then on each subsequent trial participants were asked "was that stroke the same as the first?" During each trial, participants kept their eyes open. The study took place under dimmed lights and the laser set up obscured the participant's view of the stroking procedure. During the stroking procedure the screen in front of them displayed "click when you hear the tone". After the stimulus there was a period of five seconds where participants had to think about the feel of the touch and wait for the tone. Participants were then asked whether that stroke was the same as the first in the block (see *Figure* 41).

To ensure no two consecutive trial blocks were the same, a series of five experiment randomisations were created in Matlab (Matlab 2017a, The MathWorks Inc., Natick, MA). This listed the sequential running of blocks for five versions of the study. Despite triggers being successful for four randomisations of the study, the fifth version of the randomisation resulted in unknown triggers that were not possible to decipher, thus data from five participants could not be analysed resulting in a final participant count of n=17 (males=3, M=23.5, SD=6.4).



*Figure 41.* An example of the procedure participants followed for each trial.

## 7.2.4. Data Analysis

To measure early responses to the stimuli, data were extracted from central electrodes Pz, Cz and Fz where there was a maximal peak amplitude around 500ms for non-CT-optimal stroking. For CT-optimal stroking, data were extracted both at the same point and, using the calculations for CT conduction velocity x distance from the forearm to the cortex reported in Ackerley *et al* (2013), average peak amplitudes were also taken 700ms later, ~1200msec post-stimulus onset. Using SPSS 23 (Armonk, NY, IBM corp), data from these time points were analysed in an Electrode (Pz, Cz, Fz) x Velocity (3cm/s, 30cm/s) repeated measures ANOVA. Secondly, a correlation analysis was conducted comparing individual participant's peak amplitude from this region and their scores in the questionnaires to determine whether any individual differences were associated with peak amplitude changes using a Pearson's correlation analysis.

Upon visual inspection of ERP waveforms and topographic maps of the ultra-late potentials, data were extracted from electrode F1 where the most prominent ultra-late ERP was recorded. Data were extracted from the maximal point in the ULP (between 2800 and 3200ms), and were compared in an ANOVA to data from contralateral and ipsilateral somatosensory cortices (electrodes CP3 and CP4 respectively) (Ackerley et al., 2013). Again, peak amplitudes for each participant were correlated with individual scores on the questionnaires presented.

## 7.3. Results

Table nine, shows the average, SD and min/max scores for each of the scales participants completed. These scales were used in further analysis to determine whether these scores affected participant's responses to touch.

*Table 9.* The descriptive statistics for each of the scales used in this study. Showing mean score, standard deviation and minimum/maximum scores for this sample.

Questionnaire	Mean	SD	Min	Max
AQ	17.33	7.25	7.00	32.00
STAI-S	31.14	8.60	21.00	56.00
STAI-T	41.86	11.57	27.00	68.00
STQ	27.14	13.69	4.00	48.00

## 7.3.1. Early components

Initial analyses were conducted on the early attention related components. Peak amplitude data were extracted from between 300-600ms after stimulus onset for both CToptimal and non-CT-optimal stimuli. Previous research shows that CT-optimal touch stimulates A $\beta$  and CT afferents however, the activation of A $\beta$  for non-CT-optimal stimuli is greater as their activation increases in line with stimulus velocity (Löken et al., 2009). A repeated measures ANOVA revealed a significant main effect of Electrode F(2,32)=28.57, p<.001, Velocity F(1,32)=31.57, p<.001 and a significant Electrode x Velocity interaction F(2,32)=34.68, p<.001. Simple main effects analyses revealed a significantly larger peak amplitude for stimuli delivered at non-CT-optimal velocity compared to CT-optimal stimuli (all ps<.001), thus confirming the faster stimulus results in greater activation A $\beta$  afferents. The peak amplitude measured was larger at posterior electrodes (Pz and Cz) than frontal electrodes (Fz) (*Figure 46*). For completeness, the amplitude of response to CT-optimal touch was also compared 700msec later, as this represents the longer time for the CT signal to reach the brain (Ackerley et al 2013). A repeated measured ANOVA with factors of Electrode (Cz x Fz x Pz) and Velocity (3cm/s x 30cm/s) revealed a significant main effect of Electrode F(2,32)=16.675, p<.001 and a significant main effect of Velocity F(1,16)=34.342, p<.001. Furthermore there was a significant Electrode x Velocity interaction F(2,32)=12.788, p<.001 (*Figure* 42 & 43). Further analysis of the Electrode x Velocity interaction (*Figure* 42 & 43) revealed that non-CT-optimal stimuli elicited significantly larger peak amplitude than CT-optimal at all electrode locations (all p>.001) suggesting that the faster (non-CT-optimal stimulus) is more salient and elicits a greater orienting/attentional response than slow (CT-optimal) touch.


**Figure 42**. Mean peak amplitude for the attention response to stimulation. This peak was largest at the central electrodes Fz (top), Cz (middle) and Pz (bottom). A significantly greater peak amplitude is recorded consistently for non-CT-optimal (30cm/sec, Red) compared to CT-optimal (3cm/sec, Black) velocities at all electrode locations (p<.05). However, the amplitude of response was significantly greater at Pz & Cz than Fz.



*Figure 43.* Topographical heat maps showing the increase of activity across central electrodes in response to 30cm/s touch (43b) but not during 3cm/s touch (43a).

Finally, the effect of the self-report scales on peak amplitudes was investigated. Individual ANCOVAs were run across each electrode location with each of the scales (AQ, STAI-T/S and STQ). At all electrode locations there were no significant main effect of stroking Velocity (all p>.05) and there was no interaction with scores on any of the scales (all p>.05).

#### 7.3.2. Late Components

Upon eyeballing ERP waveforms (*Figure 48*) and topographic maps (*Figure 47*) of the ULPs, data were extracted from electrode F1 where the most prominent ULP was recorded. In comparison to Ackerley et al (2013), for CT-optimal stroking the ULP was more lateral to the midline frontal (Fz) electrode. Furthermore, the largest increase in activity in this region appeared around 2900ms after stimulus onset and continued until around 200ms after stimulus offset (*Figure 44*). The peak amplitude data were extracted from a 500ms bin (2800-3300ms) from electrode F1 and both contralateral and ipsilateral electrodes situated above the somatosensory cortex (CP3 and CP4 respectively).



Figure 44. Topographic maps showing the development of the ultra-late potential over frontal electrodes up until 3200ms post stimulus onset. This ULP is strongest over electrodes in the left hemisphere i.e. contralateral to the stroking stimulus.

A repeated measures ANOVA was conducted to compare the maximal peak amplitude recorded at F1 to CP3 and CP4. There was a significant main effect of electrode site F(2,30)=7.73 p<.01,  $\eta^2$ =.42. Further analyses revealed that the ultra-late peak amplitude measure at electrode F1 was significantly larger than activity at CP3 and CP4 (both ps<.05) meaning that this ULP is not related to activity from Aβ afferents projecting to the somatosensory cortex at CP3 and CP4. *Figure* 45 depicts the temporal progression of the ULP starting around 200ms after stimulus onset and closely matching the duration of the stroking stimuli (blue box, *Figure* 45).



**Figure 45**. ERP waveform showing the ultra-late positive potential recorded maximally at ~3200ms at electrode F1. The blue box represents the duration of the stroking stimulus. The cubic line fit shows an increase in line with stimulus onset and a decrease in activity in line with stimulus offset. Shown also are the comparative activity traces at electrodes Fz and F2. The latter shows a decrease in activity in response to contra-lateral increase in activity.

Initially, correlations were run on individual scores for each questionnaire and peak ULP amplitude at F1. While peak amplitude did not correlate significantly with any of the questionnaire scores, there was a trend for a positive correlation between ULP amplitude and AQ score (r=-.47, n=17, p=.059). Given the small sample size, this trend was further examined by splitting participants into two groups (Low & High AQ) based on the median AQ score (M=11.1, SD=2.2 & M=23, SD=5.9, respectively). An independent samples T-Test with ULP as the dependent variable and AQ group at the independent variable, revealed a significantly higher amplitude ULP in the Low versus the High AQ group t (15)= 2.28, p<.05 (*Figure* 46).



*Figure 46.* There was a significantly larger peak ULP amplitude for individuals with the highest number of autistic traits compared to participants with the fewest number of autistic traits at electrode F1 in response to CT-optimal cm/s stroking (\*p<.05).

### 7.4. Discussion

One of the aims of this study outlined earlier was to measure early responses to stimuli and to determine how this, was affected by CT-optimal and non-CT-optimal stimuli. Here a P300 peak was measured for non-CT-optimal stimuli but not for CT-optimal stimuli. The P300 peak is most commonly associated with salient/novel stimuli and is measured at the central electrodes. This therefore suggests that, the weak conscious percept of CTs result in a lower orienting response than non-CT-optimal stroking, in line with GSR responses to both stimuli. Here A $\beta$  afferents generate the P300 response to stimuli as a higher velocity stimulus results in a larger peak amplitude. These differences occur both at 500ms during maximal P300 peak amplitude for non-CT-optimal stimuli and at 500ms and 1200ms where A $\beta$  and CT input are compared based on conduction velocity. This shows that both CT-optimal and non-CT-optimal stimuli do indeed affect different afferents, showing that faster velocity stroking results in a larger orienting response and more input as a result of greater A $\beta$  firing. Conversely 3cm/s stroking is measured much later in the cortex showing that this is optimal for stimulating slow conducting unmyelinated afferents.

A further aim of this study was to detect an ULP generated in response to a CToptimal stroking touch using socially laden, researcher delivered stimuli. Consistent with the findings of Ackerley et al (2013), an ULP was identified in response to CT-optimal stimuli. While in the present study the ULP was more lateral and temporally later, it did closely follow the pattern of stimulus onset and offset. Specifically, the ULP here was measured at electrode F1, beginning shortly after stimulus onset and increasing until shortly after stimulus offset. This pattern of activity was also found in Ackerley *et al* (2013). This activity was significantly different to the activity recorded in S1 where A $\beta$  afferents project, further highlighting the significance of this ULP as a mechanism specific to C-fibre activity.

It seems likely this difference between the two studies, in both the location and latency of the ULP reflects the different methods of stimulus delivery. In the previous study, a RTS was used to deliver a large number of highly controlled stimuli, in terms of both velocity and force. Here, participants received manual brush strokes delivered by the experimenter, resulting in greater variation of individual strokes. While psychophysically, these two stimulation methods have been reported to elicit similar pleasantness ratings from participants (Triscoli et al., 2013), the perceived pleasantness of CT-optimal stroking can be modulated by social context (Gazzola et al., 2012; Keizer, de Jong, Bartlema, & Dijkerman, 2017). As such both the gender of person delivering the touch (Gazzola et al., 2012) and the visual appearance of the touched surface (Keizer et al., 2017) have been shown to affect ratings of touch pleasantness as well as responses in affective brain regions such at the OFC. These top-down modulations could therefore result from each participant's individual experiences of the experiment being different and more similar to social interactions in the environment when compared to robot stroking. This adds to the understanding about how of experience and social context impacts behaviour and interactions with others.

Future research should therefore explore the effect of social context on neural responses to CT-targeted touch. It is also important to consider whether the temporal and spatial location of this ULP are specifically the result of fundamental differences in the stimulus type (RTS vs manual stroking) or the differing number of stimuli delivered. However, Ackerley et al (2013) reported that ULPs were identified in the responses of individual participants, suggesting that the number of stimuli in the grand average ERP was not likely to have affected the ULP. Comparatively this is because Ackerley et al (2013) used 200+ stimuli per participant where n=43 were used here. Overall, given the ULP measured here so closely matched the duration of skin contact, it seems likely it does reflect CT activation.

Differences in ULP peak amplitude were found between individuals with low levels of autistic traits and individuals with high levels of autistic traits, suggesting that trait sociability modulates process related to the ULP response. It was hypothesised that the social aspect of having a researcher deliver the touch manually would affect individuals in these two groups differently. On the other hand, research has shown that both ratings of pleasantness (Croy et al., 2016) and neural responses (Voos et al., 2013) are diminished in individuals with high levels of autistic traits. Also autistic traits have also been connected to self-reported responsivity to social stimuli (Bölte, Poustka, & Constantino, 2008), suggesting that perception of social stimuli is affected by autistic traits. In order to test this theory, future research should focus on participants with deficits in social perception, such as individuals with ASD. In this study, AQ scores represented reliable differences above and below the typical population mean (17) however, these scores are not typical of a population with the largest number of autistic traits (26-50) (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001), therefore it is not possible to determine the effect that high levels of autistic traits would have on ULP amplitude.

Interestingly, the lower amplitude of the ULP suggests that the neural mechanisms underlying this activity are responding differently in individuals with a large number of autistic traits compared to those with low levels of autistic traits. Thus, these differences in activity were similar to those described in Study 4 whereby activity in ZM and CS were lower for individuals with high levels of autistic traits. This suggests that the larger EEG response to CT-optimal stimulation does not translate to positive or negative affective responses to stimuli. However, it is hypothesised that these two mechanisms are related with the increase in ULP for individuals with larger levels of autistic traits, suggesting a fault in the affective valuation of stimuli and thus these objective affective responses to CT stimulation.

In this experiment it was not possible to match stimulus based on skin contact time as both 3cm/s and 30cm/s stimuli consisted of a single proximal-to-distal stroke, therefore analyses were based on the latency of signals would have reached the brain from stimulus onset. One consideration for future research is to determine whether these cortical responses to CT-optimal and non-CT-optimal touch are affected by contact time with the skin due to the development of the ULP across the duration of skin contact. However, recent evidence suggests that matching these stimuli has no effect on self-reported ratings or on physiological measures (Pawling, Cannon, et al., 2017).

