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Autistic traits modulate cortical responses to affective but not discriminative touch

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Abstract

The sense of touch is primarily considered a discriminative and exteroceptive sense, facilitating the detection, manipulation and exploration of objects, via an array of low threshold mechanoreceptors and fast conducting Aβ afferents. However, a class of unmyelinated, low threshold mechanoreceptors identified in the hairy skin of mammals have been proposed to constitute a second, anatomically distinct system coding the affective qualities of touch. Unlike Aβs, which increase their firing rate linearly with the velocity of a stimulus moving across their receptive field, the response of these C-tactile afferents (CTs) is described by an inverted 'U' curve fit, responding optimally to a skin temperature stimulus moving at between 1-10cm/s. Given the distinct velocity tuning of these fast and slow touch fibres, here we used ERPs to compare the time course of neural responses to 1st (fast) and 2nd (slow) touch systems. We identified a higher amplitude P300 in response to fast, Aβ targeted, versus slow CT-targeted, stroking touch. In contrast, we identified a previously described, C-fibre specific, ultra-late-potential (ULP) associated with CT-targeted input. Of special note as regards the function of CTs is that the amplitude of the ULP was negatively correlated with self-reported levels of autistic traits, which is consistent with the hypothesised affective and social significance of this response. Taken together these findings provide further support for distinct discriminative and affective touch systems and suggests the temporal resolution of EEG provides an as yet underutilised tool for exploring individual differences in response sensitivity to CT targeted touch.

1. Introduction

The sense of touch is typically considered discriminative and exteroceptive, supporting haptic exploration and manipulation of objects, and detection of external stimuli on the body surface. However, touch can also be emotional and interoceptive, such as the feeling of reassurance provided by a gentle touch on the back, or the pleasure of a loving caress. This distinction between the discriminative and affective functions of cutaneous senses has long been recognised for pain, where discrete classes of afferent nerves elicit different perceptual and emotional states, termed 1st and 2nd pain. First pain, conveyed by fast conducting myelinated A-delta afferents, experienced as a brief sharp or pricking sensation, facilitates reflexive withdrawal from potentially damaging stimuli. In contrast, second pain, conveyed by slowly conducting unmyelinated C-nociceptors is experienced as a longer lasting, dull, burning emotional percept, motivating protective behaviours that prevent further damage and facilitate healing (Bishop & Landau, 1958; Cross, 1994; McGlone & Reilly, 2010; Ploner, Gross, Timmermann, & Schnitzler, 2002)

Historically, the skin's sensory discriminative functions have been a focus of touch researchers (for review see McGlone & Reilly, 2010). Peripherally, large diameter, low threshold mechanosensitive A-beta afferent nerves (Aβs) conduct impulses at ~60m/s, sending spatially and temporally localised information to the central nervous system. They facilitate rapid detection, localisation, identification and discrimination of tactile stimuli. However, more recently a population of C-fibres has been identified and characterised in the hairy skin of humans that are neither nociceptive nor pruritic but respond preferentially to low force and velocity mechanical stimulation (Johansson, Trulsson, Olsson, & Westberg, 1988; Löken, Wessberg, Morrison, McGlone, & Olausson, 2009; Nordin, 1990). These C-tactile afferents (CTs), in common with other unmyelinated C-fibres, conduct at a velocity ~1 m/s. Thus, they

are too slow to provide useful discriminative tactile information and are hypothesised to form an anatomically distinct pathway for an affective "2nd touch" system of cutaneous nerves (Vallbo, Olausson, & Wessberg, 1999).

