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RESEARCH ARTICLE

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Differences in temporal profile of brain responses by pleasantness of somatosensory stimulation in autistic individuals

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ABSTRACT

Purpose/Aim. Autistic individuals may show either *hyper-* or *hypo-* responsiveness to touch compared to non-autistic individuals. These behavioural responses depend on perceptual and evaluative mechanisms, which unfold sequentially and thus can be distinguished by exploring the timing of neural responses. In this study, we examined neural response timing to pleasant, unpleasant, and affectively neutral textures, to determine whether these perceptual versus evaluative subprocesses differ in autism and how each subprocess contributes to behavioural responses.

Materials and Methods. Our sample included $n = 13$ autistic and $n = 14$ non-autistic adults who completed functional magnetic resonance imaging. We analysed early, intermediate, and late phases of the tactile response, derived from studies of noxious tactile stimulation, to three different textures.

Results. The autistic group showed distinct differences from the non-autistic group to each of the textures, showing earlier, somatosensory differences in response to the pleasantly and unpleasantly rated textures and later, frontomotor differences in response to the neutrally rated texture. Further, reduced early phase response to the pleasant texture correlated with increased sensory seeking behaviour.

Conclusions. While preliminary, these results suggest distinct patterns between autistic and non-autistic individuals in how the neural response to touch unfolds and its correspondence with the perceived pleasantness of tactile experience. The findings suggest perceptual differences in response to affectively charged textures and evaluative differences in response to neutral, ambiguous textures. These temporal properties may inform future studies of tactile processing in autism, lending a better understanding of *how* individuals differ in their sensory experiences across contexts.

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Affective touch; autism

Introduction

Autism is a neurodevelopmental condition which is diagnosed when an individual experiences significant challenges with social communication, restricted and repetitive behaviours, and sensory processing (American Psychiatric Association 2013). Of the sensory atypicalities recognised as core features of autism, atypical response to touch is both highly reported (Rogers et al. 2003; Leekam et al. 2007; Tomchek and Dunn 2007; Klintwall et al. 2011) and related to clinically meaningful features like the degree of autism-related behaviours and anxiety (Green and Ben-Sasson 2010; Cascio et al. 2012; Foss-Feig et al. 2012). Given these relationships, understanding how autistic individuals perceive and experience touch is important as part of a broader goal to support their sensory comfort and socioemotional well-being (Cascio et al. 2019). Efforts towards this goal have been challenged by the intrinsic heterogeneity in autism whereby autistic individuals may show varying levels of *hyper-* and/or *hypo-* responsiveness to touch, depending on the individual, the context, and the stimulus (Baranek and Berkson 1994; Cascio et al. 2008; Foss-Feig et al. 2012; Green et al. 2013; Ide et al. 2019). Currently, there is no cohesive mechanistic framework for these different sensory phenotypes.

One factor that influences the variability in responses to different stimuli is the organisation of the somatosensory system, with distinct pathways for processing different types of touch. Peripheral pathways responsible for painful touch, discriminative touch, and affective touch are each unique and project to distinct, but overlapping, areas of cortex. Discriminative touch is conveyed through large, myelinated Aβ fibres and is primarily processed in primary somatosensory cortex (S1). On the other hand, pain and affective touch are conveyed through smaller, unmyelinated C- and CT-fibres, respectively, and are primarily processed in the posterior insular cortex (Craig 2002; Olausson et al. 2002;

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McGlone et al. 2007). While these comprise dissociable sensory systems, many tactile stimuli have both discriminative and affective components, in which case both systems contribute to the observed behavioural response.

Additionally, individuals may perceive the same sensory stimulus differently based on prior developmental experience and ongoing cortical modulation (Knill and Richards 1996; Huang and Rao 2011; Bastos et al. 2012). This idea of Bayesian perceptual differences is among prominent explanations for sensory differences in autism (Pellicano and Burr 2012; Palmer et al. 2017). Lastly, factors such as context and cognitive/emotional evaluation influence the relation between sensation, perception, and observed responsiveness (Brown and Dunn 2010; Failla et al. 2018). Thus, analytic approaches that disentangle perceptual from evaluative contributions to sensory responsiveness are needed to fully understand why autistic individuals may differ from each other and from their non-autistic peers in their response to touch.

Examining how the response to a stimulus unfolds over time provides one such way of disentangling mechanisms that occur in subsequence (e.g. perception preceding cognitive evaluation). For example, using the temporally sensitive approach of electroencephalography (EEG), Cascio et al. (2015) investigated the neural signature of both hyper- and hypo- responsiveness to tactile stimulation in school-aged children (ages 5-17 years) and found that the neural response associated with hyper-responsiveness was earlier than the neural response associated with hypo-responsiveness. This provided initial evidence that the mechanisms underlying these different phenotypes may occur at different points of the somatosensory processing stream. Similar specificity was found by Espenhahn et al. (2021) differentially relating EEG response phases to tactile hypo- versus hyper- responsiveness in younger children (ages 3-6 years), further supporting an ability to differentiate the neural signatures of these phenotypes by analysing different processing components.

Increased insight into these different mechanisms may be gained by identifying the relevant brain regions for distinct sensory phenotypes. For example, it remains difficult to examine the interplay between discriminative and affective tactile systems in response to stimuli that are processed by both systems using EEG alone. Functional magnetic resonance imaging (fMRI) provides insight into relevant brain regions and, while limited in temporal resolution, studies have developed methods to dissect temporal components of the overall blood oxygenation level-dependent response (BOLD) signal in response to noxious or painful tactile stimulation (Moulton et al. 2012; Failla et al. 2018). One such study used a data-driven decomposition of the BOLD signal in response to noxious stimulation and found that a triphasic model (with early, intermediate, and late phases, the last of which extended past the end of stimulation) provided the best fit (Moulton et al. 2012). Further, it was only the last phase of this response that correlated with individuals' subjective pain ratings. This suggests that the data-driven approach may indeed be able to identify meaningful subprocesses that contribute uniquely to the overall subjective experience of pain. Failla et al. (2018) used this triphasic model to investigate responses to noxious thermal stimulation that was rated as similarly painful by both autistic and non-autistic participants. They found that the earliest phase of neural responses to noxious stimulation is indistinguishable between autistic and non-autistic individuals. However, neural responses in autistic individuals are greatly suppressed during the intermediate and late phases as compared to non-autistic individuals. This phase-dependent group difference challenges previously held notions that autistic individuals showed reduced perception of pain and specifically, points towards later processes (e.g. cognitive and emotional evaluation of pain) as target sub-processes to study in autism.

Previously, our lab has investigated the neural response to non-painful textures of differing affective valences in autistic compared to non-autistic adults (Cascio et al. 2012). This prior study found that autistic adults show a mix of increases and decreases in BOLD response to unpleasantly rated textures and generally diminished responses to neutrally and pleasantly rated textures. In this study, BOLD responses were averaged across the full temporal window of tactile stimulation, so it is unclear which phases of the tactile response drove group differences. Additionally, it is unknown if the suppressed intermediate and late phase processing of noxious stimuli found in Failla et al. (2018) generalises to different types of affective tactile stimuli, since emerging research suggests a high degree of stimulus specificity in how individuals respond to noxious/affective tactile stimuli (Crucianelli et al. 2022). The present study revisits the previous analysis in Cascio et al. (2012) with greater temporal specificity to address whether phase-specific differences in BOLD response generalise across affective textures in autism.

To address this question, we compared phases of the BOLD signal in response to different tactile stimuli in autistic versus non-autistic adults. Specifically, we were interested in how the affective valence (pleasant, neutral, or unpleasant) of stimulation might influence the spatiotemporal dynamics. We hypothesised that the pattern of response to the unpleasantly rated texture may resemble an attenuated version of the response to pain, such that autistic individuals show intact early processing but diminished later processing. There is a more limited literature to inform predicted temporal responses to neutrally and pleasantly rated stimuli. However, given that the autism group showed especially diminished BOLD responses to these two textures in Cascio et al. (2012), we hypothesised that neural processing may diverge between autistic and non-autistic participants at earlier time points than for unpleasantly rated stimuli.

Materials and methods

Participants

This study was approved by the Institutional Review Board of the University of North Carolina and all participants gave informed consent to participate in the study. Data from these participants have been previously analysed in Cascio et al. (2012). Participants were 27 adults (13 autistic (AUT), 14

Table 1. Participant characteristics.