Furthermore, here comparisons were drawn between CT-optimal and non-CT-optimal velocities of touch, in future as with chapter 6, it would be interesting to run this study looking at the differences between CT-innervated and non-CT-innervated locations. Research has shown that ratings of touch on the palm are comparable to CT-innervated locations (Ackerley, Carlsson, et al., 2014; Pawling, Cannon, et al., 2017) suggesting a learned value of CT-optimal touch even in the absence of CTs. This future research would then determine how this activity is represented in the brain. In fMRI research activity for CT-optimal stroking on the palm is not the same as the arm (Gordon et al., 2013; McGlone et al., 2012; Olausson et al., 2008), it would therefore be interesting to see whether time sensitive measures such as the ULP further highlight the specificity for CT-stimulation also.

In conclusion, these results further support the differences between CT-optimal and non-CT-optimal touch processing. As such, the P300 peak amplitude results in a greater attentional response in line with an increase in A $\beta$  firing frequency. Furthermore, an ULP was identified specifically for CT-optimal stroking, delivered manually, where previous research used controlled robot delivered touch. Differences were also found between the ULP in individuals with high and low levels of autistic traits suggesting these trait differences in sociability affects the processing of affective touch in the brain. Together these results show the differences between discriminative (non-CT-optimal) and affective (CT-optimal) touch processing and the impact that trait sociability has on affective processes.

### <u>Chapter 8</u>. General Discussion

### 8.1. Overview of the findings

The aim of this thesis was to determine how individual differences in trait sociability affected an individual's perception of and responses to CT-optimal affective touch. Various methods were incorporated to measure different aspects of the perception of CT-stimulation, from psychophysical ratings, to facial EMG, EEG and compare how these differed from responses to non-CT-optimal stimuli across different levels of sociability.

Three of the studies presented here investigated vicarious ratings of social touch. Research into the empathic vicarious experience of stimuli to date has primarily focused on pain sensation as this is a highly salient stimulus resulting in explicit responses to the observation of others in pain. As such, research has shown that the physiological and cortical responses to the observation of pain in others are very similar to those seen when people experience the pain first hand. However, this was not always the case. In Chapter 3 (High levels of autistic traits are not associated with reduced valuation of vicariously experienced social touch) the aim was to determine how different levels of sociability affected the vicarious experience of social touch. Adding to this in Chapter 5 (The vicarious experience of social touch does not convey affective context) these aims were measured again but with added physiological measures of affective state. With both explicit psychophysical ratings, data suggested that typically developing participants did empathically experience CT-optimal stimulation and rate this as consistently the most pleasant level of touch, as indicated by the significant quadratic relationship between touch velocity and pleasantness ratings. In contrast, the affective state arousal measured using facial EMG in Chapter 5 did not reflect a 'shared CT experience' with the individual being touched. In Chapter 4 (Childhood experience of vicarious affective touch in typically developing and autistic children) the aim was to

determine whether this vicarious experience of affective touch is present in childhood. Also in this study, individuals diagnosed with ASD were recruited to determine whether the ability to empathically perceive CT-optimal stimuli was blunted in this group. The results however, suggest that young children are not yet able to apply their own social tactile experiences to empathic ratings of observed touch. That is, their explicit affective ratings did not show the same velocity dependent relationship for vicarious as directly felt touch. Furthermore, there were no differences in affective ratings between individuals with ASD and typically developing children.

In **Chapter** 7, the early and late cortical mechanisms of tactile processing were measured. The aim of this study was to determine how the different velocities of  $CT/A\beta$ stimulation would affect the subsequent cortical measurements. Another consideration for this research is of the relative salience of CT-optimal stimuli. It is understandable that the explicit responses to observing painful stimuli is because this is a highly salient stimulus but as evidence from Chapter 7 (Early and late cortical responses to affective touch) suggests, CT-optimal stimuli are significantly less salient than fast Aβ mediated stroking touch, resulting in a smaller orienting response to CT-optimal touch compared to non-CT-optimal touch. This is likely due to the difference in relative A · activity between the two types of stimulus with grater velocity resulting in more A · activity. This could therefore explain the null results from Chapter 5 finding that the observation of CT-optimal stimuli was not enough to elicit positive affective arousal through ZM activation. Comparatively in Chapter 6 (How does that make you feel? The effect of autistic traits on implicit emotional responses to affective touch) the aim was to uncover the implicit affective responses to different types of stimuli and to determine how these responses differed across individuals with different levels of trait sociability. Individual differences in affective arousal for both CT-optimal and

non-CT-optimal stimuli were found between individuals with high levels of autistic traits and individuals with low levels of autistic traits for physiological but not subjective measures. Taken together with the differences in ULP amplitude reported in **Chapter 7**, this suggests that individuals with high levels of autistic traits experience CT-optimal stimuli differently to those with low levels of autistic traits. In addition, if the ULP is indeed a cortical measure of affective valuation of stimuli then these processes are different in individuals with high levels of autistic traits. These data therefore provide evidence that individuals with low levels of sociability may not derive the positive rewarding value of CTs that inevitably motivate individuals to partake in affiliative social tactile interactions. However, it is important to consider that the observed EMG effects were not CT specific, as the groups' responses did not differ systematically according to touch velocity or location.

# 8.2. General discussion

This thesis comprises a series of experiments designed to test the Social Touch Hypothesis in terms of how an individual's degree of trait sociability relates to responses to stimulation of CTs. It was found that social trait differences played a role in the processing and subsequent responses to affective touch. In a number of these studies the social empathic response to these stimuli were measured, showing less sensitivity to CT-optimal stimuli for individuals with high levels of autistic traits and in children. In the final experiments, the physiological and psychophysiological responses to first-hand touch were measured, each showing differential patterns of activity between individuals with low and high numbers of autistic traits.

In these studies, the measurements of sociability were made using the AQ. The AQ (Baron-Cohen et al, 2001) was originally designed to measure a range of autistic trait deficits, specifically: social skill, attention to detail, attention switching, communication and imagination. The scale, although unofficially qualifying an ASD diagnosis (Woodbury-Smith

et al., 2005), also measures a spectrum of autistic traits in the otherwise typically developing population. In particular, evidence shows that individuals in science related subjects or IT scored significantly higher than peers did from arts/humanities subjects. Considering this, it would appear that the AQ is not measuring a purely categorical clinical diagnosis but rather reflects a spectrum of traits, which vary across the entire population. This became evident in a study by Hoekstra et al, (2008). Here, the authors found that of the five aforementioned subscales of the AQ, four represented a larger factor, here referred to as "Social Interaction". This suggests that 80% of the scale is measuring a social trait with the other 20% measuring attention to detail. Thus, the scale is better referred to as a measure of social interaction than levels of autistic traits more broadly

It is important to consider that in the studies reported here, the ten questions relating to 'attention to detail' were not removed (which would have required new validation analyses) despite the fact is was used specifically as a measure of social traits within a typically developing population. In **Chapter 6**, all individuals diagnosed with ASD were also in the high AQ group showing that this scale is indeed representative of a trait that is found in ASD. Therefore, throughout this research individuals with high levels autistic traits and those diagnosed with ASD are deemed comparable in terms of their low levels of trait sociability. This is an important consideration of this research as affective touch has been hypothesised to play a fundamental role in developing affiliative behaviour between individuals.

The Social Touch Hypothesis of CT function suggests that the rewarding value of social tactile interactions is signalled by the activation of CTs. In this thesis, it this was hypothesised that poor social functioning could either result in or result from atypical responses to social touch. The causal direction of the relationship is not yet clear, however, the research reported here has shown that individual differences in trait sociability are associated with variation in physiological responses to socially relevant touch. Morrison et al (2011) stated that this touch

is consequentially similar to pain in that it has a motivational value responsible for modifying an individual's behaviour. This touch also conveys intent and emotional feeling toward another individual, which is important for social functioning. It makes sense that the optimal functioning of this touch is reliant on trait sociability and an individual's ability to process its rewarding value. This may not be the case in individuals with high levels of autistic traits and has been discussed in light of the Social Motivation Theory of ASD (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2013).

From early childhood, tactile interactions with others help to shape the social and emotional development of an individual (Cascio, Moore & McGlone, 2018). Furthermore, evidence from Harlow (1958) suggests that individuals are inclined to seek tactile support from a surrogate mother as a priority over sustenance. In light of our understanding of social interactions and their importance in early development it can be proposed that lack of appropriate motivation toward social interactions would be detrimental to an individual's development. The social motivation theory of ASD posits that lack of motivation for prosociality is linked to the social and behavioural deficits reported in ASD, here it is hypothesised that these trait deficits in sociability may also extend to the typical population. For example, in **Chapter 3**, which asked whether autistic traits affected vicarious experience of **CT**-optimal stimuli, it was the individuals with the lowest level of autistic traits and thus the highest sociability who showed greater sensitivity to affective touch.

Human behaviour is guided by motivation and experience and social interactions are reliant on positive experience and conditioning of stimuli. It was shown in **Chapter** 4, where children with and without ASD were tested, that children do not appear to have learned the value of CT-stimulation particularly as tested through empathic responses to vicarious experience. Furthermore, evidence shows that partaking in social interactions is reliant on the successful development of the regions of the brain that provide value to social stimuli (Bachevalier & Loveland, 2006; Blakemore, 2008; Dunbar & Shultz, 2014). A number of studies have proposed that social stimuli provide motivation to control behaviour in a similar way to other rewards such as monetary gain (Izuma, Saito, & Sadato, 2008; A. Lin, Adolphs, & Rangel, 2012; Saxe & Haushofer, 2008). The Social Touch Hypothesis suggests that the development of social interaction behaviours results from positive motivational processing of CT-optimal stimuli, in the same way pain (as negative motivational stimuli) inhibits behaviour. Therefore, these findings suggest that the individuals with high levels of autistic traits and subsequently lower sociability would not find these social interactions as rewarding.

In **Chapter 7**, this could explain the significant difference in ULP between high and low autistic trait groups, such that the smaller peak amplitude suggests potentially atypical processing of C-fibre input. Tied in with the results from **Chapter 6**, it is theorised that this lower peak ULP may be directly related to the lower affective responses to CT-optimal stimuli.. It seems likely therefore that these results reflect a central deficit in the processing of these social stimuli, with potential implications for the valuation and experience of social interactions. Social motivation difficulties are proposed to be the result of social anhedonia (Berthoz, Lalanne, Crane, & Hill, 2013; Carré et al., 2015), though this suggests a negative experience of stimuli, here it is proposed that there isn't necessarily a negative experience of social touch due to minimal differences in the CS activity, however more that individuals with high levels of autistic traits have a reduced affective valuation of these stimuli.

A large number of studies have provided evidence for atypical cortical development in individuals with ASD (Di Martino et al., 2009; Kaiser et al., 2015; Kohls et al., 2013; Scheele et al., 2014; Zeeland, Dapretto, Ghahremani, Poldrack, & Bookheimer, 2011) however, the link between them and social motivation deficits remains under researched (Chevallier, Grèzes, Molesworth, Berthoz, & Happé, 2012). Furthermore, individuals with the highest number of autistic traits also show similar differences in their cortical activity when compare to individuals with low levels of autistic traits (Di Martino et al., 2009; Scheele et al., 2014). Abnormalities in ACC activation would suggest wide spread deficits in motivational responses to stimuli. Interestingly in Chapter 7, individuals with high levels of autistic traits elicited a significantly larger ULP than individuals with low levels of autistic traits. It has been hypothesised both here and in Ackerley et al (2013) that this peak amplitude is related to frontal lobe activity specific to C-fibre activation or a phenotypic switch from CTs to nociceptors (with similarities between relative ULPs recorded for noxious and pleasant stimuli). Although the exact source of these signals is not known, it can be inferred from fMRI research that this potential is related to activity in the ACC, potentially reflecting higher levels of salience ascribed to CT stimuli. Alternatively, it could reflect activity in the OFC reflecting affective and motivational processing of stimuli. If this is the case, then differences in the peak amplitudes recorded in this region could suggest some deficit whether it be in the individuals with high levels of autistic traits or those with low levels. This makes sense considering research shows that the functional activations (Asada, Fukuda, Tsunoda, Yamaguchi, & Tonoike, 1999; Di Martino et al., 2009; Thakkar et al., 2008; Zeeland et al., 2011) and the gray matter density (Hadjikhani et al., 2006; Haznedar et al., 2000; Simms, Kemper, Timbie, Bauman, & Blatt, 2009) of the ACC region are atypical in individuals diagnosed with ASD (Mundy, 2003). Interestingly this is not something that has been tested regularly in individuals with different levels of autistic traits despite the functional role of the ACC in social behaviour and autistic trait measurement of social interaction (Scheele et al., 2014).

It should be noted that, consistent with the heterogeneous nature of ASD, there is wide variability in physiological differences across studies. For example, differences in brain structure vary between individuals (Amaral, Schumann, & Nordahl, 2008; Wang et al., 2013) so it is not clear how this homogeneity would affect cortical measures. How do we know whether this is not the case for individuals across the autistic trait spectrum? Comparatively research shows that the brain displays plasticity and alters regions that do not remain in regular use (Ceko et al 2013; Tecchio et al 2002; Mainhofener et al 2003). If this is the case then it is possible that social trait differences are representative of minor differences in cortical structures in the regions of the brain responsible for developing social behaviour such the ACC discussed previously. Furthermore, if this were the case, then the motivation required to partake in more social tactile interactions, typical of CT-stimulation, would not be present in individuals across the spectrum except those with the highest level of sociability.