In addition to their differing conduction velocities, these two classes of low threshold mechanoreceptors can also be distinguished by their velocity tuning. While Aβs increase their firing rate linearly with the speed of a stimulus moving across their receptive field, the response of CTs is described by an inverted 'U', responding maximally to a skin temperature stimulus moving at between 1-10cm/s - with decreased firing for faster and slower, warmer and cooler stimuli. Furthermore, there is a positive correlation between the firing frequency of CTs and psychophysical ratings of touch pleasantness (Ackerley et al., 2014; Löken et al., 2009; Morrison, Löken, & Olausson, 2010; Olausson, Wessberg, Morrison, McGlone, & Vallbo, 2010). Thus, while Aβ responses are tuned to the physical properties of a stimulus, CTs are tuned to its affective significance (McGlone, Wessberg, & Olausson, 2014).

Consistent with an emotional rather than a discriminative function, studies in two patients who, due to a rare neuronopathy, lack all large myelinated afferent fibres from the neck down have demonstrated that activation of CTs induces a sympathetic skin response accompanied by a weak conscious percept, the spatial source of which was difficult to localise (Olausson et al., 2008). Furthermore, while Aβs project to primary somatosensory cortex, fMRI studies have determined that touch which preferentially targets CTs reliably activates brain regions involved in affective processing, including the dorsal posterior insula, anterior cingulate (ACC) and orbitofrontal (OFC) cortices (Björnsdotter, Löken, Olausson, Vallbo, & Wessberg, 2009; Mcglone et al., 2012; Morrison et al., 2011; Morrison, 2016; Olausson et al., 2002). The activity in these frontal regions is believed to reflect emotional processing related to CT

activation (Francis et al., 1999; McGlone et al., 2012; Rolls et al., 2003; Trotter et al., 2016).

Their peripheral response charcterisitcs, coupled with central projections to affective rather than primary sensory regions, has led to the hypothesis that the CT system has a direct, evolutionary conserved, role in signalling socially relevant touch (Olausson et al 2010; Morrison et al 2010). Indirect support for this putative social function comes from studies which explored the relationship between autistic traits and neural responses to CT targeted touch. The Autism Quotient (AQ) is a widely used self-report measure of autistic or social traits (Baron-Cohen, Wheelwright, Skinner, Martin & Clubley; Hoekstra et al, 2008) and scores on this scale are negatively associated with BOLD responses, in the OFC and pSTS, to CT-optimal touch (Voos, Pelphrey, & Kaiser, 2013). Psychophysically too, participant ratings of CT-targeted touch pleasantness have been reported to be negatively correlated with AQ scores (Croy, Geide, Paulus, Weidner, & Olausson, 2016).

While fMRI has been widely used to contrast neural responses to CT optimal with Aβ targeted touch, there is a paucity of research examining the electrophysiological cortical correlates of CT-optimal stimulation. To date one study has reported selective changes in theta and beta cortical oscillations in response to affective touch when compared to non-affective (non-CT-optimal) touch (von Mohr et al., 2018). On one hand, this is understandable because the slow conduction velocity of CTs does not lend itself to the high temporal acuity electroencephalography (EEG) typically focuses on. However, since several previous studies have reported that late positive ERP potentials are modulated by both the affective valence of sensory stimuli and individual differences in autistic traits across various modalities (Olofsson, Nordin, Sequeira, & Polich, 2008; Schirmer & McGlone, 2019; Schupp et al., 2000), comparison of event-related potential (ERP) responses to CT versus Aβ targeted stimulation

would allow the time course of these two inputs to be separated and individual differences in affective responses to be considered.

The P300 is a well characterised ERP component evoked in response to stimulus novelty or salience. Most prominently recorded over parietal cortex , the P300 is widely used as a measure of the nature and timing of cognitive response to a stimulus and can be modulated by task demands as well as stimulus salience (Bradley, 2009; Gray, Ambady, Lowenthal, & Deldin, 2004; Johnson, 1986; Linden, 2005). Later in the ERP waveform, a component specific to input from unmyelinated afferents has been identified. This ultra-late potential (ULP), first identified as a specific response to laser evoked stimulation of C-nociceptive fibres is recorded over frontal brain regions (Bragard, Chen, & Plaghki, 1996; Bromm & Lorenz, 1998; Bromm, Neitzel, Tecklenburg, & Treede, 1983; Valeriani et al., 2002). A ULP evoked by CT targeted touch has also been reported (Ackerley, Eriksson, & Wessberg, 2013) in response to brush strokes delivered to the ventral surface of the forearm at a CT-optimal velocity (Ackerley, Eriksson, & Wessberg, 2013). The ULP peaked around 2700ms after initial skin contact and continued throughout the brushing stimulus. Furthermore, consistent with the affective significance of the input, activity at the maximally responsive frontal location, electrode Fz, was significantly greater than that recorded over somatosensory areas typically associated with discriminative tactile perception. Though the authors reported no ULP was found for non-CT optimal 30cm/s stroking, no direct comparison of ERP responses to Aβ and CT targeted stroking was made.