					Sensory Profile	
	Age (years)	FSIQ	# Male	ADOS Social	Low Registration	Sensory Sensitivity
AUT ($n = 13$)	28 (17 - 47)	103 (69 - 133)	12	9.7 (5 - 14)	36.6 (24 - 48)	35.0 (22 - 46)
NT ($n = 14$)	30 (20 - 51)	108 (81 - 128)	13		24.5 (16 - 39)	28.8 (17 - 48)

Participant characteristics are given as mean (range) for continuous variables and count for categorical variables. Abbreviations: AUT: autism; NT: non-autistic; FSIQ: Full-scale intellectual quotient as measured by the Wechsler Abbreviated Scales of Intelligence (WASI, Wechsler 1999); ADOS: Autism Diagnostic Observation Schedule (Lord et al. 1999); Sensory Profile: Adult Sensory Profile (Brown et al. 2001).

non-autistic (NT)). Participant characteristics are described in Table 1. Inclusion criteria for the study were full-scale intellectual quotient (IQ) $>$ 70 as measured by the Wechsler Abbreviated Scales of Intelligence (WASI, Wechsler 2003) and for the AUT group, a Module 4 Autism Diagnostic Observation Schedule (ADOS) score above the cut-off for autism (Lord et al. 1999), though final inclusion judgments for individuals near these score cut-offs were made by the study clinician. Participants were excluded from the study if they had any MRI contraindications (e.g. bodily metal or pacemakers) or a history of medical conditions associated with autism (e.g. Fragile X, tuberous sclerosis, and epilepsy). All included participants completed MRI scanning; $n = 1$ autistic participant was excluded from *post hoc* analyses of behavioural ratings (reported pleasantness and sensory responsiveness) due to incompletion of these measures (see below).

As reported in Cascio et al. (2012), groups did not significantly differ in age, IQ, or gender. As expected, sensory responsiveness as measured by the Adult Sensory Profile (Brown et al. 2001) did significantly differ between the groups, with the autism group self-reporting significantly greater patterns of both hypo-responsiveness ("Low Registration" domain score, $t = -4.25$, $p < 0.01$) and hyper-responsiveness ("Sensory Sensitivity" domain score, $t = -2.31$, $p = 0.03$) compared to the non-autistic group. Since sex differences in sensory processing are more likely to occur in autistic rather than non-autistic populations (Osório et al. 2021), we assessed whether the female participant in the autism group showed outlying patterns of BOLD response to texture stimulation compared to autistic males. This participant was not determined to be an outlier in any significant autism group texture by phase activations (see *Appendix 1*).

Neuroimaging data acquisition

Images were acquired on a Siemens (Erlangen, Germany) 3 Tesla Allegra head-only MRI scanner. High-resolution anatomical images were acquired with a T1-weighted MPRAGE sequence (160 axial slices, voxel size $= 1 \times 1 \times 1\,mm^3$, TR $=$ 1700 ms, FOV $= 192 \times 256\,mm^2$). Functional images were acquired using a T2*-weighted EPI sequence (50 axial slices, voxel size $= 3 \times 3 \times 3$ mm, TR $= 3$ s, FOV $= 64 \times 64\,mm^2$, interleaved acquisition).

Protocol

Two six-minute fMRI runs were acquired while participants were stimulated with three different textures: a soft cosmetic brush, a burlap fabric, and a plastic mesh material. These

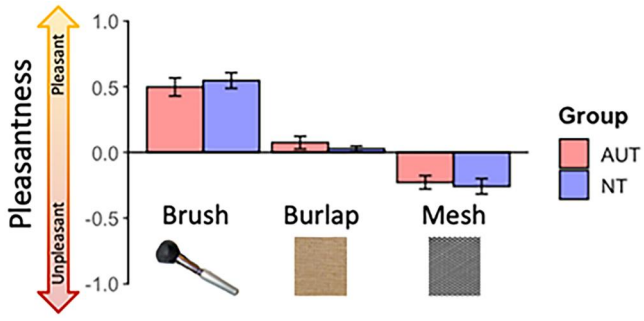

Figure 1. Reported pleasantness of each texture by group. Participants rated the perceived pleasantness of each texture on a -1 to 1 visual analog scale, with -1 being the most unpleasant and 1 being the most pleasant score. The bars indicate the mean and standard error of ratings by group, with autistic participants in red and non-autistic participants in blue.

textures were chosen according to their perceived pleasantness in a large normative sample of neurotypical adults (Essick et al. 2010). The brush is typically perceived as pleasant, the burlap is typically perceived as neutral, and the mesh is typically perceived as mildly unpleasant. Importantly, the autistic adults included in this study rated the pleasantness of these textures similarly to non-autistic adults (Figure 1), allowing us to examine group differences in brain response patterns within the targeted affective gradient (i.e. from unpleasant to pleasant).

Textures were presented in pseudorandom blocks of 30 s each, during which participants were instructed to lie still and pay attention to the texture. During these 30 s, the experimenter manually stroked each texture continuously along the dorsal surface of the participant's right forearm, with a moderate force and speed of approximately 5 cm/s. The location of stimulation was jittered by a few millimetres on each stroke to minimise receptor fatigue. Texture blocks were alternated with 30-second rest blocks, during which the participants were instructed to relax and lie still. Participants completed 2 experimental runs that each included two blocks per texture type.

fMRI preprocessing

Images were analysed using FMRI Expert Analysis Tool (FEAT) version 6.00, part of FMRIB's Software Library (FSL, www.fmrib.ox.ac.uk/fsl, version 5.0). Functional data were registered to the high-resolution structural image using a boundary-based registration algorithm (Greve and Fischl 2009) and then normalised to the Montreal Neurological Institute (MNI) 152-T1 $2\,mm^3$ template using FMRIB's linear image registration tool (FLIRT, linear; Jenkinson and Smith 2001; Jenkinson et al. 2002) and further refined with FMRIB's nonlinear image

Table 2. Motion parameters during functional scans.

Group	% Confounds	Translation X	Translation Y	Translation Z
AUT	2.5 (0-9.8)	0.33 (0.44)	0.58 (0.83)	1.11 (1.60)
NT	2.5 (0-9.0)	0.16 (0.12)	0.18 (0.17)	0.46 (0.34)

Motion parameters per diagnostic group are presented as median (range) for confounds and mean (standard deviation) for translation parameters. Variables include the percent of volumes modelled as confound regressors and millimetres of translation in X, Y, and Z directions. Abbreviations: AUT: autism; NT: non-autistic.

registration tool algorithms (FNIRT; Andersson et al. 2007). Preprocessing of functional images included brain extraction with FSL's brain extraction tool (Smith 2002), a 200 Hz high-pass filter, grand-mean intensity normalisation, and spatial smoothing with a Gaussian kernel of 5 mm full width at half maximum. Standard and extended motion parameters were extracted during preprocessing and included in the general linear model (GLM). Additionally, confound regression was used for volumes determined as outliers on both DVARS (D, temporal derivatives of time courses; VARS, variance of root mean squares of head motion across voxels) and frame-wise displacement (FD) metrics for head motion (Power et al. 2012). No participant had more than 10% of volumes as confound regressors (Table 2).

Task-based fMRI analysis

We analysed temporal phases in accordance with established protocols in pain processing studies (Moulton et al. 2012; Failla et al. 2018). Three different phases of the BOLD response were analysed as: 1. an early phase (1-15s), 2. an intermediate phase (16-30s) within the 30s texture stimulation period, and 3) a late phase immediately following texture stimulation (31-40s) to capture post-stimulus evaluation. See Figure 2 for a diagram of these three response phases. Each phase was convolved with a double-gamma hemodynamic response function as part of the general linear model (GLM), with temporal filtering added. In the first level of analyses, BOLD responses to each texture were each modelled as a single contrast: phase versus rest. Second-level analyses combined runs for each subject using a fixed-effect model in FSL (FLAME; Beckmann et al. 2003; Woolrich et al. 2004; Woolrich 2008).

Group-level statistics were calculated at the whole-brain level for the following contrasts: Texture Phase > Rest per diagnostic group (AUT, NT) and group contrasts (AUT > NT and NT > AUT) per texture phase. Given the small sample size and exploratory nature of these analyses, these maps were created using both a conservative and liberal approach. For primary analyses, we implemented a conservative approach using permutation testing *via* FSL's randomise with $n = 5000$ replicates, threshold-free cluster enhancement (TFCE), and family-wise error corrected p-value = 0.05 (Winkler et al. 2014). For exploratory analyses, we implemented a liberal approach using a mixed-effect FLAME 1 model in FSL with a cluster threshold of $z = 2.3$ and p-value = 0.05 (family-wise error corrected based on clusters defined by Gaussian random field theory; Worsley 2001). Clusters were assigned to specific regions based on the highest overlap with the Harvard-Oxford Cortical Atlas at peak and/or local maximum voxels.