# 8.3. Methodological Limitations.

Throughout this thesis, there are a number of considerations for methodological changes that may have affected the results reported. Initially the first three studies used videos depicting one female actor touching the upper body of a male actor. Furthermore, in **Chapter 5**, an additional set of male-to-male touch videos were included. It is important to consider that these videos were used across a number of different studies where different groups of individuals were recruited. For example, in **Chapter 4** these videos were used in an experiment with children. A consideration for this research is that the children may not be able to empathise with the actors in the videos because they are all adults. Furthermore, the touch these children would have experienced in their lives would have specific context, such as the comforting embrace of a parent or a peer. These contextual differences would undoubtedly have a top-down effect on the experience of these stimuli. These videos were specifically created to remove social context (i.e. removing facial expressions or external context), this should therefore allow for the participant's focus to be on the action of the touch. However, future research should consider that children may be more inclined to focus on the touch when it is contextually similar to the touch they would have received.

Secondly, in **Chapter 4** participants in the typically developing group all completed the video task together. Although it was possible to have participants complete the BPVS

independently, issues on the day meant that each participant in this group observed the videos together in the same order on a projector screen. Each of the children used an tablet computer to make their individual ratings. This raises a number of issues, first of which is the proximity of each child to a member of their peer group whilst completing these questions about touch. Furthermore, in comparison to the ASD group, who were sat with their parents in a lab space, these experiences would be different for the groups. In future it would be important to consider how these issues may be improved, for example, testing each of the groups at a school or in the lab would reduce the differences between groups.

The stimuli delivered in **Chapters 5 & 6** were fundamentally different (one vicarious, one first hand touch) however; it is still possible that the EMG measure will have recorded noise from the post stimulus period that was present in both studies. Eye blinks are unlikely to have caused enough noise to show an increase in activity throughout the post-stroking period, especially as in **Chapter 6** participants had their eyes closed throughout the stroking and post-stroking period. A further theory is that these increases are the result of participants moving once the stimuli is finished; this could be the result of the stimulus in general making the participants wince, laugh or smirk but again this is only likely in **Chapter 6** (physical stimuli) but not **Chapter 5** (video stimuli). Combining these two methods in one study would enable a full picture of these effects to be measured across vicarious and first-hand experience of the touch. Theoretically, these two studies independently show that activity is greater post stimulus, suggesting an evaluation of the stimulus and the subsequent affective responses. This interpretation is not increase late in the stroking period and peaked in the post-stroking period.

A final methodological consideration is with **Chapter 7**. Here, participants experienced individual manual brush stroke to their arms. This experiment was an extension

of that conducted by Ackerley et al (2013). In the previous study, over 200 individual strokes were delivered to participants, which elicited individual ULPs for each participant. In this study as the stimuli were delivered manually, only 43 strokes were delivered at each velocity. This meant that the ULP was only present in the grand average ERP across participants. In future this study should be completed using an RTS to both maximise the number of strokes possible and to achieve accurate velocity and pressure from stimuli.

## 8.4. Future Directions

Evidence is presented in this thesis from studies using a range of methodologies to determine the effect of social trait differences on Affective Touch perception. Since the inception of this project, some researchers have published evidence supporting or disputing the evidence found here. For example, Croy et al (2017) found that children around the same age as those recruited in Chapter 4, showed preference for CT-optimal stimuli that we did not find. There are a number of methodological differences between these studies for example, Croy et al (2017) used physical tactile stimulation whereas here participants observed videos depicting CT-optimal and non-CT-optimal touch. Furthermore, in Chapter 4, individuals diagnosed with ASD were recruited to further test trait sociability and its effect on responses to CT-optimal touch. Future research should consider how children with and without ASD process first-hand CT-optimal touch longitudinally, to determine when the responses to CT-optimal stimuli are present and when the learned value of these behaviours allow for the empathic experience of these stimuli. It was hypothesised that the preference for CT-optimal stimuli in Chapter 3 and 5 reflect a learned value CT-optimal stimuli and thus participants perceive the benefits during the observation of the stimuli. However, it is likely that these observational benefits are not present in early childhood.

Furthermore, incorporating more objective measures into this research would benefit the outcome. In studies such as Kida and Shinohara (2013), CT-optimal stimuli elicits

patterns of cortical activation in infants similar to those measured in adults suggesting that children do indeed process CT-optimal stimuli, however it is not clear what these cortical metrics mean. By measuring affective response to stimuli as discussed in **Chapter 6**, it would be possible to determine whether these cortical responses reflect valuation of affective arousal responses to CT-optimal stimuli observed in adults. In line with the studies presented here, another method to measure affective arousal to stimuli is the facial action coding system (Ekman & Friesen, 1978). This is even less invasive than EMG by measuring the movement of muscles on the face during specific stimuli. Participants would be video recorded and an individual trained to determine how observed muscle activity relates to affective state changes then observes these.

A key finding in this thesis was that participants with high number of autistic traits show an increased ULP amplitude in response to CT-optimal stimuli. Future research should develop this line of investigation. For instance, one improvement would be to recruit participants diagnosed with ASD as in **Chapter 6**, this would improve the spread of AQ scores with more participants eliciting poorer social trait abilities. If this ULP is indeed the measure of activity in the OFC or ACC then this would be the first instance where activation of these areas have been shown in participants with ASD. A number of researchers have shown deficits in this region through fMRI research (Barnea-Goraly et al 2004; Cascio et al 2012; Kohls et al 2013) however, this is not something that has been found using more temporally sensitive measures such as EEG. The importance of EEG in this instance is that it allows us to specifically measure stimuli that are fundamentally different in their conduction velocities. As such, the research presented in Chapter 7, specifically highlights the differences in A $\beta$  and CT stimuli processing and the subsequent cortical processing of these inputs.

Furthermore, measuring the effect that trait sociability has on responses to CT-optimal touch is very much the first stage in testing the Social Touch Hypothesis. In the introduction, it was hypothesised that not getting the positive rewarding benefits to social touch would not motivate individuals to partake in such interactions, however this needs to be further tested to determine exactly how trait deficits in sociability affect an individual's ability to perceive social reward in general and CT activating touch specifically.

## 8.5. Conclusion

The main aim of this thesis was to determine whether trait differences in sociability affected individual's responses to affective touch. It has been shown that individual responses, both self-report and physiological do vary as a function of trait sociability. This however, was not the case in children who showed similar patterns of blunted affect in response to the observation of affective touch in others regardless of whether they were autistic or typically developing. This suggests that the mechanisms responsible for empathic responses to social stimuli may remain undeveloped in the young children tested here.

Furthermore, the data from physiological and psychophysiological measures suggest that the responses of individuals with high levels of autistic traits differ from individuals with low levels of autistic traits, and thus greater sociability. It is hypothesised that these differences reflect atypical reward processing in individuals with poor sociability that result in CT-optimal stimuli being perceived as less rewarding or no more rewarding than other types of tactile interactions. The social touch hypothesis states that these stimuli are necessary for the development of social bonds., The data reported here, highlighting a relationship between trait levels of sociability and responses to socially relevant touch, suggest it is possible that genetically determined differences in responses to affective touch during early development could potentially lead to reduced motivation for social tactile interactions in later life.

## **References**

- Ackerley, R., Backlund Wasling, H., Liljencrantz, J., Olausson, H., Johnson, R. D., & Wessberg, J. (2014). Human C-Tactile Afferents Are Tuned to the Temperature of a Skin-Stroking Caress. *Journal of Neuroscience*, *34*(8), 2879–2883. https://doi.org/10.1523/JNEUROSCI.2847-13.2014
- Ackerley, R., Carlsson, I., Wester, H., Olausson, H., & Backlund Wasling, H. (2014). Touch perceptions across skin sites: differences between sensitivity, direction discrimination and pleasantness. *Frontiers in Behavioral Neuroscience*, 8(February), 54. https://doi.org/10.3389/fnbeh.2014.00054
- Ackerley, R., Eriksson, E., & Wessberg, J. (2013). Ultra-late EEG potential evoked by preferential activation of unmyelinated tactile afferents in human hairy skin. *Neuroscience Letters*, 535, 62–6. https://doi.org/10.1016/j.neulet.2013.01.004
- Ackerley, R., Saar, K., McGlone, F., & Backlund Wasling, H. (2014). Quantifying the sensory and emotional perception of touch: differences between glabrous and hairy skin. *Frontiers in Behavioral Neuroscience*, 8(February), 34. https://doi.org/10.3389/fnbeh.2014.00034
- Alvarez, P., Levine, J. D., & Green, P. G. (2015). Neonatal handling (resilience) attenuates water-avoidance stress induced enhancement of chronic mechanical hyperalgesia in the rat. *Neuroscience Letters*, 591, 207–211. https://doi.org/10.1016/j.neulet.2015.01.066
- Amaral, D. G., Schumann, C. M., & Nordahl, C. W. (2008). Neuroanatomy of autism. *Trends in Neurosciences*, 31(3), 137–145. https://doi.org/10.1016/j.tins.2007.12.005
- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders : DSM-5. Washington, D.C: American Psychiatric Association. doi:10.1176/appi.books.9780890425596.744053
- Asada, H., Fukuda, Y., Tsunoda, S., Yamaguchi, M., & Tonoike, M. (1999). Frontal midline theta rhythms reflect alternative activation of prefrontal cortex and anterior cingulate cortex in humans. *Data Processing*, 274, 29–32. DOI: 10.1016/S0304-3940(99)00679-5
- Austin, E. J. (2005). Personality correlates of the broader autism phenotype as assessed by the Autism Spectrum Quotient (AQ). *Personality and Individual Differences*, 38(2), 451–460. https://doi.org/10.1016/j.paid.2004.04.022

- Avenanti, A., Minio-Paluello, I., Bufalari, I., & Aglioti, S. M. (2009). The pain of a model in the personality of an onlooker: Influence of state-reactivity and personality traits on embodied empathy for pain. *NeuroImage*, 44(1), 275–283. https://doi.org/10.1016/j.neuroimage.2008.08.001
- Bachevalier, J., & Loveland, K. A. (2006). The orbitofrontal-amygdala circuit and selfregulation of social-emotional behavior in autism. *Neuroscience and Biobehavioral Reviews*, 30(1), 97–117. https://doi.org/10.1016/j.neubiorev.2005.07.002
- Balconi, M., Vanutelli, M. E., & Finocchiaro, R. (2014). Multilevel analysis of facial expressions of emotion and script: Self-report (arousal and valence) and psychophysiological correlates. *Behavioral and Brain Functions*, 10(1), 1–14. https://doi.org/10.1186/1744-9081-10-32
- Barnea-Goraly, N., Kwon, H., Menon, V., Eliez, S., Lotspeich, L., & Reiss, A. L. (2004).
  White matter structure in autism: Preliminary evidence from diffusion tensor imaging. *Biological Psychiatry*, 55(3), 323–326. https://doi.org/10.1016/j.biopsych.2003.10.022
- 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*, 17, 5–17. DOI: 10.1023/A:1005653411471
- Baumeister, R. F., Bratslavsky, E., Finkenauer, C., & Vohs, K. D. (2001). Bad Is Stronger Than Good. *Review of General Psychology*, 5(4), 323–370. https://doi.org/10.1037//1089-2680.5.4.323
- Bennett, R. H., Bolling, D. Z., Anderson, L. C., Pelphrey, K. a, & Kaiser, M. D. (2014). fNIRS detects temporal lobe response to affective touch. *Social Cognitive and Affective Neuroscience*, 9(4), 470–6. https://doi.org/10.1093/scan/nst008
- Berger, H. (1929). über das elektrenkephalogramm des menschen. Archiv Fur Psychiatrie Und Nervenkrankheiten, 87, 527–570. doi:10.1007/BF01797193.
- Berridge, K. C., Robinson, T. E., & Aldridge, J. W. (2009). Dissecting components of reward: "liking", "wanting", and learning. *Current Opinion in Pharmacology*, 9(1), 65– 73. https://doi.org/10.1016/j.coph.2008.12.014
- Berthoz, S., Lalanne, C., Crane, L., & Hill, E. L. (2013). Investigating emotional impairments

in adults with autism spectrum disorders and the broader autism phenotype. *Psychiatry Research*, 208(3), 257–264. https://doi.org/10.1016/j.psychres.2013.05.014

- Bettleheim, B. (1967). The Empty Fortress: Infantile Autism and the Birth of the Self. London: Collier-Macmillan. doi:10.1001/archpsyc.1967.01730280126018
- Björnsdotter, M., Gordon, I., Pelphrey, K. A, Olausson, H., & Kaiser, M. D. (2014).
  Development of brain mechanisms for processing affective touch. *Frontiers in Behavioral Neuroscience*, 8(February), 24. https://doi.org/10.3389/fnbeh.2014.00024
- Björnsdotter, M., Löken, L., Olausson, H., Vallbo, A., & Wessberg, J. (2009). Somatotopic organization of gentle touch processing in the posterior insular cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 29(29), 9314–9320. https://doi.org/10.1523/JNEUROSCI.0400-09.2009
- Björnsdotter, M., Morrison, I., & Olausson, H. (2010). Feeling good: On the role of C fiber mediated touch in interoception. *Experimental Brain Research*, 207(3–4), 149–155. https://doi.org/10.1007/s00221-010-2408-y
- Blake, R., Turner, L. M., Smoski, M. J., Pozdol, S. L., & Stone, W. L. (2003). Visual Recognition of Biological Motion is Impaired in Children With Autism. *Psychological Science (Wiley-Blackwell)*, 14(2), 151–157. DOI: 10.1111/1467-9280.01434 e
- Blakemore, S.-J. (2008). The social brain in adolescence. *Nature Reviews. Neuroscience*, 9(4), 267–277. https://doi.org/10.1038/nrn2353
- Blakemore, S.-J., Tavassoli, T., Calò, S., Thomas, R. M., Catmur, C., Frith, U., & Haggard, P. (2006). Tactile sensitivity in Asperger syndrome. *Brain and Cognition*, 61(1), 5–13. https://doi.org/10.1016/j.bandc.2005.12.013
- Bolognini, N., Rossetti, A., Fusaro, M., Vallar, G., & Miniussi, C. (2014). Sharing social touch in the primary somatosensory cortex. *Current Biology*, 24(13), 1513–1517. https://doi.org/10.1016/j.cub.2014.05.025
- Bölte, S., Poustka, F., & Constantino, J. N. (2008). Assessing autistic traits: Cross-cultural validation of the social responsiveness scale (SRS). *Autism Research*, 1(6), 354–363. https://doi.org/10.1002/aur.49
- Boxtel, A. Van. (2010). Facial EMG as a Tool for Inferring Affective States. In Spink AJ, Grieco F., Krips O. E., Loijens L. W. S., Noldus L. P. J. J. & Zimmerman P.