The aim of the present study was to compare ERPs evoked by Aβ targeted and CT targeted touch (i.e. 1st and 2nd touch, respectively). It was hypothesised that, consistent with the stronger conscious percept and higher amplitude sympathetic skin response previously reported

(Olausson et al., 2008, 2010; Pawling, Trotter, et al., 2017), a larger amplitude P300 will be measured in response to Aβ targeted (30cm/s) versus CT-targeted (3cm/s) touch. Secondly, consistent with the previous report of Ackerley et al (2013), CT optimal (3cm/s) stroking is hypothesised to evoke a ULP over frontal electrodes, while 30cm/s strokes, a stronger stimulus for Aβs, will not. Finally, we explored whether, in line with previous psychophysical and fMRI data (Croy et al., 2016; Voos et al., 2013), cortical responses to CT-targeted touch are correlated with self-reported levels of autistic traits.

2. Method

2.1 Participants:

Twenty-two healthy participants (Females=18, Mean age =23.7, SD=6.8), with no history of neurological or neurodevelopmental disorder, 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 provided written informed consent prior to beginning the study. The study was performed according to the Declaration of Helsinki on Biomedical Research Involving Human Subjects and was granted ethical approval by Liverpool John Moores University research ethics committee.

2.2 Materials & Measures:

2.2.1 Delivery of tactile stimuli

The layout of the laboratory where participants were seated during the experiment is shown in Figure 1a. 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, 10cm apart, were drawn on the dorsal surface of their right forearm. Intersection of a laser beam by the brush provided a time locking signal to the EEG. The laser deflection screen served both to minimise the distance the laser travelled, optimising timing accuracy, and occlude the participant's view of the stroked area.

A visual metronome presented on a computer screen behind the participant (Pawling et al, 2017), guided the researcher in delivering the brush strokes at each of three velocities: CT-

optimal (3cm/s), non-CT-optimal (30cm/s) and a midrange oddball (15cm/s). The metronome used 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 velocity required for each trial (Fig 1d). Specifically, for stimuli delivered at 3cm/s the box filled over 3000ms (10cm stroking area x 3cm/s), for stimuli delivered at 30cm/s the metronome box filled in 300ms (10cm stroking area x 30cm/s). On each trial, a single proximal-to-distal stroke was delivered 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.

Participants sat facing a laptop computer controlled by the mouse in their right hand, irrespective of dominant hand, as the task only required a left or right mouse click. This ran a separate E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) programme unconnected to the other computers in the experiment. The participants 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 to the first one. Thus, immediately after the 2nd to 5th trial of each block participants were asked, "Was that touch the same as the first". Blocks contained between 0 & 2 oddball strokes (Fig 1c). Accuracy of oddball detection was high, 92.8% (SD=8.96).

(Figure 1)

2.2.2 EEG

EEG data were collected using a 64-channel active-electrode BioSemi (BioSemi, Amsterdam) system and recorded using ActiView (BioSemi, Amsterdam). An online filter of

0.1Hz and a subsequent offline 0.1Hz-40Hz bandpass filter were applied to the data. A custom-made cable (Cortech Solutions, Wilmington, NC) was used to split signals and send trial triggers from the PC displaying the visual metronome and the laser over the participant's arm. Triggers from the metronome computer were coded for each velocity of the stroking, sending a signal for the start of the trial. Following the onset of the tactile stimulus the broken laser beam sent another trigger to the data acquisition computer, allowing the concurrent trial epochs to be locked precisely to the stimulus.