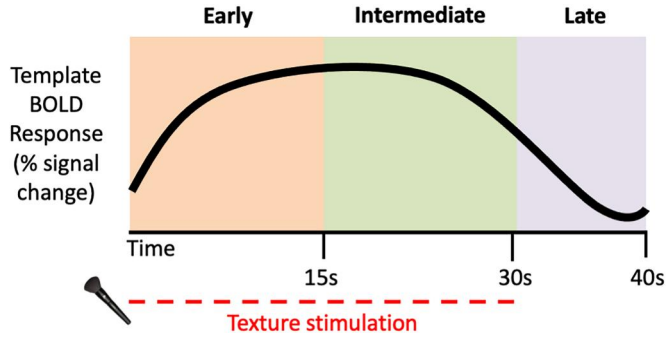

Figure 2. Diagram of template blood oxygenation level-dependent (BOLD) response by texture stimulation phase. Temporal phases correspond to the following time periods: early (orange, stimulation, 0-15s), intermediate (green, stimulation, 16-30s), and late (purple, post-stimulus offset, 31-40s).

Post hoc analyses

fMRI time course analysis

The BOLD response time course of key regions was analysed to provide greater temporal specificity in understanding group differences. These key regions included areas of 1) discriminative tactile responses: left postcentral gyrus, 2) affective tactile responses: bilateral parietal operculum, and 3) frontal/evaluative responses: middle frontal gyrus, all defined *via* the Harvard-Oxford Cortical Atlas in FSL. These clusters were analysed for each texture using Perl Event-related Timecourse Extraction (PEATE, Kaplan 2013, http://www.jonaskaplan.com/peate/index.php, version 3.01) to construct the average time course of response for each diagnostic group. These responses were constructed for the 30 s texture window plus the following 30 s rest block, for a total of 60 s. Percent signal change was analysed in comparison to a 2s window before stimulus onset. Spline interpolation was used, with a final resolution of one second. Bootstrapping with $n = 1000$ repetitions was used to construct 90% confidence bands for the average time series. Specific time points of BOLD signal divergence between groups were defined as when the 90% constructed confidence interval for group difference in mean did not include 0 (indicating significance at the $p < 0.10$ level, though there were no adjustments for multiple comparisons among time points).

Behavioural rating correlations

Correlations were analysed between BOLD responses and i) average pleasantness ratings per texture and ii) Sensory Profile domain scores (Brown et al. 2001). For these analyses, we included all four domain scores, reflecting hypo- ("Low Registration") and hyper- responsiveness ("Sensory Sensitivity") and conceptually related approach ("Sensory Seeking") and avoidant ("Sensory Avoidance") behaviours. For these correlations, we chose narrower anatomical ROIs to better distinguish contributions from primary points of the affective versus discriminatory tactile processing paths. Since the posterior insular cortex is a primary sensory area for this type of stimulation, which has been shown in prior work (Cascio et al. 2012), this region was the focus of behavioural rating correlations. To

reflect the different somatosensory processing streams and their temporal relationship with affective tactile processing, we considered additional regions by phase for the specific texture ratings: S1 for the early phase and S2 for both the early and intermediate phases. The posterior insula ROI was defined following Farb et al. (2013) cytoarchitectonically defined subdivisions, mapping onto the posterior long gyrus of the insula. Primary somatosensory cortex (SI, 1 only due to emerging specificity of this area for texture discrimination, Randolph and Semmes 1974; Geyer et al. 2000) and secondary somatosensory cortex (S2) were defined by the Juelich atlas (Eickhoff et al. 2006; 2006). Given expected non-linearities between BOLD response and behavioural report, we computed Spearman correlations for each of these associations.

Results

Unpleasantly rated texture (plastic mesh)

The conservative (permutation test) results aligned with the liberal (threshold) approach findings for the early phase such that both groups showed significant BOLD responses in affective sensory areas (including the insular cortex and parietal operculum, Figure 3a-b, peak coordinates in Table 3). During the intermediate phase, the NT group showed significant responses in a parietal operculum/supramarginal gyrus region when applying the conservative approach (Figure 3a). When applying the liberal approach, the spatial extent of this region was extended in the NT group and the AUT group showed significant BOLD responses in a similar opercular region, bilaterally (Figure 3b, peak coordinates in Table 3). During the late phase, both groups showed areas of significant responses when applying the conservative test approach. These late-phase activations were found in frontal regions for the AUT group and opercular/insular regions for the NT group. However, the liberal approach did not identify any significant responses for the late phase. No significant group differences in response were identified in any phase (early, intermediate, or late), using either approach.

When comparing the BOLD response time course in the three chosen regions: left postcentral gyrus, parietal operculum, and middle frontal gyrus (Figure 3c), the AUT group showed a greater BOLD response than the NT group during the first few seconds of texture stimulation across regions: 0-2s for parietal operculum and 1-4s for left postcentral gyrus and middle frontal gyrus. Qualitatively, the AUT group showed a bimodal pattern of response, including significantly greater post-stimulus responses than the NT group after texture offset (49-50s) for the parietal operculum region. In contrast, the NT group showed a graded, ramping pattern particularly in the two sensory areas (postcentral gyrus and parietal operculum).

Neutrally rated texture (burlap fabric)

The conservative (permutation test) approach was especially limited when analysing the neutrally rated texture, such that for both groups, no significant clusters were identified across any phase (Figure 4a). Thus, results are presented solely from the liberal (threshold) approach. During the early phase, the NT group showed significant BOLD responses in sensory and frontal areas (Figure 4b, peak coordinates in Table 3). The AUT group showed no significant BOLD responses in the early phase. Group responses significantly differed in a paracingulate cortex cluster, with greater responses in the NT group than the AUT group (Figure 4b, peak coordinates in Table 3). During the intermediate phase, the NT group showed significant BOLD responses in sensory and frontal areas, including S1, parietal operculum, and inferior frontal gyrus (IFG). The AUT group did not show significant BOLD responses in the intermediate phase. Additionally, there were no significant group comparison differences in the intermediate phase. During the late phase, both groups showed significant frontal region BOLD responses, but in different areas (frontal pole in NT, paracingulate in AUT, peak coordinates in Table 3). The late-phase AUT group response pattern is spatially proximal to the cluster of increased NT early-phase processing.

Like the unpleasantly rated mesh texture, the pattern of postcentral gyrus, parietal operculum, and middle frontal gyrus responses showed common trends across all three regions. In the NT group, the temporal pattern mirrors the unpleasantly rated texture (i.e. a graded ramping pattern). The three regions' time course compared between the NT and AUT groups shows a strong divergence in pattern which was significant for most time points between 6-35 s (Figure 4c). The AUT group's response was lower than the NT group during this period, consistent with the whole brain analyses. This divergence was sustained for the greatest duration in the middle frontal gyrus (6-30s) and parietal operculum (10-12, 14, 17-20, 22-24, 29-35s) and emerged later in the postcentral gyrus (17-26, 28-30, 34s).

Pleasantly rated texture (soft cosmetic brush)

The conservative (permutation test) approach only identified significant responses during the intermediate (NT, NT > AUT) and late phases (AUT); thus, the early phase responses are only reported from the liberal (threshold) approach. However, the response patterns identified were highly consistent between the early and intermediate phases. During these two phases, the NT group showed significant BOLD responses in similar sensory and frontal areas as to the other two textures, including the primary somatosensory cortex and parietal operculum (Figure 5a-b, peak coordinates in Table 3). The AUT group showed no clusters of statistically significant BOLD responses during either phase. During the intermediate phase, the NT group showed a significantly greater BOLD response in the primary somatosensory cortex (S1) than the AUT group when using the conservative approach (Figure 5a, peak coordinates in Table 3). Using the liberal approach, this S1 difference was significant across both the early and intermediate phases. During the late phase, the AUT group showed a significant middle temporal gyrus (MTG) response (Figure 5a).