Proceedings of Measuring Behavior, 2010, 104–108.

- Bradley, M. M., Keil, A., & Lang, P. J. (2012). Orienting and emotional perception: Facilitation, attenuation, and interference. *Frontiers in Psychology*, 3(NOV), 1–6. https://doi.org/10.3389/fpsyg.2012.00493
- Bromm, B., Neitzel, H., Tecklenburg, A., & Detlef-Treede, R. (1983). Evoked cerebral potential correlates of c-fibre activity. *Neuroscience Letters*, 43, 109–114. https://doi.org/10.1016/0304-3940(83)90137-4
- Bromm, B., & Treede, R. D. (1987). Pain related cerebral potentials: late and ultralate components. *International Journal of Neuroscience*, 33(1–2), 15–23. https://doi.org/10.3109/00207458708985926
- Brooks, J. C. W., 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. https://doi.org/10.1016/j.neuroimage.2005.03.041
- Bufalari, I., & Ionta, S. (2013). The social and personality neuroscience of empathy for pain and touch. *Frontiers in Human Neuroscience*, 7(July). https://doi.org/10.3389/fnhum.2013.00393
- Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends.Cogn Sci.*, 4(6), 215–222. https://doi.org/10.1016/S1364-6613(00)01483-2
- Butterworth, S., Francis, S., Kelly, E., McGlone, F., Bowtell, R. & Sawle, G. V. (2003).
  Abnormal cortical sensory activation in Dystonia: An fMRI study. *Movement Disorders*, 8 (6), 673-682. 10.1002/mds.10416
- Bystrova, K. (2009). Novel mechanism of human fetal growth regulation: A potential role of lanugo, vernix caseosa and a second tactile system of unmyelinated low-threshold Cafferents. *Medical Hypotheses*, 72(2), 143–146. https://doi.org/10.1016/j.mehy.2008.09.033
- Cacioppo, J. T., Petty, R. E., Losch, M. E., & Kim, H. S. (1986). Electromyographic Activity Over Facial Muscle Regions Can Differentiate the Valence and Intensity of Affective Reactions. *Journal of Personality and Social Psychology*, 50(2), 260–268.

https://doi.org/10.1037/0022-3514.50.2.260

- Campagnoli, R. R., Krutman, L., Vargas, C. D., Lobo, I., Oliveira, J. M., Oliveira, L., ... Volchan, E. (2015). Preparing to caress: a neural signature of social bonding. *Frontiers in Psychology*, 6(January), 1–9. https://doi.org/10.3389/fpsyg.2015.00016
- Cannon, P. R., Hayes, A. E., & Tipper, S. P. (2009). An electromyographic investigation of the impact of task relevance on facial mimicry. *Cognition and Emotion*, 23(5), 918–929. https://doi.org/10.1080/02699930802234864
- Carré, A., Chevallier, C., Robel, L., Barry, C., Maria, A.-S., Pouga, L., ... Berthoz, S. (2015). Tracking Social Motivation Systems Deficits: The Affective Neuroscience View of Autism. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-015-2498-2
- Cascio, C. J., Foss-feig, J. H., Heacock, J. L., Newsom, C. R., Cowan, R. L., Benningfield, M. M., ... Cao, A. (2012). Response of neural reward regions to food cues in autism spectrum disorders. *Journal of Neurodevelopmental Disorders*, 4(1), 9. https://doi.org/10.1186/1866-1955-4-9
- Cascio, C. J., Lorenzi, J., & Baranek, G. T. (2016). Self-reported Pleasantness Ratings and Examiner-Coded Defensiveness in Response to Touch in Children with ASD: Effects of Stimulus Material and Bodily Location. *Journal of Autism and Developmental Disorders*, 46(5), 1528–1537. https://doi.org/10.1007/s10803-013-1961-1
- Cascio, C. J., Lorenzi, J., & Baranek, G. T. (2016). Self-reported Pleasantness Ratings and Examiner-Coded Defensiveness in Response to Touch in Children with ASD: Effects of Stimulus Material and Bodily Location. *Journal of Autism and Developmental Disorders*, 1528–1537. https://doi.org/10.1007/s10803-013-1961-1
- Cascio, C. J., Moana-filho, E. J., Guest, S., Nebel, M. B., Baranek, G. T., & Essick, G. K. (2012). Perceptual and neural response to affective tactile texture stimulation in adults with Autsim Spectrum Disorders. *Autism Research*, 5(4), 231–244. https://doi.org/10.1002/aur.1224.Perceptual
- Cascio, C., McGlone, F., Folger, S., Tannan, V., Baranek, G., Pelphrey, K. a, & Essick, G. (2008). Tactile perception in adults with autism: a multidimensional psychophysical study. *Journal of Autism and Developmental Disorders*, 38(1), 127–137.

https://doi.org/10.1007/s10803-007-0370-8

- Cascio, C. J., Moore, D. & McGlone, F. (2018). Social Touch and Human Development. Developmental Cognitive Development, https://doi.org/10.1016/j.dcn.2018.04.009
- Case, L. K., Laubacher, C. M., Olausson, H., Wang, B., Spagnolo, P. A., & Bushnell, M. C. (2016). Encoding of Touch Intensity But Not Pleasantness in Human Primary Somatosensory Cortex. *Journal of Neuroscience*, *36*(21), 5850–5860. https://doi.org/10.1523/JNEUROSCI.1130-15.2016
- Ceko, M., Seminowicz, D. a., Catherine Bushnell, M., & Olausson, H. W. (2013). Anatomical and functional enhancements of the insula after loss of large primary somatosensory fibers. *Cerebral Cortex*, 23(9), 2017–2024. https://doi.org/10.1093/cercor/bhs157
- Champagne, F. A., & Meaney, M. J. (2007). Transgenerational effects of social environment on variations in maternal care and behavioral response to novelty. *Behavioral Neuroscience*, *121*(6), 1353–63. https://doi.org/10.1037/0735-7044.121.6.1353
- Chapman, H. A., Kim, D. A., Susskind, J. M., & Anderson, A. K. (2009). In bad taste: Evidence for the oral origins of moral disgust. *Science*, 323(5918), 1222–1226. https://doi.org/10.1126/science.1165565
- Chatel-Goldman, J., Congedo, M., Jutten, C., & Schwartz, J.-L. (2014). Touch increases autonomic coupling between romantic partners. *Frontiers in Behavioral Neuroscience*, 8(March), 95. https://doi.org/10.3389/fnbeh.2014.00095
- Cheng, Y., Chen, C., Lin, C. P., Chou, K. H., & Decety, J. (2010). Love hurts: An fMRI study. *NeuroImage*, *51*(2), 923–929. https://doi.org/10.1016/j.neuroimage.2010.02.047
- Chevallier, C., Grèzes, J., Molesworth, C., Berthoz, S., & Happé, F. (2012). Brief report:
  Selective social anhedonia in high functioning autism. *Journal of Autism and Developmental Disorders*, 42(7), 1504–1509. https://doi.org/10.1007/s10803-011-1364-0
- Chevallier, C., Kohls, G., Troiani, V., Brodkin, E. T., & Schultz, R. T. (2013). The social motivation theory of autism. *Trends in Cognitive Neuroscience*, 16(4), 231–239. https://doi.org/10.1016/j.tics.2012.02.007.

Chevallier, C., Parish-Morris, J., McVey, A., Rump, K. M., Sasson, N. J., Herrington, J. D.,

& Schultz, R. T. (2015). Measuring social attention and motivation in autism spectrum disorder using eye-tracking: Stimulus type matters. *Autism Research*, n/a-n/a. https://doi.org/10.1002/aur.1479

- Chiesa, P. A., Liuzza, M. T., Macaluso, E., & Aglioti, S. M. (2017). Brain activity induced by implicit processing of others' pain and pleasure. *Human Brain Mapping*, 0(July). https://doi.org/10.1002/hbm.23749
- Coan, J. a, Schaefer, H. S., & Davidson, R. J. (2006). Lending a Hand of the Neural Response to Threat. *Psychological Science*, 17(12), 1032–1039. https://doi.org/10.1111/j.1467-9280.2006.01832.x
- Coben, R., Clarke, A. R., Hudspeth, W., & Barry, R. J. (2008). EEG power and coherence in autistic spectrum disorder. *Clinical Neurophysiology*, *119*(5), 1002–1009. https://doi.org/10.1016/j.clinph.2008.01.013
- Conde-Agudelo, A., Belizán, J. M., & Diaz-Rossello, J. (2011). Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. *Cochrane Database of Systematic Reviews (Online)*, (3), CD002771. https://doi.org/10.1002/14651858.CD002771.pub2
- Coskun, M. A., Varghese, L., Reddoch, S., Castillo, E. M., Pearson, D. a, Loveland, K. a, ...
  Sheth, B. R. (2009). How somatic cortical maps differ in autistic and typical brains. *Neuroreport*, 20(2), 175–179. https://doi.org/10.1097/WNR.0b013e32831f47d1
- Courchesne, E., Karns, C. M., Davis, H. R., Ziccardi, R., Carper, R. A., Tigue, Z. D., ... Courchesne, R. Y. (2011). Unusual brain growth patterns in early life in patients with autistic disorder: An MRI study. *Neurology*, 76(24), 2111. https://doi.org/10.1212/01.wnl.0000399191.79091.28
- Craig, A. D. (2009). How do you feel now? The anterior insula and human awareness. *Nature Reviews Neuroscience*, *10*(1), 59–70. https://doi.org/10.1038/nrn2555
- Crane, L., Goddard, L., & Pring, L. (2009). Sensory processing in adults with autism spectrum disorders. *Autism : The International Journal of Research and Practice*, 13(3), 215–228. https://doi.org/10.1177/1362361309103794
- Croy, I., Geide, H., Paulus, M., Weidner, K., & Olausson, H. (2016). Affective touch awareness in mental health and disease relates to autistic traits? An explorative

neurophysiological investigation. *Psychiatry Research*, 245, 491–496. https://doi.org/10.1016/j.psychres.2016.09.011

- Croy, I., Luong, A., Triscoli, C., Hofmann, E., Olausson, H., & Sailer, U. (2016). Interpersonal stroking touch is targeted to C tactile afferent activation. *Behavioural Brain Research*, 297, 37–40. https://doi.org/10.1016/j.bbr.2015.09.038
- Croy, I., Sehlstedt, I., Wasling, H. B., Ackerley, R., & Olausson, H. (2017). Gentle touch perception: From early childhood to adolescence. *Developmental Cognitive Neuroscience*. https://doi.org/10.1016/j.dcn.2017.07.009
- Crusco, A. H., & Wetzel, C. G. (1984). The Midas Touch The Effects of Interpersonal touch on Restaurant Tipping. *Personality and Social Psychology Bulletin*, 10(4), 512–517. https://doi.org/0803973233
- Davis, M. H. (1980). Interpersonal Reactivity Index. JSAS Catalog of Selected Documents in *Psychology*, 10(1980), 14–15. https://doi.org/10.1037/t01093-000
- de Groot, J. H. B., Smeets, M. A. M., Rowson, M. J., Bulsing, P. J., Blonk, C. G., Wilkinson,
  J. E., & Semin, G. R. (2015). A Sniff of Happiness. *Psychological Science*, 26(6), 684–700. https://doi.org/10.1177/0956797614566318
- Decety, J., Echols, S., & Correll, J. (2010). The Blame Game: The Effect of Responsibility and Social Stigma on Empathy for Pain. *Journal of Cognitive Neuroscience*, 22(5), 985– 997. https://doi.org/10.1162/jocn.2009.21266
- Decety, J., & Jackson, P. L. (2004). The functional architecture of human empathy. Behavioral and cognitive neuroscience reviews (Vol. 3). https://doi.org/10.1177/1534582304267187
- Decety, J., Michalska, K. J., & Akitsuki, Y. (2008). Who caused the pain? An fMRI investigation of empathy and intentionality in children. *Neuropsychologia*, 46(11), 2607–2614. https://doi.org/10.1016/j.neuropsychologia.2008.05.026
- Delmonte, S., Balsters, J. H., McGrath, J., Fitzgerald, J., Brennan, S., Fagan, A. J., & Gallagher, L. (2012). Social and monetary reward processing in autism spectrum disorders. *Molecular Autism*, 3(1), 7. <u>https://doi.org/10.1186/2040-2392-3-7</u>
- Delorme, A. & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of singletrial EEG dynamics. *Journal of Neuroscience Methods*, 134, 9-21.

doi:10.1016/j.jneumeth.2003.10.009.