2.2.3 Questionnaires

Upon completing the EEG task, participants were asked to complete three questionnaires presented using custom scripts running in PsychoPy (Pierce, 2007) on the laptop in front of them. Participants completed the Autism Spectrum Quotient (AQ, Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001), Social Touch Questionnaire (STQ, Wilhelm, Kochar, Roth & Gross 2001) and the State/Trait Anxiety Index (STAI, Spielberger, Gorsuch, Lushene, Vagg & Jacobs, 1983). These questionnaires measure self-reported levels of autistic traits, touch preference and anxiety respectively.

The AQ is a 50-item scale that measures autistic traits within a typical population (Baron-Cohen et al., 2001; Bölte et al., 2011; Voos et al., 2013). Here participants rate how much they agree or disagree with a statement on a four-point Likert scale, ranging from strongly agree (1) to strongly disagree (4). Typical questions relate to the responder's experience of social situations for example "I prefer to do things with others rather than on my own". Answers are scored as one (strongly / slightly agree) or a zero (strongly / slightly disagree) with half the questions being negatively scored. The scale has a Cronbach's alpha of $\alpha = 0.88$ (Austin, 2005).

Data from the STQ & STAI are not reported here as this data was collected as part of a wider project measuring the association between affective state and traits on perceptions of social touch.

2.3 Procedure:

Participants were seated in a comfortable chair with their right arm resting on a foam cushion. This foam cushioning was adjusted so participants did not have to reach for the mouse with their right hand, reducing the effect of muscle activity on the EEG measurement, it also ensured that the participant's arm would remain in the same position with the dorsal surface accessible. The task consisted of 20 blocks of five trials. In each block participants received either CT-optimal (3cm/s) or Aβ targeted (30cm/s). To focus participant's attention on the sensation of the stroking, they were asked to complete and oddball task. Oddball strokes were delivered at 15cm/s and participants were informed that there could be between 0-2 oddballs within in each block of 5 strokes (*Figure 1b*). Across 20 blocks participants experienced 43 CT-optimal strokes, 43 Aβ targeted strokes and 14 oddball strokes, split evenly between CT-optimal and Aβ targeted blocks. The first trial in each block was always CT-optimal or Aβ targeted stroke, then on each subsequent trial participants were asked "was that stroke the same as the first?" on the computer in front of them (*Figure 1c*).

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" (*Figure 1c*). After each stimulus there was a period of five seconds where participants had to think about the feel of the touch and wait for the tone, which prompted them to indicate

whether the stroke just received was the same as the first in the block.

Participants were randomly assigned to receive the experimental blocks in one of 5 pseudorandomised orders, which ensured no two consecutive trial blocks were the same. The 5 running orders were created in Matlab (Matlab 2017a, The MathWorks Inc., Natick, MA). A bug in the programme for one of the randomisations resulted in additional triggers being sent 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, Right handed=15).

2.4 Data Treatment & Analysis

2.4.1 EEG Data Treatment

Offline, EEG data were down sampled to 256Hz (Ackerley et al., 2013). Data were then re-referenced to an average of all electrodes. Stimulus-locked epochs (500ms to 4000ms) were extracted from the continuous data. Data were baseline corrected to an average of the 500ms period prior to stimulus onset, these were averaged by stimulus type within participants. Excessively noisy trials were removed by visual inspection. 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 Aβ-targeted trials. Oddball trials were not analysed.