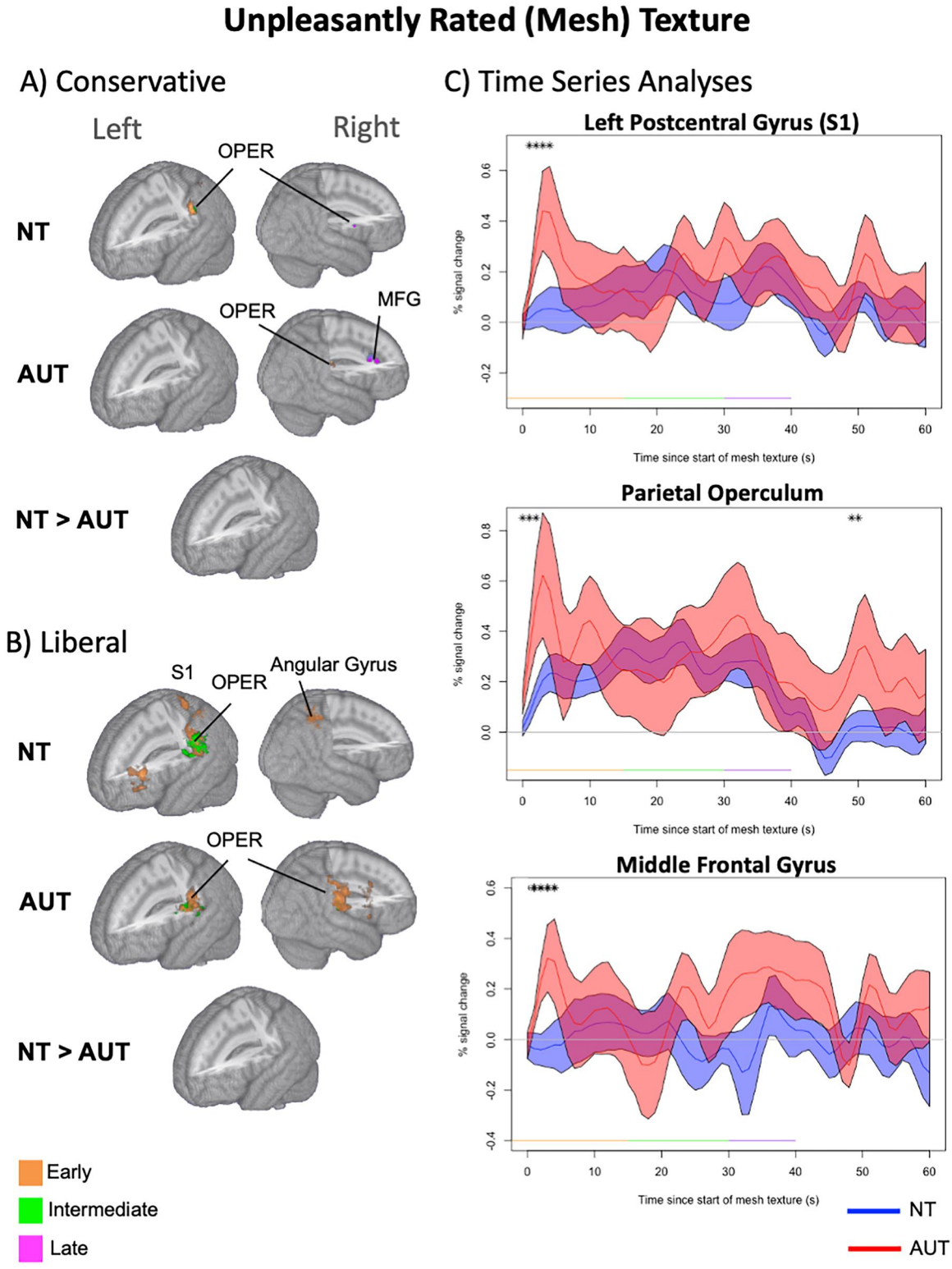

Figure 3. Unpleasantly rated (mesh) texture responses by group and phase. (A) Significant clusters by group using conservative permutation testing approach (permutation testing, threshold-free cluster enhancement (TFCE), and family-wise error corrected p-value = 0.05). (B) Significant clusters by group using the liberal threshold approach (mixed-effect FLAME 1 with a cluster threshold of $z = 2.3$ and p-value = 0.05, family-wise error corrected based on clusters defined by Gaussian random field theory). there were no significant regions of group differences in response to this texture, using either approach. (C) Time course of 1) left postcentral gyrus (S1), 2) parietal operculum, and 3) middle frontal gyrus response by group. Coloured lines indicate early (orange) and intermediate (green) phases of 30s period of texture stimulation and late (purple) post-texture responses. Average AUT response plotted in red; average NT response plotted in blue, including 90% confidence bands per group. The AUT group shows an increased early response (between 0-2s in parietal operculum and 1-4s in S1 and middle frontal gyrus, indicated by asterisks) in all three regions compared to the non-autistic group. Abbreviations: NT: non-autistic, AUT: autism, S1: primary somatosensory cortex, OPER: parietal operculum, MFG: middle frontal gyrus.

Table 3. Summary of significant BOLD responses, including brain region and peak coordinates, per texture phase.

Task activation	Group contrast	Brain region	R/L	Coordinates			Cluster size	Max Z
Mesh early > rest				X	Y	Z		
Z = 2.3, p<.05	AUT	SMG	R	66	−26	34	1597	4.09
		Insular cortex	L	−38	−18	14	1147	4.4
		S1	L	−22	−40	48	337	3.54
	NT	SMG	L	−50	−30	38	1951	4.17
		PO	L	−46	40	20	497	4.16
		Angular gyrus	R	48	−52	46	492	3.29
Permuted	AUT	SMG	R	54	−26	34	85	4.95
		Central opercular cortex	R	50	−2	6	25	4.25
	NT	SMG	L	−62	−26	36	250	5.21
		Angular gyrus	L	−42	−58	54	235	4.58
		PO	L	−60	−34	20	42	3.76
		SMG	L	−34	−44	34	4	3.86
Mesh intermediate > rest								
Z = 2.3, p<.05	AUT	Central opercular cortex	L	−50	−22	14	597	4.28
		Parietal operculum cortex	R	44	−30	28	344	3.95
	NT	SMG/PO	L	−64	−30	34	707	3.58
Permuted	NT	SMG	L	−64	−28	38	49	5.23
Mesh late > rest								
Z = 2.3, p<.05	n.s.							
Permuted	AUT	Middle frontal gyrus	R	32	32	24	241	7.27
		Superior frontal gyrus	R	22	24	44	9	4.25
		Frontal pole	R	36	44	22	5	3.98
	NT	Central opercular cortex	R	54	0	14	156	5.06
		Temporal pole	R	50	14	−4	51	4.75
		Insular cortex	R	40	16	0	1	3.73
Burlap early > rest								
Z = 2.3, p<.05	NT	Frontal pole	R	50	50	4	840	3.8
		Central opercular cortex	L	−52	−18	14	478	3.75
		Superior frontal gyrus	R	4	22	50	335	3.41
	NT > AUT	Paracingulate gyrus	L	−6	28	40	346	3.53
Permuted	n.s.							
Burlap intermediate > rest								
Z = 2.3, p<.05	NT	SMG/PO	L	−62	−38	34	920	3.77
		SMG/PO	R	54	−32	40	827	3.69
		Superior parietal lobule	L	−36	−38	74	456	3.62
		Central opercular cortex	R	54	8	0	382	3.95
Permuted	n.s.							
Burlap late > rest								
Z = 2.3, p<.05	AUT	Supplementary Motor Cortex	L	−6	−6	60	476	3.52
	NT	Frontal pole	R	50	48	6	485	3.74
Permuted	n.s.							
Brush early > rest								
Z = 2.3, p<.05	NT	SMG/S1	L	−50	−32	32	568	3.33
		Middle Frontal Gyrus	L	−46	32	20	486	3.44
	NT > AUT	SMG/Superior Parietal Lobule	R	48	−40	58	825	3.56
		S1	L	−50	−28	54	812	3.4
Permuted	n.s.							
Brush intermediate > rest								
Z = 2.3, p<.05	NT	S1	L	−46	−32	56	452	3.58
		PO	L	−62	−28	18	400	3.17
	NT > AUT	S1	L	−46	−34	46	1434	3.77
		Lateral occipital cortex	R	32	−60	56	922	3.78
Permuted	NT	S1	L	−42	−36	56	24	5.1
	NT > AUT	S1	L	−46	−34	46	113	5.64
		Occipital pole	R	30	−93	−8	18	4.89
Brush late > rest								
Z = 2.3, p<.05	n.s.							
Permuted	AUT	Middle temporal gyrus	R	44	−54	8	6	7.05

Significant regions of brain response are described per texture and phase. Group contrast lists the relevant contrast out of AUT (Texture phase > rest), NT (Texture phase > rest), AUT > NT, NT > AUT, which were each tested for all textures/phases. Clusters were assigned to brain regions based on the highest regional association from the Harvard-Oxford cortical atlas at peak voxel/local maxima. Coordinates are reported for the peak voxel, in MNI space. Cluster size is listed as the number of voxels per cluster. Z max is listed as the z-score at the peak voxel. Abbreviations: R/L: right or left hemisphere, MNI: Montreal Neurological Institute, NT: non-autistic, AUT: autistic, S1: primary somatosensory cortex, SMG: supramarginal gyrus, PO: parietal operculum.