- Di Martino, A., Ross, K., Uddin, L. Q., Sklar, A. B., Castellanos, F. X., & Milham, M. P. (2009). Functional brain correlates of social and non-social processes in autism spectrum disorders: an ALE meta-analysis. *Biological Psychiatry*, 65(1), 63–74. https://doi.org/10.1016/j.biopsych.2008.09.022.Functional
- Di Martino, A., Shehzad, Z., Kelly, C., Roy, A. K., Gee, D. G., Uddin, L. Q...Milham, M. P. (2009). Relationship between cingulo-insular functional connectivity and autistic traits in neurotypical adults. *The American Journal of Psychiatry*, 166 (8), 891-899 https://doi.org/10.1176/appi.ajp.2009.08121894.
- Diamond, M. C., Krech, D., & Rosenzweig, M. R. (1964). The effects of an enriched environment on the histology of the rat cerebral cortex. *Journal of Comparative Neurology*, *123*(1), 111–119. https://doi.org/10.1002/cne.901230110
- Diego, M. A., Field, T., & Hernandez-Reif, M. (2014). Preterm infant weight gain is increased by massage therapy and exercise via different underlying mechanisms. *Early Human Development*, 90(3), 137–140. https://doi.org/10.1016/j.earlhumdev.2014.01.009
- Djouhri, L. (2016). Electrophysiological evidence for the existence of a rare population of Cfiber low threshold mechanoreceptive (C-LTM) neurons in glabrous skin of the rat hindpaw. *Neuroscience Letters*, *613*, 25–29. https://doi.org/10.1016/j.neulet.2015.12.040
- Dunbar, A. R. I. M., & Shultz, S. (2014). Evolution in the Social Brain. *Science*, *317*(5843), 1344–1347. https://doi.org/10.1126/science.1145463
- Dunn, L. M., Dunn, L. M., Whetton, K., & Burley, J. (1997). *British Picture Vocabulary Scale* (2nd ed.). Windsor: NFER-NELSON.
- Dunn, W. (1999). Sensory Profile: Caregiver Questionnaire. Pearson.
- Dziobek, I., Rogers, K., Fleck, S., Bahnemann, M., Heekeren, H. R., Wolf, O. T., & 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), 464–73. https://doi.org/10.1007/s10803-007-0486-x
- Ebenezer, G. J., McArthur, J. C., Thomas, D., Murinson, B., Hauer, P., Polydefkis, M., & Griffin, J. W. (2007). Denervation of skin in neuropathies: The sequence of axonal and Schwann cell changes in skin biopsies. *Brain*, *130*(10), 2703–2714.

https://doi.org/10.1093/brain/awm199

- Ebisch, S. J. H., Perrucci, M. G., Ferretti, A., Del Gratta, C., Romani, G. L., & Gallese, V. (2008). The sense of touch: embodied simulation in a visuotactile mirroring mechanism for observed animate or inanimate touch. *Journal of Cognitive Neuroscience*, 20(9), 1611–1623. <u>https://doi.org/10.1162/jocn.2008.20111</u>
- Edin, B. B., Essick, G. K., Trulsson, M. & Olsson, K. A. (1995). Receptor encoding of moving tactile stimuli in humans I. temporal pattern of discharge of individual lowthreshold mechanoreceptors. *The Journal of Neuroscience*, 15(1), 830-847, doi.org/10.1523/JNEUROSCI.15-01-00830.1995
- Edin, B. B. (2001). Cutaneous afferents provide information about knee joint movements in humans. *Journal of Physiology*, *531*(1), 289–297. https://doi.org/10.1111/j.1469-7793.2001.0289j.x
- Ekman, P. & Friesen, W. (1978). Facial action coding system: A technique for the measurement of facial movement. *Consulting Psychologists Press*, Palo Alto, 1978.
- Elbert, T., Flor, H., Birbaumer, N., Knecht, S., Hampson, S., Larbig, W., & Taub, E. (1994). Extensive reorganization of the somatosensory cortex in adult humans after nervous system injury. *NeuroReport*, 5(18), 2593–2597. <u>https://doi.org/10.1097/00001756-199412000-00047</u>
- Ellingsen, D.-M., Wessberg, J., Eikemo, M., Liljencrantz, J., Endestad, T. & Olausson, H. (2013). Placebo improves pleasure and pain through opposite modulation of sensory processing. *Proceedings of the National Academy of Sciences, U.S.A, 110,* 17993-17998, doi: 10.1073/pnas.1305050110
- Ellingsen, D. –M., Leknes, S., Løseth, G., Wessberg, J. & Olausson, H. (2016). The neurobiology shaping affective touch: Expectation, motivation and meaning in the multisensory context. *Frontiers in Psychology*, 6 (1986). doi:10.3389/fpsyg.2015.01986
- Epstein, L. H. (1990). Perception of Activity in the Zygomaticus Major and Corrugator Supercilii Muscle Regions. *Psychophysiology*, 27(1), 68–72. https://doi.org/10.1111/j.1469-8986.1990.tb02181.x
- Escalona, A., Field, T., Singer-Strunck, R., Cullen, C., & Hartshorn, K. (2001). Improvements in the behavior of children with autism following massage therapy.

Journal of Autism and Developmental Disorders, 31(5), 513–516. https://doi.org/10.1023/A:1012273110194

- Essick, G. K., James, A., & McGlone, F. P. (1999). Psychophysical assessment of the affective components of non-painful touch. *Neuroreport*, 10(10), 2083–2087. https://doi.org/10.1097/00001756-199907130-00017
- Etzi, R., Carta, C., & Gallace, A. (2018). Stroking and tapping the skin: behavioral and electrodermal effects. *Experimental Brain Research*, 236(2), 453–461. https://doi.org/10.1007/s00221-017-5143-9
- Fairhurst, M. T., Löken, L., & Grossmann, T. (2014). Physiological and behavioral responses reveal 9-month-old infants' sensitivity to pleasant touch. *Psychological Science*, 25(5), 1124–31. https://doi.org/10.1177/0956797614527114
- Falck-Ytter, T. (2015). Gaze performance during face-to-face communication: A live eye tracking study of typical children and children with autism. *Research in Autism Spectrum Disorders*, 17, 78–85. https://doi.org/10.1016/j.rasd.2015.06.007
- Feldman, R., & Eidelman, A. I. (2003). Skin-to-skin contact (Kangaroo Care) accelerates autonomic and neurobehavioural maturation in preterm infants. *Developmental Medicine & Child Neurology*, 45(4), 274–281. https://doi.org/10.1017/S0012162203000525
- Fisher, J. D., Rytting, M., & Heslin, R. (1976). Hands Touching Hands : Affective and Evaluative Effects of an Interpersonal Touch. In, Fisher, J. D , Rytting, M. and Heslin, R. American Sociological Association Stable URL : http://www.jstor.org/stable/3033506, *Sociometry*, *39*(4), 416–421. DOI: 10.2307/3033506
- Francis, S., Rolls, E. T., Bowtell, R., Mcglone, F., O'Doherty, J., Browning, a, ... Smith, E. (1999). The representation of pleasant touch in the brain and its relationship with taste and olfactory areas. *Neuroreport*, 10(3), 453–459. https://doi.org/10.1097/00001756-199902250-00003
- Freitag, C. M., Konrad, C., H\u00e4berlen, M., Kleser, C., von Gontard, A., Reith, W., ... Krick, C. (2008). Perception of biological motion in autism spectrum disorders. *Neuropsychologia*, 46(5), 1480–1494.

https://doi.org/10.1016/j.neuropsychologia.2007.12.025

- 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
- Gardner, E. P. (1988). Somatosensory cortical mechanisms of feature detection in tactile and kinesthetic discrimination. *Canadian Journal of Physiology and Pharmacology*, 66(4), 439–454. DOI: 10.1139/y88-074
- Gazzola, V., Spezio, M. L., Etzel, J. a, Castelli, F., Adolphs, R., & Keysers, C. (2012).
   Primary somatosensory cortex discriminates affective significance in social touch.
   Proceedings of the National Academy of Sciences of the United States of America, 109(25), E1657-66. https://doi.org/10.1073/pnas.1113211109
- Golarai, G., Grill-Spector, K., & Reiss, A. L. (2006). Autism and the development of face processing. *Clinical Neuroscience Research*, 6(3–4), 145–160. https://doi.org/10.1016/j.cnr.2006.08.001
- Goodwin, M. S., Groden, J., Velicer, W. F., Lipsitt, L. P., Baron, M. G., Hofmann, S. G., & Groden, G. (2006). Cardiovascular Arousal in Individuals With Autism. *Focus on Autism and Other Developmental Disabilities*, 21(2), 100–123. https://doi.org/10.1177/10883576060210020101
- Gordon, I., Voos, A. C., Bennett, R. H., Bolling, D. Z., Pelphrey, K. A., & Kaiser, M. D. (2013). Brain mechanisms for processing affective touch. *Human Brain Mapping*, 34(4), 914–922. https://doi.org/10.1002/hbm.21480
- Gray, H. M., Ambady, N., Lowenthal, W. T., & Deldin, P. (2004). P300 as an index of attention to self-relevant stimuli. *Journal of Experimental Social Psychology*, 40(2), 216–224. https://doi.org/10.1016/S0022-1031(03)00092-1
- Hadjikhani, N., Joseph, R. M., Snyder, J., & Tager-Flusberg, H. (2006). Anatomical differences in the mirror neuron system and social cognition network in autism. *Cerebral Cortex*, 16(9), 1276–1282. https://doi.org/10.1093/cercor/bhj069
- Hadjikhani, N., Zürcher, N. R., Rogier, O., Hippolyte, L., Lemonnier, E., Ruest, T., ... Prkachin, K. M. (2014). Emotional contagion for pain is intact in autism spectrum disorders. *Translational Psychiatry*, 4(November 2013), e343.

https://doi.org/10.1038/tp.2013.113

- Haigh, S. M. (2018). Variable sensory perception in autism. *European Journal of Neuroscience*, 47(6), 602–609. https://doi.org/10.1111/ejn.13601
- Hamilton, A. F. D. C., Brindley, R. M., & Frith, U. (2007). Imitation and action understanding in autistic spectrum disorders : How valid is the hypothesis of a deficit in the mirror neuron system ?, 45(8), 1859–1868. https://doi.org/10.1016/j.neuropsychologia.2006.11.022
- Harlow, H. F. (1958). The nature of love. *American Psychologist*, *13*(12), 673–685. https://doi.org/10.1037/h0047884
- Harlow, H. F., Dodsworth, R. O., & Harlow, M. K. (1965). Total Social Isolation in Monkeys. Proceedings of the National Academy of Sciences of the United States of America, 54, 90–97. PMID:4955132
- Harlow, H. F., & Zimmermann, R. R. (1959). Affectional in. *Science*, *130*(3373), 421–432. https://doi.org/10.1126/science.130.3373.421
- Haznedar, M. M., Buchsbaum, M. S., Wei, T.-C., Hof, P. R., Cartwright, C., Bienstock, C. a, & Hollander, E. (2000). Limbic Circuitry in Patients With Autism Spectrum Disorders Studied With Positron Emission Tomography and Magnetic Resonance Imaging. *American Journal of Psychiatry*, *157*(12), 1994–2001. https://doi.org/10.1176/appi.ajp.157.12.1994
- Hertenstein, M. J., Keltner, D., App, B., Bulleit, B. A, & Jaskolka, A. R. (2006). Touch communicates distinct emotions. *Emotion (Washington, D.C.)*, 6(3), 528–33. https://doi.org/10.1037/1528-3542.6.3.528
- Hietanen, J. K., Surakka, V., & Linnankoski, I. (1998). Facial electromyographic responses to vocal affect expressions. *Psychophysiology*, 35(5), 530–536. https://doi.org/10.1017/S0048577298970445
- Hilton, C. L., Harper, J. D., Kueker, R. H., Lang, A. R., Abbacchi, A. M., Todorov, A., & Lavesser, P. D. (2010). Sensory responsiveness as a predictor of social severity in children with high functioning autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 40(8), 937–945. https://doi.org/10.1007/s10803-010-0944-8

Hoekstra, R. A., Bartels, M., Cath, D. C., & Boomsma, D. I. (2008). Factor structure,
reliability and criterion validity of the autism-spectrum quotient (AQ): A study in Dutch population and patient groups. *Journal of Autism and Developmental Disorders*, *38*(8), 1555–1566. https://doi.org/10.1007/s10803-008-0538-x