2.4.2 Discriminative cortical mechanisms

To measure early responses to the stimuli, data for all participants were extracted from central electrodes Pz, Cz and Fz with mean amplitudes being taken from a 250ms time bin

from 250-500ms, based on a standard optimal window for orienting responses to salient stimuli (Polich, 2007). For CT-optimal stroking, data were extracted both at the same point (250-500ms) and, using the calculations for CT conduction velocity x distance from the forearm to the cortex reported in Ackerley *et al* (2013) *(distance from forearm to cortex with ~1m/s conduction velocity = 700ms),* average amplitudes were also taken 700ms later, 950-1200ms post-stimulus onset for all participants. 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, Pearson's correlations probed the relationship between mean amplitude from these electrodes and AQ scores.

2.4.3 Ultra-Late Potential

Upon visual inspection of ERP waveforms (*Figure 5*) and topographic maps (*Figure 4*) of the ultra-late potentials, data from CT-optimal stroking, were extracted from electrodes F1, Fz and F2 then averaged together where the most prominent ultra-late ERPs were recorded. Data were extracted from the mean amplitude in the ULP between 3000 and 3400ms based on the ULP peak following stimulus offset at 3000ms (as with Ackerley et al 2013). These averaged ULP data were compared in an ANOVA to data from electrodes located over the somatosensory cortices, specifically the regions associated with touch perception on the forearm (electrodes CP3 and CP4 respectively) (Ackerley et al., 2013). Again, mean amplitudes for each participant were correlated with scores on the AQ.

Though no ULP was visible, as a control, data from Aβ targeted trials were extracted from the same 3000-34000ms time window, averaged over the same electrodes (F1, Fz and F2) and in an ANOVA mean peak amplitude compared to activity over CP3 and CP4.

Results

The mean AQ score was 17.3 (S.D. 7.25) which is consistent with average scores previously reported in large, typically developing samples (Baron-Cohen et al., 2001). In the present study, despite the small sample, there was a broad range of AQ scores (7-32), reflecting high and low levels of autistic traits.

3.1 Discriminative touch - ERP component

A repeated measures ANOVA with factors of Electrode (Cz, Fz, Pz) and Velocity (3cm/s,30cm/s) revealed a significant main effect of Electrode $F(2,32)=19.46$, $p<.001$, $\eta^2 =.55$, Velocity $F(1,16)=44.03$, $p<.001$, $\eta^2 =.73$ and an Electrode x Velocity interaction $F(2,32)=18.26$, $p<.001$, $\eta^2 =.53$, reflecting greater activity for Aβ targeted stimuli across posterior and central electrodes compared to CT-optimal stimuli ($p<.001$) (Figure 2 & 3). Pairwise comparisons showed, activity at Fz was significantly less than both Cz ($p<.001$) and Pz ($p<.001$). There was also no significant difference between activity at Cz and Pz ($p>.05$).

For completeness, the amplitude of response to CT-optimal touch was also compared 700ms later, as this represents the longer time for the CT signal to reach the brain (Ackerley et al 2013; Nordin, 1990). Again, a repeated measures ANOVA revealed a significant main effect of Electrode (Cz, Fz, Pz) $F(2,32)=9.95$, $p<.001$, $\eta^2 =.38$, and a significant main effect of Velocity Velocity $F(1,16)=30.43$, $p<.001$, $\eta^2 =.66$. Furthermore, there was a significant Electrode x Velocity interaction $F(2,32)=20.71$, $p<.001$, $\eta^2 =.56$, (*Figure* 2). Further analysis of the Electrode x Velocity interaction (*Figure* 2) revealed that the faster Aβ stimulation elicited a significantly larger mean amplitude than CT-optimal stimuli at all electrode

locations (all *p<.001*), suggesting that the faster (Aβ targeted) touch is more salient and elicits a greater orienting/attentional response than slow (CT-optimal) touch. Furthermore, this mean amplitude is significantly lower at the frontal electrode (Fz) than Cz (*p<.001*) or Pz (*p<.01*).

(Figure 2)

(Figure 3)

Finally, the association between AQ and mean amplitudes at electrodes Fz, Cz an Pz was investigated. Here, there were no significant correlations (all *p's>.20*).