The temporal response pattern in the NT group for all three regions was similar to the previous two textures, showing a graded ramping response (Figure 5c). In the S1 region, the AUT group showed a slightly decreased response compared to the NT group, which was significant at 17 s. The responses within the other two regions (middle frontal gyrus and parietal operculum) did not significantly diverge between the two groups.

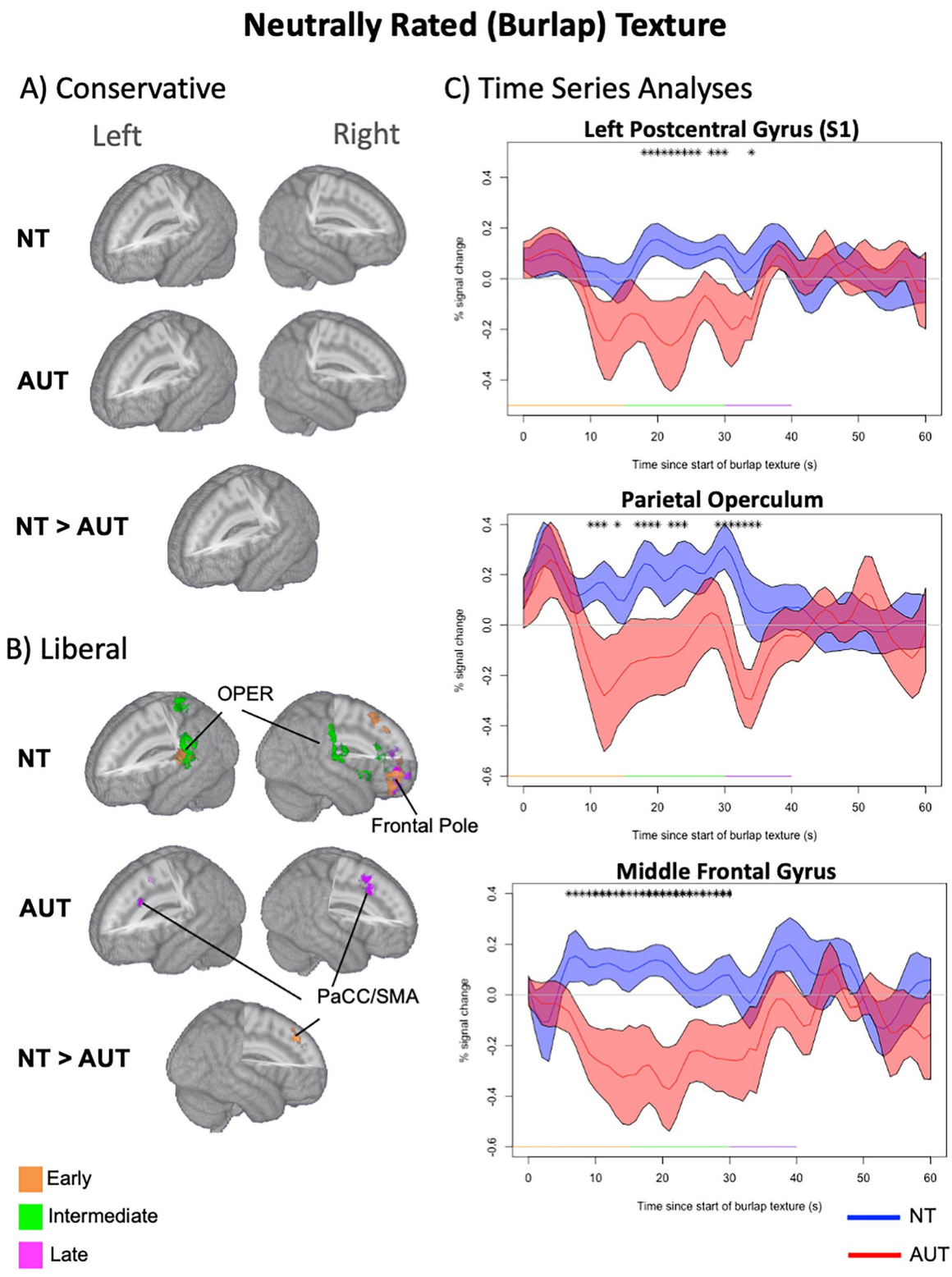

Figure 4. Neutrally rated (burlap) texture responses by group and phase. (A) No significant clusters were identified for either group using the conservative approach (permutation testing, threshold-free cluster enhancement (TFCE), and family-wise error corrected p-value = 0.05), for any time phase. (B) Significant clusters by group and phase using the liberal approach (mixed-effect FLAME 1 with a cluster threshold of $z = 2.3$ and p-value = 0.05, family-wise error corrected based on clusters defined by Gaussian random field theory), including one region (paracingulate) of decreased early response in the AUT group compared to the NT group. (C) Time course of 1) left postcentral gyrus (S1), 2) parietal operculum, and 3) middle frontal gyrus response by group. Average autistic response plotted in red; average non-autistic response plotted in blue, including 90% confidence bands per group. Coloured lines indicate early (orange) and intermediate (green) phases of 30s period of texture stimulation and late (purple) post-texture responses. Both groups show comparable early responses, but the autistic group shows decreased intermediate responses than the non-autistic group for all regions (middle frontal gyrus: 6-30s, parietal operculum: 10-12, 14, 17-20, 22-24, 29-35s, left postcentral gyrus: 17-26, 28-30, 34s, indicated by asterisks).

Abbreviations: NT: non-autistic, AUT: autism, S1: primary somatosensory cortex, OPER: central/parietal operculum, PaCC: paracingulate cortex, SMA: supplemental motor area.