- Hoksbergen, R., ter Laak, J., Rijk, K., van Dijkum, C., & Stoutjesdijk, F. (2005). Post-Institutional Autistic Syndrome in Romanian adoptees. *Journal of Autism and Developmental Disorders*, 35(5), 615–23. <u>https://doi.org/10.1007/s10803-005-0005-x</u>
- Hommel, B. (1993). Attentional scanning in the selection of central targets from mulitsymbol strings. *Visual Cognition*, 2(2-3). doi.org/10.1080/13506289508401727.
- Hunt, F. (2008). The importance of kangaroo care on infant oxygen saturation levels and bonding. *Journal of Neonatal Nursing*, 14(2), 47–51. <u>https://doi.org/10.1016/j.jnn.2007.12.003</u>
- Hurst, R. M., Mitchell, J. T., Kimbrel, N. A., Kwapil, T. K. & Nelson-Gray, R. O. (2007). Examination of the relibility and factor structure of the Autism Spectrum Quotient (AQ) in a non-clinical sample. *Personality and Individual Differences*, 43 (7), 1938-1949. doi.org/10.1007/s10803-013-1827-6
- Izuma, K., Saito, D. N., & Sadato, N. (2008). Processing of Social and Monetary Rewards in the Human Striatum. *Neuron*, 58(2), 284–294. https://doi.org/10.1016/j.neuron.2008.03.020
- Jackson, P. L., Meltzoff, A. N., & Decety, J. (2005). How do we perceive the pain of others? A window into the neural processes involved in empathy. *NeuroImage*, 24(3), 771–9. https://doi.org/10.1016/j.neuroimage.2004.09.006
- Jackson, P. L., Rainville, P., & Decety, J. (2006). To what extent do we share the pain of others? Insight from the neural bases of pain empathy. *Pain*, 125(1–2), 5–9. https://doi.org/10.1016/j.pain.2006.09.013
- Jasper, H. H. (1958). The ten-twenty electrode system of the International Federation. *Electroencephalography and Clinical Neurophysiology*, 10, 371–375. DOI: 10.1080/00029238.1961.11080571
- Johansson, R. S., Trulsson, M., Olsson, K. a, & Westberg, K. G. (1988). Mechanoreceptor activity from the human face and oral mucosa. *Experimental Brain Research*, 72(February), 204–8. https://doi.org/10.1007/BF00248518

- Johnson, S. M., Moser, M. B., Beckes, L., Smith, A., Dalgleish, T., Halchuk, R., ... Coan, J. A. (2013). Soothing the threatened brain: Leveraging contact comfort with emotionally focused therapy. *PLoS ONE*, 8(11), 1–10. <u>https://doi.org/10.1371/journal.pone.0079314</u>
- Jönsson. E. H., Kotilahti, K., Heiskala, J., Backlund-Wasling, H., Olausson, H., Croy, I., et al. (2018). Affective and non-affective touch evoke differential brain response in 2-month old infants. *Neuroimage*, 169, 162-171. https://doi.org/10.1016/j.neuroimage.2017.12.024.
- Kaiser, M. D., Hudac, C. M., Shultz, S., Lee, S. M., Cheung, C., Berken, A. M., ... Pelphrey,
  K. a. (2010). Neural signatures of autism. *Proceedings of the National Academy of Sciences of the United States of America*, 107(49), 21223–8.
  https://doi.org/10.1073/pnas.1010412107
- Kaiser, M. D., Yang, D. Y.-J., Voos, A. C., Bennett, R. H., Gordon, I., Pretzsch, C., ...
  Pelphrey, K. A. (2015). Brain Mechanisms for Processing Affective (and Nonaffective)
  Touch Are Atypical in Autism. *Cerebral Cortex*, (2002), 1–10.
  <u>https://doi.org/10.1093/cercor/bhv125</u>
- Kakigi, R., Inui, K., Tran, D. T., Qiu, Y., Wang, X., Wantanabe, S. & Hoshiyama, M. (2004).
  Human Brain Processing and Central Mechanisms of Pain as Observed by Electro and
  Magneto-encephalography. *Journal of the Chinese Medical Association*, 67 (8), 377-386.
  PMID: 15553795.
- Kaplan, J. T., & Iacoboni, M. (2006). Getting a grip on other minds: mirror neurons, intention understanding, and cognitive empathy. *Social Neuroscience*, 1(3–4), 175–183. https://doi.org/10.1080/17470910600985605
- Keizer, A., de Jong, J. R., Bartlema, L., & Dijkerman, C. (2017). Visual perception of the arm manipulates the experienced pleasantness of touch. *Developmental Cognitive Neuroscience*, (September), 0–1. https://doi.org/10.1016/j.dcn.2017.09.004
- Kennedy, W. R., Wendelschafer-Crabb, G., Polydefkis, M. & McArthur, J. C. (2005). Pathology and Quantification of Cutaneous Innervation. *Peripheral Neuronopathy*, 1, 869-895. 0.1016/B978-0-7216-9491-7.50037-5
- Keysers, C., Kaas, J. H., & Gazzola, V. (2010). Somatosensation in social perception. *Nature Reviews. Neuroscience*, 11(6), 417–428. https://doi.org/10.1038/nrn2919

- Kida, T., & Shinohara, K. (2013). Gentle touch activates the anterior prefrontal cortex: an NIRS study. *Neuroscience Research*, 76(1–2), 76–82. https://doi.org/10.1016/j.neures.2013.03.006
- Kikuchi, Y., Senju, A., Tojo, Y., Osanai, H., & Hasegawa, T. (2009). Faces do not capture special attention in children with autism spectrum disorder: a change blindness study, 80(5), 1421–1433. https://doi.org/10.1111/j.1467-8624.2009.01342.x
- Kirsch, L. P., Krahé, C., Blom, N., Crucianelli, L., Moro, V., Jenkinson, P. M., & Fotopoulou, A. (2017). Reading the Mind in the Touch: Neurophysiological Specificity in the Communication of Emotions by Touch. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2017.05.024
- Kirsch, L. P., Snagg, A., Heerey, E., & Cross, E. S. (2016). The Impact of Experience on Affective Responses during Action Observation. *PloS One*, *11*(5), e0154681. https://doi.org/10.1371/journal.pone.0154681
- Klin, A., & Jones, W. (2008). Altered face scanning and impaired recognition of biological motion in a 15-month-old infant with autism: REPORT. *Developmental Science*, 11(1), 40–46. https://doi.org/10.1111/j.1467-7687.2007.00608.x
- Klin, A., Lin, D. J., Gorrindo, P., Ramsay, G., & Jones, W. (2009). Two-year-olds with autism orient to non-social contingencies rather than biological motion. *Nature*, 459(7244), 257–261. https://doi.org/10.1038/nature07868
- Kohls, G., Schulte-Rüther, M., Nehrkorn, B., Müller, K., Fink, G. R., Kamp-Becker, I., ...
  Konrad, K. (2013). Reward system dysfunction in autism spectrum disorders. *Social Cognitive and Affective Neuroscience*, 8(5), 565–572.
  https://doi.org/10.1093/scan/nss033
- Krahé, C., Drabek, M. M., Paloyelis, Y., & Fotopoulou, A. (2016). Affective touch and attachment style modulate pain: a laser-evoked potentials study. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 371(1708), 20160009. https://doi.org/10.1098/rstb.2016.0009
- Kress, I. U., Minati, L., Ferraro, S. & Critchley, H. D. (2012). Direct skin-to-skin vs. indirect touch modulates neural responses to stroking vs. tapping. *Neuroreport*, 22(13), 646-651, doi:10.1097/WNR.0b013e328349d166.

- Kringelbach, M. L. (2005). The human orbitofrontal cortex: Linking reward to hedonic experience. *Nature Reviews Neuroscience*, 6(September), 691–702. https://doi.org/10.1038/nrn174
- Lamm, C., Porges, E. C., Cacioppo, J. T., & Decety, J. (2008). Perspective taking is associated with specific facial responses during empathy for pain. *Brain Research*, 1227, 153–161. https://doi.org/10.1016/j.brainres.2008.06.066
- Lamm, C., Silani, G., & Singer, T. (2015). Distinct neural networks underlying empathy for pleasant and unpleasant touch. *Cortex*, 1–11. https://doi.org/10.1016/j.cortex.2015.01.021
- Lamm, C., & Singer, T. (2010). The role of anterior insular cortex in social emotions. *Brain Structure and Function*, *214*, 1–13. https://doi.org/10.1007/s00429-010-0251-3
- Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997). International Affective Picture System (IAPS): Technical Manual and Affective Ratings. *NIMH Center for the Study of Emotion and Attention*, 39–58. https://doi.org/10.1027/0269-8803/a000147
- Larsen, J. T., Norris, C. J., & Cacioppo, J. T. (2003). Effects of positive and negative affect on electromyographic activity over zygomaticus major and .... *Psychophysiology*, 40(5), 776–785. https://doi.org/10.1111/1469-8986.00078
- 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. https://doi.org/10.1007/s10803-006-0218-7
- Legisa, J., Messinger, D. S., Kermol, E., & Marlier, L. (2013). Emotional Responses to Odors in Children with High- Functioning Autism: Autonomic Arousal, Facial Behavior and Self-Report. *Autism Speaks*, *43*(4), 869–879. https://doi.org/10.1007/s10803-012-1629-2.
- Levine, T. P., Sheinkopf, S. J., Pescosolido, M., Rodino, A., Elia, G., & Lester, B. (2012).
  Physiologic arousal to social stress in children with Autism Spectrum Disorders: A pilot study. *Research in Autism Spectrum Disorders*, 6(1), 177–183.
  https://doi.org/10.1016/j.rasd.2011.04.003
- Liljencrantz, J., Björnsdotter, M., Morrison, I., Bergstrand, S., Ceko, M., Seminowicz, D. A., ... Olausson, H. (2013). Altered C-tactile processing in human dynamic tactile

allodynia. Pain, 154(2), 227-234. https://doi.org/10.1016/j.pain.2012.10.024

- Lin, A., Adolphs, R., & Rangel, A. (2012). Social and monetary reward learning engage overlapping neural substrates. *Social Cognitive and Affective Neuroscience*, 7(3), 274– 281. https://doi.org/10.1093/scan/nsr006
- Linden, D. E. J. (2005). The p300: where in the brain is it produced and what does it tell us? *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, 11(6), 563–576. https://doi.org/10.1177/1073858405280524
- Lindgren, L., Westling, G., Brulin, C., Lehtipalo, S., Andersson, M., & Nyberg, L. (2012). Pleasant human touch is represented in pregenual anterior cingulate cortex. *NeuroImage*, 59(4), 3427–32. https://doi.org/10.1016/j.neuroimage.2011.11.013
- Liu, Q., Vrontou, S., Rice, F. L., Zylka, M. J., Dong, X., & Anderson, D. J. (2007). Molecular genetic visualization of a rare subset of unmyelinated sensory neurons that may detect gentle touch. *Nature Neuroscience*, 10(8), 946–948. https://doi.org/10.1038/nn1937
- Lloyd-Fox, S., Blasi, A., Elwell, C. E., Charman, T., Murphy, D., & Johnson, M. H. (2013).
  Reduced neural sensitivity to social stimuli in infants at risk for autism. *Proceedings. Biological Sciences / The Royal Society*, 280(1758), 20123026.
  https://doi.org/10.1098/rspb.2012.3026
- Löken, L. S., Evert, M., & Wessberg, J. (2011). Pleasantness of touch in human glabrous and hairy skin: order effects on affective ratings. *Brain Research*, 1417, 9–15. https://doi.org/10.1016/j.brainres.2011.08.011
- Löken, L. S., Wessberg, J., Morrison, I., McGlone, F., & Olausson, H. (2009). Coding of pleasant touch by unmyelinated afferents in humans. *Nature Neuroscience*, *12*(5), 547–8. https://doi.org/10.1038/nn.2312
- Loveland, K. A., Bachevalier, J., Pearson, D. A., & Lane, D. M. (2008). Fronto-limbic functioning in children and adolescents with and without autism. *Neuropsychologia*, 46(1), 49–62. https://doi.org/10.1016/j.neuropsychologia.2007.08.017
- Lucas, M. V, Anderson, L. C., Bolling, D. Z., Pelphrey, K. A., Kaiser, M. D., & Lucas, M. V. (2015). Dissociating the Neural Correlates of Experiencing and Imagining Affective Touch, (September), 2623–2630. https://doi.org/10.1093/cercor/bhu061

Luck, S. J. (2014). An introduction to the Event-Related Potential Technique (2nd ed.).

Cambridge, MA: The MIT Press.

- Lundqvist, L.-O. (2015). Hyper-responsiveness to touch mediates social dysfunction in adults with autism spectrum disorders. *Research in Autism Spectrum Disorders*, 9, 13–20. https://doi.org/10.1016/j.rasd.2014.09.012
- Lydon, S., Healy, O., Reed, P., Mulhern, T., Hughes, B. M., & Goodwin, M. S. (2014). A systematic review of physiological reactivity to stimuli in autism. *Developmental Neurorehabilitation*, 8423, 1–21. https://doi.org/10.3109/17518423.2014.971975
- Maihöfner, C., Handwerker, H. O., Neundörfer, B., & Birklein, F. (2003). Patterns of cortical reorganization in complex regional pain syndrome. *Neurology*, 61(12), 1707–1715. https://doi.org/10.1212/01.WNL.0000098939.02752.8E
- Mailhot, J. P., Vachon-Presseau, E., Jackson, P. L., & Rainville, P. (2012). Dispositional empathy modulates vicarious effects of dynamic pain expressions on spinal nociception, facial responses and acute pain. *European Journal of Neuroscience*, 35(2), 271–278. https://doi.org/10.1111/j.1460-9568.2011.07953.x
- Marco, E. J., Hinkley, L. B. N., Hill, S. S., & Nagarajan, S. (2011). Sensory processing in autism: A review of neuropsychologic findings. *Pediatric Research*, 69(5), 48–54.
- Marco, E. J., Khatibi, K., Hill, S. S., Siegel, B., Arroyo, M. S., Dowling, A. F., ... Nagarajan,
  S. S. (2012). Children with Autism show reduced somatosensory response. *Changes*, 29(6), 997–1003. https://doi.org/10.1016/j.biotechadv.2011.08.021.Secreted
- Marshall, P. J., & Meltzoff, A. N. (2015). Body maps in the infant brain. *Trends in Cognitive Sciences*, *19*(9), 499–505. https://doi.org/10.1016/j.tics.2015.06.012
- Mathersul, D., McDonald, S., & Rushby, J. A. (2013). Automatic facial responses to affective stimuli in high-functioning adults with autism spectrum disorder. *Physiology and Behavior*, 109(1), 14–22. https://doi.org/10.1016/j.physbeh.2012.10.008
- Mayer, J. L. (2017). The Relationship Between Autistic Traits and Atypical Sensory Functioning in Neurotypical and ASD Adults: A Spectrum Approach. *Journal of Autism* and Developmental Disorders, 47(2), 316–327. https://doi.org/10.1007/s10803-016-2948-5
- Mazefsky, C. A., Herrington, J., Siegel, M., Scarpa, A., Maddox, B. B., Scahill, L., & White,S. W. (2013). The Role of Emotion Regulation in Autism Spectrum Disorder.