3.2 Affective touch - Ultra-Late Potential

For CT optimal trials, an increase in activity at ULP electrodes appeared around 2600ms after stimulus onset and continued until around 200ms after stimulus offset (i.e. 3200ms, *Figure 5*). The mean peak amplitude data were therefore extracted from a 400ms time bin around this peak amplitude (3000-3400ms) from an average of electrodes F1, Fz and F2 and both contralateral and ipsilateral electrodes situated above the somatosensory cortex (CP3 and CP4 respectively as with Ackerley et al., 2013).

(Figure 4)

A repeated measures ANOVA was conducted to compare the mean amplitude recorded at an average of F1, Fz, F2 to CP3 and CP4. There was a significant main effect of Electrode $F(2,30)=10.71$ $p<.001$, $\eta^2 = .42$. Further analyses revealed that the ultra-late mean amplitude measured at the fontal electrodes was significantly larger (M=1.37, SD= 3.04) than activity at CP3 and CP4 (both ps<.05) (M=.97, SD=1.89; M=-1.20, SD=3.80) suggesting that this ULP is not related to activity from Aβ afferents projecting to the somatosensory cortex. Figure 5

depicts the temporal progression of the ULP starting around 200ms after stimulus onset and closely matching the duration of the CT-optimal stroking stimuli (*Figure 5*) in comparison to the two somatosensory control site electrodes. The same analysis of Aβ targeted trials confirmed that, as expected 2700ms after stimulus offset, here there was no main effect of electrode $F(2,32) = 2.53$, $p>.05$.

(Figure 5)

There was a significant negative correlation between ULP amplitude and AQ score (r=-66, n=17, $p<.01$) (*Figure 6*). Given the small sample size, this effect was further examined by splitting participants into two groups (Low (n=8) & High AQ (n=9)) based on the median AQ score (med=18, Low AQ: M=11.1, SD=2.2 & High AQ: 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 $t(15)= 2.68$, $p=.01$ (*Figure* 6).

(Figure 6)

3. Discussion

This study finds that ERPs can differentiate the time course of neuroelectric responses to 1st and 2nd touch. An ERP response at posterior mid-line electrodes, representative of a P300 peak associated with novel and salient input, was recorded in response to fast Aβ targeted brush strokes, but not for slower, CT targeted stimulation. This is consistent with the significantly higher amplitude sympathetic skin response previously reported to this stimulus (Pawling, Trotter et al, 2017). Importantly, these differences are apparent both 500ms post-stimulus onset, where the P300 peak amplitude was maximal for 30cm/s strokes, and at 1200ms post stimulus onset, when CT input from the forearm would be predicted to reach the cortex. This distinction is consistent with the weak, poorly localized conscious percept elicited by CT stimulation in neuronopathy patients lacking fast myelinated fibers (Olausson et al 2008). Furthermore, consistent with thei findings of Ackerley et al (2013), an ULP was identified in response to the slower CT-optimal stimulus. While in the present study the ULP was more lateral and delayed, it did closely follow the pattern of stimulus onset and offset. Specifically, the ULP here was measured at frontal electrodes, beginning shortly after stimulus onset and increasing until shortly after stimulus offset. This activity was significantly different to the activity recorded during the same period from electrodes positioned over S1 where Aβ afferents project, further indicating this response is C-fibre specific (Ackerley et al, 2013).

The difference in both the location and latency of the ULP reported here compared to Ackerley et al (2013) possibly reflects the different methods of stimulus delivery used. In the previous study, a Rotary Tactile Stimulator (RTS, “stroking robot”) delivered a large number of highly controlled brush strokes. In this study participants received manual brush strokes delivered by the experimenter, which while as consistent as possible, will have been inherently more variable in terms of timing, force and velocity. It is also possible the temporal and spatial

differences in ULP reflect the differing number of stimuli delivered between studies. However, with RTS delivered strokes, Ackerley et al (2013) reported 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. Overall, despite these small differences in the timing and location of the ULPs across studies, in both cases a response closely linked to the duration of the touch delivered was identified. This supports the use of manual stimulation, as is widely used in this field of research, in eliciting CT specific neural response. Importantly, no ULP was recorded following the faster 30cm/s strokes which are typically used as control stimuli (Jönsson et al., 2018; Pawling, Cannon et al, 2017; Triscoli, Akerley & Sailer, 2014).