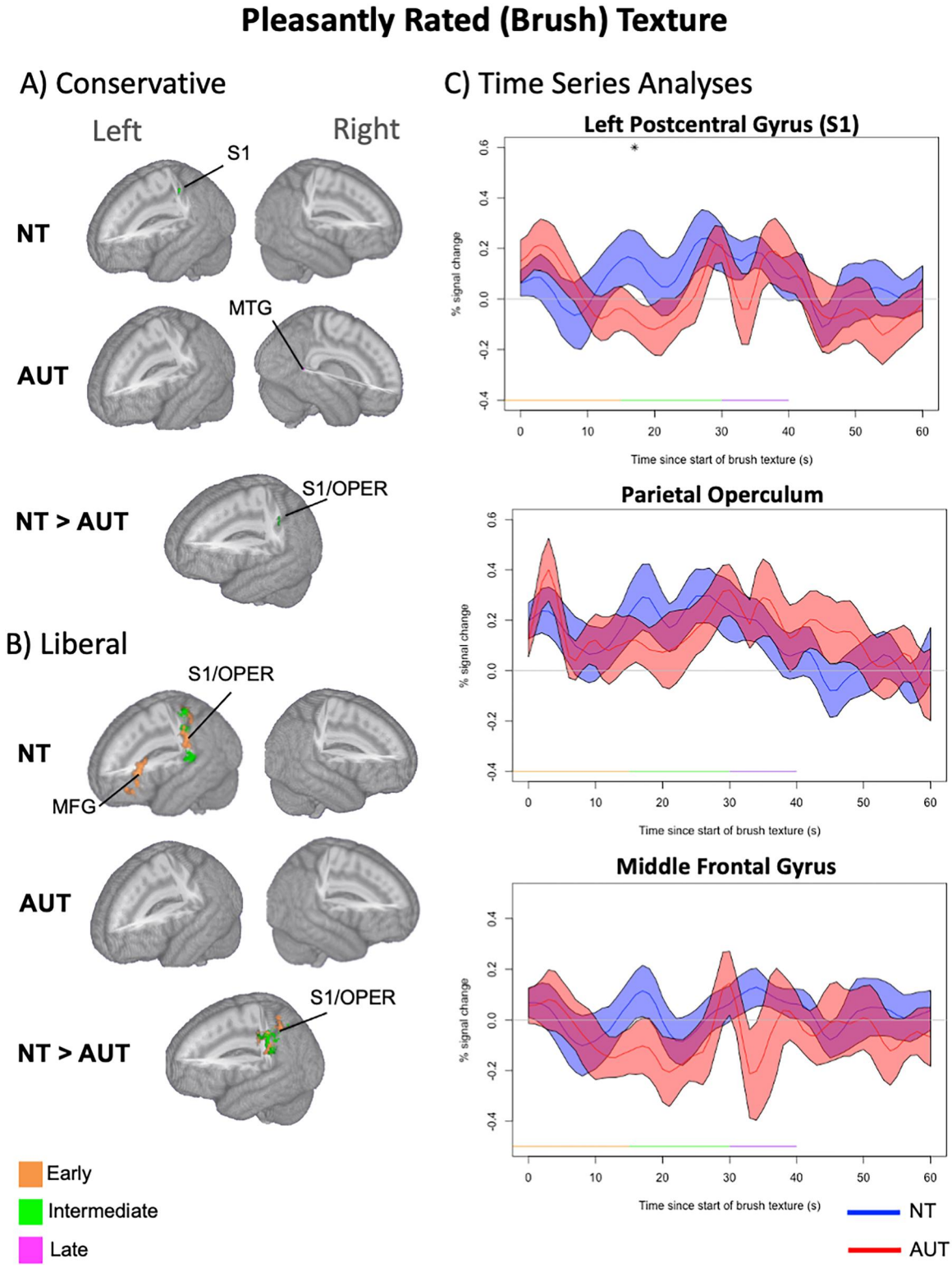

Figure 5. Pleasantly rated (brush) texture responses by group and phase. (A) Significant clusters by group and phase using conservative approach (permutation testing, threshold-free cluster enhancement (TFCE), and family-wise error corrected p-value = 0.05), including one region (left somatosensory cortex) of decreased intermediate response in the AUT group compared to the NT group. (B) Significant clusters by group and phase using the liberal approach (mixed-effect FLAME 1 with a cluster threshold of $z = 2.3$ and p-value = 0.05, family-wise error corrected based on clusters defined by Gaussian random field theory), including regions (left and right somatosensory cortex) of decreased early/intermediate responses in the AUT compared to the NT group. (C) Time course of 1) left postcentral gyrus (S1), 2) parietal operculum, and 3) middle frontal gyrus response by group. Average autistic response plotted in red; average non-autistic response plotted in blue, including 90% confidence bands per group. Coloured lines indicate early (orange) and intermediate (green) phases of 30s period of texture stimulation and late (purple) post-texture responses. Though responses are comparable in both groups, the AUT group shows a decreased intermediate postcentral gyrus response (17s, indicated by an asterisk) compared to the NT group. Abbreviations: NT: non-autistic, AUT: autism, MFG: middle frontal gyrus, S1: primary somatosensory cortex, OPER: parietal operculum, MTG: middle temporal gyrus.

Behavioural correlations

Correlations with pleasantness ratings

There were no significant relationships between BOLD response and texture pleasantness ratings for any region, texture, or response phase at the $p < 0.05$ level (Figure 6). When ranking the size of the coefficients, the intermediate phase posterior insula response showed the strongest relationships with pleasantness ratings for all three textures. Across textures, the direction of this finding was such that individuals who showed the most extreme ratings (e.g. close to −1 indicating most unpleasant for the unpleasantly rated texture and close to +1 indicating most pleasant for the pleasantly rated texture) showed the *lowest* BOLD responses and individuals with more moderate ratings (i.e. close to 0 indicating neither pleasant nor unpleasant) showed greater BOLD responses. Though correlations between S1, S2, and behavioural ratings were weaker than for the posterior

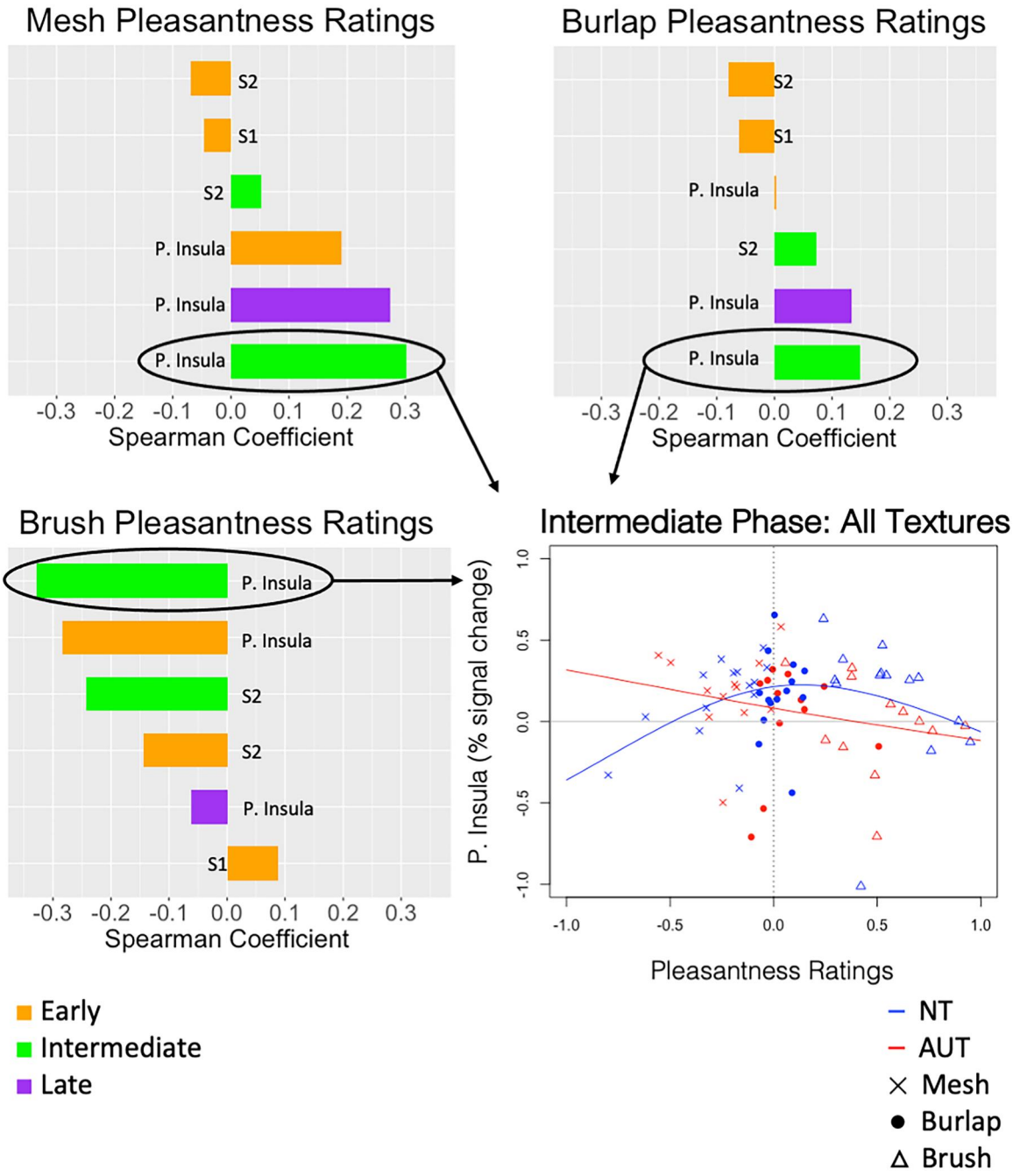

Figure 6. Correlations between affective (posterior insula) and discriminative (S1/S2) somatosensory BOLD response and texture pleasantness ratings, by response phase. For each texture, Spearman correlation coefficients are plotted in order from strongest negative correlation to strongest positive correlation. Each coefficient is colour-coded according to response phase, with orange = early phase response, green = intermediate phase response, and purple = late phase response. The plot in panel 4 reflects the relationship between texture pleasantness ratings and intermediate posterior insula responses (percent signal change) across textures. Textures are coded by shapes (with crosses = mesh, circles = burlap, and triangles = brush) and groups are coded by colour, with red = autistic and blue = non-autistic. Trend lines per group were fit as natural splines with a knot at 0, allowing the relationship to diverge between negative ratings (mostly mesh texture) and positive ratings (mostly brush texture), though only the NT group was better fit by a diverging trend. Abbreviations: NT: non-autistic, AUT: autism, P. Insula = posterior insula, S2 = secondary somatosensory cortex, S1 = primary somatosensory cortex.

insula, these relationships were often in the opposite direction such that individuals who showed greater S1/S2 BOLD responses tended to rate these textures on the more extreme ends of the scale. When visualising individual patterns by group, however, this pattern seems driven by non-autistic participants, who show diverging response relationships for positive (mostly brush texture) versus negative (mostly mesh texture) ratings, whereas autistic participants seem to show the same linear trend across textures.