*J.Am.Acad.Child Adolesc.Psychiatry*, *52*(1527–5418 (Electronic)), 679–688. https://doi.org/10.1016/j.jaac.2013.05.006.The

- Mazza, M., Pino, M. C., Mariano, M., Tempesta, D., Ferrara, M., De Berardis, D., ... Valenti, M. (2014). Affective and cognitive empathy in adolescents with autism spectrum disorder. *Frontiers in Human Neuroscience*, 8(October), 791. https://doi.org/10.3389/fnhum.2014.00791
- McCabe, C., Rolls, E. T., Bilderbeck, A., & McGlone, F. (2008). Cognitive influences on the affective representation of touch and the sight of touch in the human brain. *Social Cognitive and Affective Neuroscience*, 3(2), 97–108. https://doi.org/10.1093/scan/nsn005
- McCain, G. C., Ludington-Hoe, S. M., Swinth, J. Y., & Hadeed, A. J. (2007). Heart rate variability responses of a preterm infant to kangaroo care. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*, 34(6), 689–94. https://doi.org/10.1177/0884217505281857
- McGlone, F., Olausson, H., Boyle, J., Jones-Gotman, M., Dancer, C., Guest, S., & Essick, G. (2012). Touching and feeling: differences in pleasant touch processing between glabrous and hairy skin in humans. *The European Journal of Neuroscience*, 35(11), 1782–8. https://doi.org/10.1111/j.1460-9568.2012.08092.x
- McGlone, F., Wessberg, J., & Olausson, H. (2014). Discriminative and affective touch: sensing and feeling. *Neuron*, 82(4), 737–55. https://doi.org/10.1016/j.neuron.2014.05.001
- 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. https://doi.org/10.1111/j.1467-7687.2006.00492.x
- McMahon, S. B., & Koltzenburg, M. (1992). Itching for an explanation. *Trends in Neurosciences*, 15(12), 497–501. https://doi.org/10.1016/0166-2236(92)90102-E
- Miguel, H. O., Lisboa, I. C., Gonçalves, Ó. F., & Sampaio, A. (2017). Brain mechanisms for processing discriminative and affective touch in 7-month-old infants. *Developmental Cognitive Neuroscience*, (October), 0–1. https://doi.org/10.1016/j.dcn.2017.10.008

- Miguel, H. O., Sampaio, A., Martínez, R., Gómez, L., Cristina, G., López, G., ... Fernández, M. (2017). Touch Processing and Social Behavior in ASD. *Journal of Autism and Developmental Disorders*, 0(0), 0. https://doi.org/10.1007/s10803-017-3163-8
- Minde, J., Toolanen, G., Andersson, T., Nennesmo, I., Remahl, I. N., Svensson, O., & Solders, G. (2004). Familial insensitivity to pain (HSAN V) and a mutation in the NGFB gene. A neurophysiological and pathological study. *Muscle and Nerve*, 30(6), 752–760. https://doi.org/10.1002/mus.20172
- Minio-Paluello, I., Baron-Cohen, S., Avenanti, A., Walsh, V., & Aglioti, S. M. (2009).
  Absence of Embodied Empathy During Pain Observation in Asperger Syndrome. *Biological Psychiatry*, 65(1), 55–62. https://doi.org/10.1016/j.biopsych.2008.08.006
- Miyazaki, M., Fujii, E., Saijo, T., Mori, K., Hashimoto, T., Kagami, S., & Kuroda, Y. (2007). Short-latency somatosensory evoked potentials in infantile autism: Evidence of hyperactivity in the right primary somatosensory area. *Developmental Medicine and Child Neurology*, 49(1), 13–17. https://doi.org/10.1017/S0012162207000059.x
- Moore, D. J. (2014). Acute pain experience in individuals with autism spectrum disorders: A review. *Autism*, (March). https://doi.org/10.1177/1362361314527839
- Moraga-Amaro, R., & Stehberg, J. (2012). The Insular Cortex and the Amygdala: Shared Functions and Interactions. *The Amygdala - A Discrete Multitasking Manager*. https://doi.org/10.5772/2973
- Morelli, S. A., & Lieberman, M. D. (2013). The role of automaticity and attention in neural processes underlying empathy for happiness, sadness, and anxiety. *Frontiers in Human Neuroscience*, 7(May), 1–15. https://doi.org/10.3389/fnhum.2013.00160
- Morrison, I. (2016). Keep Calm and Cuddle on : Social Touch as a Stress Buffer. *Adaptive Human Behavior and Physiology*, (2), 344–362. https://doi.org/10.1007/s40750-016-0052-x
- Morrison, I., Björnsdotter, M., & Olausson, H. (2011). Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 31(26), 9554–62. https://doi.org/10.1523/JNEUROSCI.0397-11.2011

Morrison, I., Lloyd, D., di Pellegrino, G., & Roberts, N. (2004). Vicarious responses to pain

in anterior cingulate cortex: is empathy a multisensory issue? *Cognitive, Affective & Behavioral Neuroscience*, 4(2), 270–278. https://doi.org/10.3758/CABN.4.2.270

- Morrison, I., Löken, L. S., Minde, J., Wessberg, J., Perini, I., Nennesmo, I., & Olausson, H. (2011). Reduced C-afferent fibre density affects perceived pleasantness and empathy for touch. *Brain : A Journal of Neurology*, 134(Pt 4), 1116–26. https://doi.org/10.1093/brain/awr011
- Morrison, I., Löken, L. S., & Olausson, H. (2010). The skin as a social organ. *Experimental Brain Research*, 204(3), 305–314. https://doi.org/10.1007/s00221-009-2007-y
- Morrison, I., Tipper, S. P., Fenton-Adams, W. L., & Bach, P. (2013). "Feeling" others' painful actions: The sensorimotor integration of pain and action information. *Human Brain Mapping*, 34(8), 1982–1998. https://doi.org/10.1002/hbm.22040
- Mountcastle, V. B. (2005). The Sensory Hand: Neural mechanisms of somatic sensation. Cambridge, MA, US, University Press.
- 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 and Allied Disciplines*, 44(6), 793–809. https://doi.org/10.1111/1469-7610.00165
- Nelson, R. J., Sur, M., Felleman, D. J., & Kaas, J. H. (1980). Representations of the body surface in postcentral parietal cortex of *Macaca fascicularis*. J Comp Neurol, 192(4), 611–643. https://doi.org/10.1002/cne.901920402
- Nordin, M. (1990). Low-Threshold Mechanoreceptive and Nociceptive Units With Unmyelinated (C) Fibres in the Human Supraorbital Nerve. *Journal of Physiology*, 426, 229–240. https://doi.org/10.1113/jphysiol.1990.sp018135
- Nordin, M., & Hagbarth, K. -E. (1989). Mechanoreceptive units in the human infra-orbital nerve. Acta Physiologica Scandinavica, 135(2), 149–161. https://doi.org/10.1111/j.1748-1716.1989.tb08562.x
- O'Riordan, M., & Passetti, F. (2006). Discrimination in autism within different sensory modalities. *Journal of Autism and Developmental Disorders*, 36(5), 665–675. https://doi.org/10.1007/s10803-006-0106-1
- Oberman, L. M., Hubbard, E. M., McCleery, J. P., Altschuler, E. L., Ramachandran, V. S., &

Pineda, J. a. (2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. *Cognitive Brain Research*, *24*(2), 190–198. https://doi.org/10.1016/j.cogbrainres.2005.01.014

- 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. https://doi.org/10.1111/j.1467-7687.2008.00796.x
- Olausson, H., Cole, J., Rylander, K., Mcglone, F., Lamarre, Y., Wallin, B. G., ... Vallbo, Å. (2008). Functional role of unmyelinated tactile a V erents in human hairy skin : sympathetic response and perceptual localization, 135–140. https://doi.org/10.1007/s00221-007-1175-x
- Olausson, H., Cole, J., Rylander, K., McGlone, F., Lamarre, Y., Wallin, B. G., ... Vallbo, Å. (2008). Functional role of unmyelinated tactile afferents in human hairy skin:
  Sympathetic response and perceptual localization. *Experimental Brain Research*, 184(1), 135–140. https://doi.org/10.1007/s00221-007-1175-x
- Olausson, H., Cole, J., Rylander, K., McGlone, F., Lamarre, Y., Wallin, B. G., ... Vallbo, Å. (2008). Functional role of unmyelinated tactile afferents in human hairy skin:
  Sympathetic response and perceptual localization. *Experimental Brain Research*, 184(1), 135–140. https://doi.org/10.1007/s00221-007-1175-x
- Olausson, H., Lamarre, Y., Backlund, H., Morin, C., Wallin, B. G., Starck, G., ... Bushnell, M. C. (2002). Unmyelinated tactile afferents signal touch and project to insular cortex. *Nature Neuroscience*, 5(9), 900–4. https://doi.org/10.1038/nn896
- Olausson, H. W., Cole, J., Vallbo, Å., McGlone, F., Elam, M., Krämer, H. H., ... Bushnell, M. C. (2008). Unmyelinated tactile afferents have opposite effects on insular and somatosensory cortical processing. *Neuroscience Letters*, *436*(2), 128–132. https://doi.org/10.1016/j.neulet.2008.03.015
- Ornitz, E. M. (1973). Childhood autism. A review of the clinical and experimental literature. *California Medicine*, *118*(4), 21–47. PMID:4120820
- Parron, C., Da Fonseca, D., Santos, A., Moore, D. G., Monfardini, E., & Deruelle, C. (2008).Recognition of biological motion in children with autistic spectrum disorders. *Autism* :

*The International Journal of Research and Practice*, *12*(3), 261–274. https://doi.org/10.1177/1362361307089520

- Pawling, R., Cannon, P. R., McGlone, F. P., & Walker, S. C. (2017). C-tactile afferent stimulating touch carries a positive affective value. *PLoS ONE*, 12(3), 1–15. https://doi.org/10.1371/journal.pone.0173457
- Pawling, R., Trotter, P. D., McGlone, F. P., & Walker, S. C. (2017). A positive touch: Ctactile afferent targeted skin stimulation carries an appetitive motivational value. *Biological Psychology*, 129(March), 186–194. https://doi.org/10.1016/j.biopsycho.2017.08.057
- Peled-Avron, L., & Shamay-Tsoory, S. G. (2017). Don't Touch Me! Autistic Traits Modulate Early and Late ERP Components during Visual Perception of Social Touch, (March), 1141–1154. https://doi.org/10.1002/aur.1762
- Pelphrey, K. A, & Carter, E. J. (2008). Charting the typical and atypical development of the social brain. *Development and Psychopathology*, 20(4), 1081–1102. https://doi.org/10.1017/S0954579408000515
- Penfield, W., & Rasmussen, T. (1953). The cerebral cortex of man. American Journal of Physical Anthropology, 11(3), 441–444.
- Perini, I., Morrison, I., & Olausson, H. (2015). Seeking pleasant touch: neural correlates of behavioral preferences for skin stroking. *Frontiers in Behavioral Neuroscience*, 9(February), 1–9. https://doi.org/10.3389/fnbeh.2015.00008
- Pierce, J. W. (2007). PsychoPy Psychophyics software in Python. Journal of Neuroscience Methods, 162(1–2), 8–13.
- Pitcher, M., Le Pichon, C. E., & Chesler, A. (2016). Functional properties of C-Low Threshold Mechanoreceptors (C-LTMRs) in Nonhuman Mammals. In H. Olausson, J. Wessberg, I. Morrison, & F. McGlone (Eds.), *Affective Touch and the Neurophysiology* of CT Afferents (pp. 1–430). https://doi.org/10.1007/978-1-4939-6418-5
- Prescott, S. A., Ma, Q., & De Koninck, Y. (2014). Normal and abnormal coding of somatosensory stimuli causing pain. *Nature Publishing Group*, 17(2), 183–191. https://doi.org/10.1038/nn.3629

Robertson, A. E., & Simmons, D. R. (2013). The relationship between sensory sensitivity and

autistic traits in the general population. *Journal of Autism and Developmental Disorders*, 43(4), 775–784. https://doi.org/10.1007/s10803-012-1608-7