In the present study, significantly lower mean ULP peak amplitude was observed in participants with high compared to those with low levels of autistic traits. Though the small sample size in the present study prevents strong conclusions being drawn about this effect, it is consistent with previous research reporting that both psychophysical ratings of pleasantness (Croy et al., 2016) and neural responses (Voos et al., 2013) to CT targeted touch are negatively correlated with levels of autistic traits. In the present 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 mean ULP amplitude. Therefore, in future, comparing individuals with a diagnosis of ASD to neurotypical controls would be of interest.

While psychophysically, robot and experimenter delivered stimulation methods have been reported to elicit similar pleasantness ratings (Triscoli et al., 2013), the perceived pleasantness

of and neural responses to CT-optimal stroking has been shown to be modulated by social context (Gazzola et al., 2012; Keizer, de Jong, Bartlema, & Dijkerman, 2017). For example, both the gender of the person delivering the touch (Gazzola et al., 2012) and the visual appearance of the touched surface (Keizer et al., 2017) can affect ratings of touch pleasantness as well as responses in affective brain regions such at the OFC. Given that the social context of a sensory experience is likely to affect those with low and high levels of autistic traits differently (Bölte, Poustka, & Constantino, 2008; Lassalle & Itier, 2014; Peled-Avron & Shamay-Tsoory, 2017), future research should investigate whether these groups show differential neural responses to robot versus experimenter delivered touch.

It is noteworthy that, slow, gentle stroking touch applied to the glabrous skin of the palm where CTs have not been found electrophysiologically, is often rated as pleasant as the same stimulus applied to hairy, CT innervated skin (Ackerley, Carlsson, et al., 2014; Pawling, Cannon, et al., 2017). Also, while touch delivered at CT optimal velocity reliably produces a reduction in heart-rate, this is also true when the touch is delivered either to the CT innervated forearm or the non-CT innervated palm. Taken together these findings suggest that CT input alone is not responsible for the affective value of touch. In contrast, neural and implicit affective response to the two types of stimulation are distinct (Gordon et al., 2013; McGlone et al., 2012; Olausson et al., 2008; Pawling et al 2017), thus it would be interesting to explore whether time sensitive measures such as the early and late positive potentials identified in the present study provide another means of differentiating these two inputs. Given, the palm is more densely innervated by Aβ afferents than the forearm, here an early P300 response would be predicted in response to CT optimal stroking touch, in the absence of a later C-fibre specific ULP. So future research should incorporate stroking to both the palm and forearm to measure differential cortical responses to these two inputs.

In conclusion, the results of the present study provide further support for the distinction between first and second touch. The stimulus delivered to elicit greater Aβ stimulation was associated with a higher amplitude P300, consistent with the higher perceptual salience of this stimulus. In contrast, an ULP was identified specifically for manually delivered CT-optimal stroking, which is consistent with previous research using highly controlled robot delivered touch. Consistent with the hypothesis that this ULP reflects the affective significance of CT input, differences in ULP amplitude were associated with differences in self-reported levels of autistic traits.

Author Contributions

CH, SW and FM conceived and designed the study. CH collected and analyzed the data. PM supported CH with laboratory set up and data processing. CH & SW drafted the manuscript. All authors reviewed and approved the final manuscript prior to submission.

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Data Sharing

Data can be provided upon request to the corresponding author, figures have been provided via Figshare: https://doi.org/10.6084/m9.figshare.9864065.v2

Conflicts of Interest

The Authors acknowledge no conflicts of interest with this research.

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