Correlations with Sensory Profile domains

For posterior insula responses by texture and phase, there was one statistically significant relationship between higher "Sensory Seeking" domain scores with lower posterior insula early phase BOLD responses to the brush texture at the $p < 0.05$ level (Figure 7). When ranking the size of the correlation coefficients, responses to the brush texture tended to correlate most strongly with Sensory Profile scores across all domains. Unlike for the pleasantness ratings, early and late phase responses tended to show the highest correlation with Sensory Profile domains, such that reduced early responses but enhanced later responses were seen in individuals with the highest degree of sensory challenges across multiple domains. However, there was also a lot of variability between domain scores as to the strength and direction of relationships with posterior insula BOLD response phases.

Discussion

These results preliminarily characterise the spatiotemporal pattern of response to affective textures in non-autistic individuals and point towards distinct patterns of differences in autism for each texture type: early increase in sensory region response to unpleasantly rated textures, sustained/delayed processing of neutrally rated textures, and suppressed processing of pleasantly rated textures. Tentatively, the nuanced neural findings in response to these affective textures emphasise that magnitude of neural processing may relate closely to the experience of affectively charged textures (both pleasantly and unpleasantly rated) and the timing of neural processing may relate to the experience of neutrally rated textures. Further, these findings suggest complex interactions between regions and timing of response to shape reported sensory experiences, that larger studies may begin to investigate with greater power than was available in this preliminary work.

Non-autistic pattern of texture responses

Few studies have previously investigated how the spatiotemporal response to textures relates to the pleasantness or unpleasantness of experiences. Of the studies that have, a few common themes emerge. First, there are consistent findings of a sustained neural response past texture offset, especially in frontal regions (Chen et al. 2002; Kitada et al. 2005; Gordon et al. 2013). Second, prior findings introduce the possibility that in some cases, BOLD response may correspond *inversely* with perceived roughness/smoothness, specifically when participants are asked to provide a rating and thus may be focusing additional attention to cognitive evaluation (Kitada et al. 2005).

The findings in this study are both consistent with and extend these prior findings. Regions of significant texture responses were generally consistent with prior accounts (Chen et al. 2002; Kitada et al. 2005; Gordon et al. 2013), with the NT group showing BOLD responses in primary and associative sensory regions for all texture types. In continuous analyses focusing on response patterns in the parietal operculum and somatosensory cortex during texture stimulation, NT individuals tended to show the strongest BOLD response increases during the first twenty seconds of texture stimulation and a graded ramping in the last ten seconds. One prominent way in which these results extend prior findings is comparing the spatiotemporal responses between pleasantly rated, neutrally rated, and unpleasantly rated textures. For instance, these current results point towards different evaluative regions in response to neutral versus affectively charged textures, implicating a more ventral/anterior region for the affectively charged brush and mesh textures than for the neutrally rated burlap texture.

Further, the post-stimulus evaluative responses tended to become less prominent as stimuli become increasingly pleasant, as the NT group showed a late phase response to the unpleasantly rated texture (as identified *via* the conservative approach) in affective regions such as the insula and central operculum. The NT group also showed a tentative (as identified *via* the liberal approach) late phase response to the neutrally rated texture in the frontal pole. On the other hand, NT group BOLD responses to pleasantly rated texture stimulation was limited to stimulus presentation (early and intermediate phases).

General trends: relationships between neural response and behavioural ratings

Though there were several stimulus- and phase- specific patterns in how BOLD responses related to texture ratings and overall sensory responsiveness, there were a few key themes that emerged from these findings. In general, the intermediate posterior insula response related most strongly to texture pleasantness ratings for all textures. However, this relationship was close to absent for the burlap texture for either group, supporting a distinction between the relationships between perceptual brain region responses and experienced pleasantness between neutral and affectively charged textures. In addition, visualised patterns by individuals/groups suggest that there may be an interaction effect of how group status mediates the response between BOLD response and texture pleasantness ratings. This potential interaction may be a promising area of future, larger scale research. Lastly, though *hypo-* and *hyper-* responsiveness may be thought of as more proximal behavioural ratings to the perceptual paradigm in this study, the relatively stronger relationships were seen between BOLD responses and approach

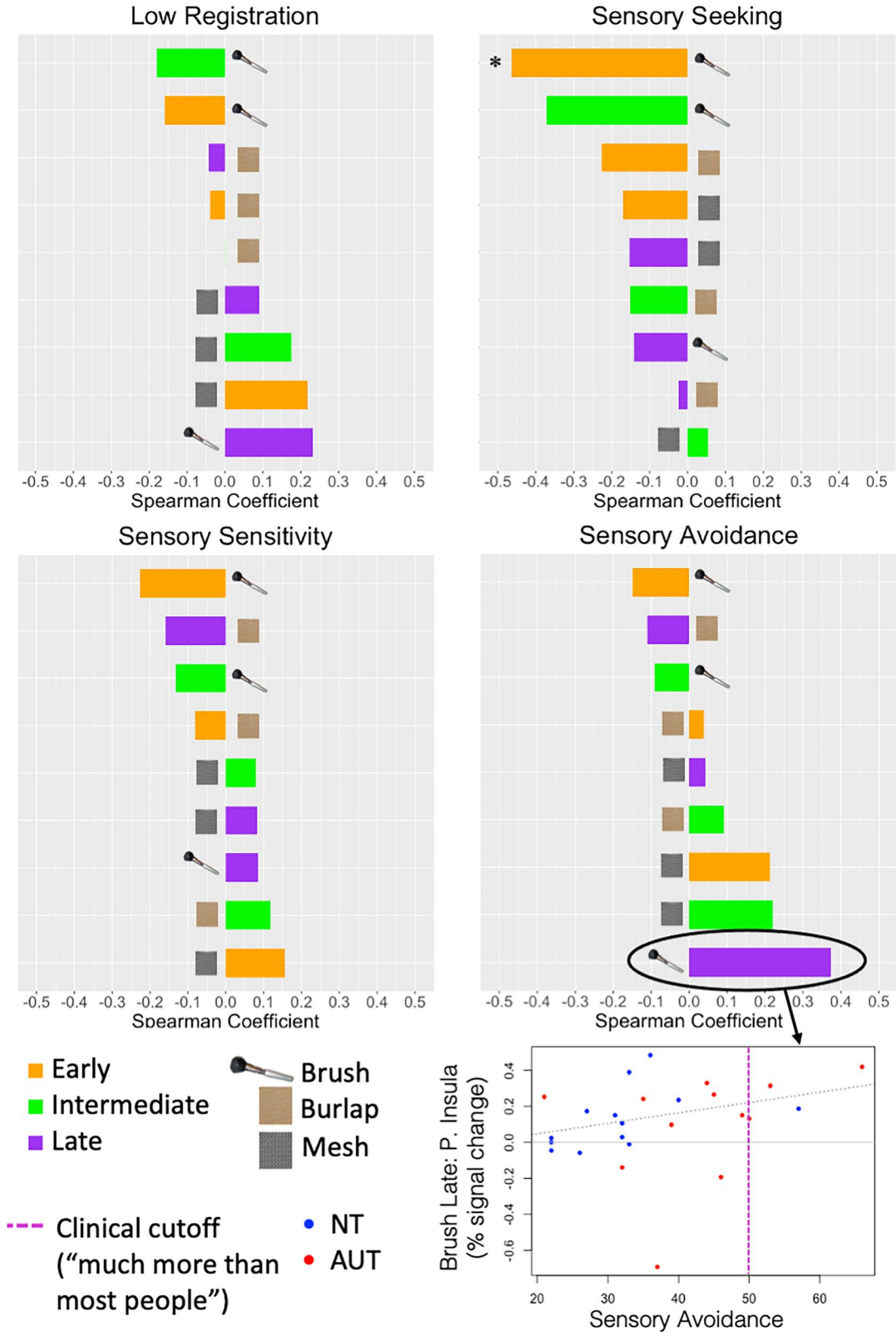

Figure 7. Correlations between posterior insula BOLD response and Sensory Profile domain scores, by response phase. For each Sensory Profile domain, Spearman correlation coefficients are plotted in order from strongest negative correlation to strongest positive correlation. Each coefficient is colour-coded according to response phase, with orange = early phase response, green = intermediate phase response, and purple = late phase response. Asterisk indicates significant correlation at $p < 0.05$. The inset correlation plot below panel 4 reflects the individual-level data for the correlation between sensory avoidance ratings and late-phase posterior insula responses to the brush texture (percent signal change), with individuals coloured by group (red = autistic and blue = non-autistic). The clinical cut-off of 50 is plotted in pink, reflecting the scores over which sensory avoidance becomes "much more than most people" based on normalised scores (Brown et al. 2001). Abbreviations: NT: non-autistic, AUT: autism, P. Insula = posterior insula.