- Rolls, E. T., O'Doherty, J., Kringelbach, M. L., Francis, S., Bowtell, R., & McGlone, F. (2003). Representations of pleasant and painful touch in the human orbitofrontal and cingulate cortices. *Cerebral Cortex*, *13*(3), 308–317. https://doi.org/10.1093/cercor/13.3.308
- Rose, J. K., Sangha, S., Rai, S., Norman, K. R., & Rankin, C. H. (2005). Decreased Sensory Stimulation Reduces Behavioral Responding, Retards Development, and Alters Neuronal Connectivity in Caenorhabditis elegans. *Journal of Neuroscience*, 25(31), 7159–7168. https://doi.org/10.1523/JNEUROSCI.1833-05.2005
- 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*, (August), 1–14. https://doi.org/10.1080/17405629.2014.950221
- Rule, R. R., Shimamura, A. P., & Knight, R. T. (2002). Orbitofrontal cortex and dynamic filtering of emotional stimuli. *Cognitive, Affective, & Behavioral Neuroscience*, 2(3), 264–270. <u>https://doi.org/10.3758/CABN.2.3.264</u>
- Ruzich, E. Allison, C., Smith, P., Watson, P., Auyeung, B., Ring, H. & Baron-Cohen, S. (2015). Measuring autistic traits in the general population: a systematic review of the Autism-Spectrum Quotient (AQ) in a nonclinical population sample of 6,900 typical adult males and females. *Molecular Autism*, 6 (2). https://doi.org/10.1186/2040-2392-6-2
- Saby, J. N., Meltzoff, A. N., & Marshall, P. J. (2013). Infants 'Somatotopic Neural Responses to Seeing Human Actions : I've Got You under My Skin. *PLOSone*, 8(10), 1– 6. https://doi.org/10.1371/journal.pone.0077905
- Saby, J. N., Meltzoff, A. N., & Marshall, P. J. (2015). Neural body maps in human infants: Somatotopic responses to tactile stimulation in 7-month-olds. *NeuroImage*, 118, 74–78. https://doi.org/10.1016/j.neuroimage.2015.05.097
- Samson, A. C., Huber, O., & Gross, J. J. (2012). Emotion regulation in Asperger's syndrome and high-functioning autism. *Emotion*, *12*(4), 659–665.

https://doi.org/10.1037/a0027975

- Samson, A. C., Wells, W. M., Phillips, J. M., Hardan, A. Y., & Gross, J. J. (2014). Emotion regulation in autism spectrum disorder: evidence from parent interviews and children's daily diaries. *Journal of Child Psychology and Psychiatry*, 8, n/a-n/a. https://doi.org/10.1111/jcpp.12370
- Saxe, R., & Haushofer, J. (2008). For Love or Money: A Common Neural Currency for??Social and Monetary Reward. *Neuron*, 58(2), 164–165. https://doi.org/10.1016/j.neuron.2008.04.005
- Schaefer, M., Heinze, H. J., & Rotte, M. (2012). Embodied empathy for tactile events: Interindividual differences and vicarious somatosensory responses during touch observation. *NeuroImage*, 60(2), 952–957. https://doi.org/10.1016/j.neuroimage.2012.01.112
- Scheele, D., Kendrick, K. M., Khouri, C., Kretzer, E., Schläpfer, T. E., Stoffel-Wagner,
  B., ... Hurlemann, R. (2014). An oxytocin-induced facilitation of neural and emotional responses to social touch correlates inversely with autism traits. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*, 39(9), 2078–85. https://doi.org/10.1038/npp.2014.78
- Schirmer, A., Reece, C., Zhao, C., Ng, E., Wu, E., & Yen, S. C. (2014). Reach out to one and you reach out to many: Social touch affects third-party observers. *British Journal of Psychology*, 117570, 107–132. https://doi.org/10.1111/bjop.12068
- Sehlstedt, I., Ignell, H., Wasling, H. B., Ackerley, R., Olausson, H., & Croy, I. (2016). Gentle Touch Perception Across the Lifespan. *Psychology and Aging*, 31(2), 176–184. doi: 10.1037/pag0000074.
- Senju, A., & Johnson, M. H. (2009). Atypical eye contact in autism: Models, mechanisms and development. *Neuroscience and Biobehavioral Reviews*, 33(8), 1204–1214. https://doi.org/10.1016/j.neubiorev.2009.06.001
- Silva, C., Da Fonseca, D., Esteves, F., & Deruelle, C. (2015). Motivational approach and avoidance in autism spectrum disorder: A comparison between real photographs and cartoons. *Research in Autism Spectrum Disorders*, 17, 13–24. https://doi.org/10.1016/j.rasd.2015.05.004

- Simms, M. L., Kemper, T. L., Timbie, C. M., Bauman, M. L., & Blatt, G. J. (2009). The anterior cingulate cortex in autism: Heterogeneity of qualitative and quantitative cytoarchitectonic features suggests possible subgroups. *Acta Neuropathologica*, *118*(5), 673–684. https://doi.org/10.1007/s00401-009-0568-2
- Singer, T., Seymour, B., O'Doherty, J., Dolan, R. J., Kaube, H., Frith, C. D., ... 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. https://doi.org/10.1126/science.1093535
- Sivamani, R. K., Goodman, J., Gitis, N. V., & Maibach, H. I. (2003). Friction coefficient of skin in real-time. *Skin Research and Technology*, 9(3), 235–239. https://doi.org/10.1034/j.1600-0846.2003.20361.x
- Spapé, M. M., Harjunen, V., & Ravaja, N. (2017). Effects of touch on emotional face processing: A study of event-related potentials, facial EMG and cardiac activity. *Biological Psychology*, 124, 1–10. https://doi.org/10.1016/j.biopsycho.2017.01.002
- Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual* for the State-Trait Anxiety Inventory. Consulting Psychologists Press. Palo Alto.
- Sterman, A. B., Schaumburg, H. H., & Asbury, A. K. (1980). The acute sensory neuronopathy syndrome: A distinct clinical entity. *Annals of Neurology*, 7(4), 354–358. https://doi.org/10.1002/ana.410070413
- Sugiura, Y., Lee, C. L., & Perl, E. R. (1984). Central Projections of Identified , Unmyelinated
  (C) Afferent Fibres Innervating Mammalian Skin. *Science*, 234(4774), 358–361. PMID: 3764416
- Suvilehto, J. T., Glerean, E., Dunbar, R. I. M., Hari, R. & Nummenmaa, L. (2015). Topograpgy of social touching on emotional bonds between humans. *Proceedings of the National Academy of Sciences*, doi: 10.1073/pnas.1519231112
- Tan, J.-W., Walter, S., Scheck, A., Hrabal, D., Hoffmann, H., Kessler, H., & Traue, H. C. (2012). Repeatability of facial electromyography (EMG) activity over corrugator supercilii and zygomaticus major on differentiating various emotions. *Journal of Ambient Intelligence and Humanized Computing*, 3(1), 3–10. https://doi.org/10.1007/s12652-011-0084-9

- Tarbox, J., Wilke, A., Najdowski, A., Findel-Pyles, R., Balasanyan, S., Caveney, A., ... Tia, B. (2009). Comparing indirect descriptive, and experimental functional assessments of challenging behaviour in children with Autism. *Journal of Developmental and Physical Disabilities*, 21(6), 493–514. https://doi.org/10.1007/s10882-009-9154-8
- Tecchio, F., Padua, L., Aprile, I., & Rossini, P. M. (2002). Carpal tunnel syndrome modifies sensory hand cortical somatotopy: A MEG study. *Human Brain Mapping*, 17(1), 28–36. https://doi.org/10.1002/hbm.10049
- Tessier, R., Cristo, M., Velez, S., Giron, M., Ruiz-Palaez, J. G., Charpak, Y., & Charpak, N. (1998). Kangaroo Mother Care and the Bonding Hypothesis. *Pediatrics*, 102(2), e17– e17. https://doi.org/10.1542/peds.102.2.e17
- Thakkar, K. N., Polli, F. E., Joseph, R. M., Tuch, D. S., Hadjikhani, N., Barton, J. J. S., & Manoach, D. S. (2008). Response monitoring, repetitive behaviour and anterior cingulate abnormalities in autism spectrum disorders (ASD). *Brain*, 131(9), 2464–2478. https://doi.org/10.1093/brain/awn099
- Tommerdahl, M., Tannan, V., Cascio, C. J., Baranek, G. T., & Whitsel, B. L. (2007).
   Vibrotactile adaption fails to enhance spatial localization in adults with autism. *Brain Research*, *18*(1154), 116–123. https://doi.org/10.1109/TMI.2012.2196707.Separate
- Triscoli, C., Ackerley, R., & Sailer, U. (2014). Touch satiety: differential effects of stroking velocity on liking and wanting touch over repetitions. *PloS One*, 9(11), e113425. https://doi.org/10.1371/journal.pone.0113425
- Triscoli, C., Olausson, H., Sailer, U., Ignell, H., & Croy, I. (2013). CT-optimized skin stroking delivered by hand or robot is comparable. *Frontiers in Behavioral Neuroscience*, 7(December), 208. https://doi.org/10.3389/fnbeh.2013.00208
- Troller-Renfree, S., McDermott, J. M., Nelson, C. a., Zeanah, C. H., & Fox, N. a. (2014). The effects of early foster care intervention on attention biases in previously institutionalized children in Romania. *Developmental Science*, 5, n/a-n/a. https://doi.org/10.1111/desc.12261
- Uddin, L. Q. (2014). Salience processing and insular cortical function and dysfunction. *Nature Publishing Group*, (November). https://doi.org/10.1038/nrn3857

Vachon-Presseau, E., Roy, M., Martel, M. O., Albouy, G., Chen, J., Budell, L., ... Rainville,

P. (2012a). Neural processing of sensory and emotional-communicative information associated with the perception of vicarious pain. *NeuroImage*, *63*(1), 54–62. https://doi.org/10.1016/j.neuroimage.2012.06.030

- Vachon-Presseau, E., Roy, M., Martel, M. O., Albouy, G., Chen, J., Budell, L., ... Rainville,
  P. (2012b). Neural processing of sensory and emotional-communicative information associated with the perception of vicarious pain. *NeuroImage*, 63(1), 54–62. https://doi.org/10.1016/j.neuroimage.2012.06.030
- Vallbo, Å. B., Olausson, H. & Wessberg, J. (1999). Unmyelinated Afferents Constitute a Second System Coding Tactile Stimuli of the Human Hairy Skin Unmyelinated Afferents Constitute a Second System Coding Tactile Stimuli of the Human Hairy Skin. *Journal of Neurophysiology*, 2753–2763. DOI:10.1152/jn.1999.81.6.2753
- Vallbo, Å., Olausson, H., Wessberg, J., & Norrsell, U. (1993). A system of unmyelinated afferents for innocuous mechanoreception in the human skin. *Brain Research*, 628(1–2), 301–304. https://doi.org/10.1016/0006-8993(93)90968-S
- Vallbo, Å. B., & Hagbarth, K. E. (1968). Activity from skin mechanoreceptors recorded percutaneously in awake human subjects. *Experimental Neurology*, 21(3), 270–289. https://doi.org/10.1016/0014-4886(68)90041-1
- Vieira, A. I., Ramos, A. V., Cavalheiro, L. M., Almeida, P., Nogueira, D., Reis, E., ... Castro-Caldas, A. (2016). Reliability and Validity of the European Portuguese Version of the Social Touch Questionnaire. *Journal of Nonverbal Behavior*, 40(4), 363–377. https://doi.org/10.1007/s10919-016-0239-7
- Voos, A. C., Pelphrey, K. a, & Kaiser, M. D. (2013). Autistic traits are associated with diminished neural response to affective touch. *Social Cognitive and Affective Neuroscience*, 8(4), 378–86. https://doi.org/10.1093/scan/nss009
- Walker, S. C., Trotter, P. D., Woods, A., & McGlone, F. (2017). Vicarious ratings of social touch reflect the anatomical distribution & velocity tuning of C-tactile afferents: A hedonic homunculus? *Behavioural Brain Research*, 320, 91–96. https://doi.org/10.1016/j.bbr.2016.11.046
- Walsh, V., & Cowey, A. (2000). Transcranial Magnetic Stimulation and Cognitive Neuroscience. *Nature Reviews Neuroscience*, 1, 73–80. DOI:10.1038/35036239

- Wang, J., Barstein, J., Ethridge, L. E., Mosconi, M. W., Takarae, Y., & Sweeney, J. a. (2013).
  Resting state EEG abnormalities in autism spectrum disorders. *Journal of Neurodevelopmental Disorders*, 5(1), 1–14. https://doi.org/10.1186/1866-1955-5-24
- Weekes, D. P., Kagan, S. H., James, K., & Seboni, N. (1993). The phenomenon of hand holding as a coping strategy in adolescents experiencing treatment-related pain. J *Pediatr Oncol Nurs*, 10(1), 19–25. https://doi.org/10.1177/104345429301000105
- Wilhelm, F. H., Kochar, A. S., Roth, W. T., & Gross, J. J. (2001). Social anxiety and response to touch: incongruence between self-evaluative and physiological reactions. *Biological Psychology*, 58(3), 181–202. https://doi.org/10.1016/S0301-0511(01)00113-2
- 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. https://doi.org/10.1007/s10803-005-3300-7
- Zeeland, A. A. S., Dapretto, M., Ghahremani, D. G., Poldrack, R. A., & Bookheimer, S. Y. (2011). Reward Processing in Autism. *Autism*, 3(2), 53–67. https://doi.org/10.1002/aur.122.Reward
- Zwaigenbaum, L., Thurm, A., Stone, W., Baranek, G., Landa, R., Rogers, S., & Sigman, M. (2007). Studying the Emergence of Autism Spectrum Disorders in High-risk Infants : Methodological and Practical Issues, 466–480. https://doi.org/10.1007/s10803-006-0179-x