("seeking")/avoidant behaviours, which may be contextualised under active inference paradigms that characterise perception *as* active (Palmer et al. 2017). Alternatively, it may be somewhat easier for individuals to report this kind of observation (seeking or avoiding something) than a more subjective observation of high or low sensitivity.

Perceptual differences in autism: pleasantly rated (brush) texture

The most prominent group differences were found in response to the pleasantly rated brush texture. Unlike the other two textures, group differences in response to the brush stimulation spanned multiple regions, multiple response phases, and both liberal and conservative approaches. In response to this texture, the AUT group showed significantly decreased bilateral primary somatosensory responses compared to the NT group, across the entire texture stimulation period (early and intermediate phases). Most studies operationalise social touch as the type of stimulation that maximally activates CT afferents which correlates with higher pleasantness ratings (Olausson et al. 2002; McGlone et al. 2007); thus, the pleasantly rated brush texture may provide the most comparable stimulation to prior social touch studies. Sustained sensory region decreases in response to the pleasantly rated stimulus are in correspondence with the literature suggesting that autistic individuals may show primary sensory and perceptual differences in processing social touch rather than purely evaluative differences (Cascio et al. 2016; Kaiser et al. 2016).

Further, pleasantly rated brush texture BOLD responses tended to show the strongest correlation with behavioural sensory responsiveness as assessed by the Sensory Profile, especially between the early response phase and sensory seeking. This latter relationship (between BOLD response to the brush texture and sensory seeking behaviours) is consistent with individuals who find this sensation to be most pleasant being most likely to seek out additional sensation. More surprisingly, responses in the early and late phases to the brush texture were among the most highly correlated with sensory sensitivity and sensory avoidance behaviours as well. This likely relates to a general tendency for different types of sensory phenotypes to occur within the same individual (Williams et al. 2018; Baranek et al. 2022; Lee et al. 2022), also shown by our current AUT group reporting increased hypo- *and* hyper- responsiveness. One potential explanation is that reduced sensory habituation (as indicated by increased late phase responses) may relate both to increased seeking of pleasant sensations and increased avoidance of negative sensations. However, current behavioural rating analyses focused on the posterior insula as a key region that is highly active in response to all three textures studies. Future studies focusing on a distributed texture response network may better leverage variance in the other two textures' responses for explaining behavioural responsiveness.

Perceptual/evaluative differences in autism: unpleasantly rated (mesh) texture

In response to the unpleasantly rated mesh texture, AUT individuals showed increased regional responses in the first few seconds of the early phase, the degree of which did show a small, but not significant, correlation with greater sensory sensitivities. In addition, the AUT group showed a qualitatively bimodal response pattern in parietal opercular areas, similar to the shape found in response to noxious stimulation in the neurotypical population (Moulton et al. 2012). There was a tentative relationship such that the strength of this late phase response across groups related inversely to finding the mesh texture to be more unpleasant. Combined, this bimodal processing pattern and its relationship to both the experience of the mesh texture and sensory behaviours more broadly, suggest both perceptual and evaluative differences in autistic individuals' responses to this mildly unpleasant texture.

However, the shape of this response was surprising to observe given that autistic individuals did *not* show a bimodal response to stimuli that they rated as painful in a prior study (Failla et al. 2018). Since prior data-driven accounts characterise the later phase of the bimodal pain response as relating to stimulus evaluation and coping techniques (Moulton et al. 2012), Failla et al. (2018) suggested that this prior finding may reflect reduced pain coping techniques in autistic individuals. We speculate that one explanation for the current findings may be that in response to mildly aversive stimulation, autistic individuals may indeed enact cognitive coping techniques (such as attempting to distract themselves) that non-autistic individuals do not, but their ability to use coping techniques may be diminished as stimuli become increasingly painful. However, a replication of Moulton et al. (2012) approach decomposing the BOLD response into meaningful phases for innocuous textures is needed to confirm the extent to which late phase responses to unpleasantly-rated stimulation resemble late phase responses to noxious stimulation. If this relationship is confirmed, this bimodal response pattern may indicate a meaningful index of sensory sensitivities to mildly aversive stimuli.

Evaluative differences in autism: neutrally rated (burlap) texture

Of all three textures investigated, the AUT group showed the greatest qualitative pattern of temporal differences from the NT group in response to the neutrally rated burlap texture, though the regions identified per group were only significant using the liberal analysis approach. Both groups showed significant post-stimulus evaluative responses to the burlap texture, supporting a tendency in both groups to take additional time to interpret and evaluate the texture reported as the least affectively charged and thus, most ambiguous (Cascio et al. 2012). Given that the AUT group demonstrated decreased early-phase processing compared to the NT group in the paracingulate cortex but then showed significant later processing in a similar area, this suggests

that the AUT group may be taking relatively longer than the NT group to interpret this kind of ambiguous stimulation. Though the response to this texture was less clearly related to sensory experiences as measured by the Sensory Profile, it may be relevant to consider for more granular studies of daily sensory experiences, such as decreased tolerance for uncomfortable clothing.

Limitations

While this study provides the first spatiotemporal characterisation of responses to non-painful tactile stimulation in autism, it is not without limitations. This study was primarily limited by its small sample size; thus, there may be additional group differences in the spatiotemporal pattern of processing tactile stimuli that this study was insufficiently powered to address. The small sample size especially limits us in addressing the heterogeneity in the autism group, who report both increased sensory hyper-responsiveness and increased hypo-responsiveness. This heterogeneity may potentially relate to greater neural variability among autistic participants, which may explain the limited number of whole brain findings.

Relatedly, we chose a limited number of repetitions per texture type (four) to limit the effect of receptor fatigue. Particularly, the sustained response dynamics of these receptors are impacted in response to more than four repeated stimuli (Vallbo et al. 1999). However, this also limits our power to observe robust within-individual effects. Due to these power limitations, our temporal windows of analysis were defined *a priori*, following established studies in pain processing (Moulton et al. 2012; Failla et al. 2018). Future studies with larger samples (both in stimulus repetitions and in number of participants) may take data-driven approaches to identify a more specific temporal signature of texture processing and improve the ability to relate response phases to individual sensory responsivity. This sample was also limited to predominantly males with typical IQ scores; thus, studies with greater generalisability across a wider range of the autism spectrum are needed. Given these limitations, these results are presented as exploratory findings for future studies to investigate with larger sample sizes.

Future directions

Group differences in patterns of neural response occurred despite prior findings that our autistic participants generally rated these textures' pleasantness within similar ranges as their non-autistic peers (Cascio et al. 2012). Thus, these findings indicate that the differential neural responses occurred when these textures are experienced in accordance with the targeted valence. Given the high degree of individual variability in how specific tactile stimuli are experienced by individuals across the autism spectrum (Cascio et al. 2016), it is unlikely that a single tactile stimulus will evoke a uniformly exaggerated response in all autistic participants. Future research may investigate how the regions/networks identified in this study respond to stimuli that are experienced as extreme or unusual by individual participants.

Additionally, though we were not powered to do so in the current study, comparing the responses *between* textures may provide valuable insight into the mechanisms that guide varied tactile experiences within individuals. Further, approaches such as magnetoencephalogram (MEG) may have the ideal combination of spatial and temporal resolution to further investigate the response timing of these relevant brain regions with the level of temporal detail that may be linked to specific neuronal mechanisms.

While the current study investigated response patterns in autistic adults (without intellectual disability), differences in affective touch processing may have developmental relevance (Gliga et al. 2019) and may be among some of the earliest signs of autism (Baranek 1999). Future studies may use similar analytic approaches to investigate the developmental trajectory of these neural response patterns, which may further inform the basis of affective tactile learning differences in autism.

Conclusions

These results suggest that the timing of neural responses to non-painfully rated textures may index different aspects of tactile responsiveness. These findings additionally provide preliminary evidence of unique spatiotemporal patterns in response to affective touch in autism; specifically, autistic individuals showed preliminary differences in the timing and/or magnitude of brain response that were distinct for textures of different affective valence. Based on our results, we propose that distinct phases of the neural response may relate to different aspects of *how* tactile responsiveness in autism compares to non-autistic peers, pointing towards perceptual differences in response to affectively charged textures and evaluative differences in response to neutral, ambiguous textures. Future studies are needed with larger sample sizes and with younger participants to better understand the developmental progression of sensory versus evaluative components of tactile responsiveness. Finally, these results suggest that data-driven decompositions of the neural response to innocuous textures may be an important future research direction to better understand the relationship between tactile processing and individual sensory experiences.

Disclosure statement

The authors have no disclosures to report.

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Appendix 1

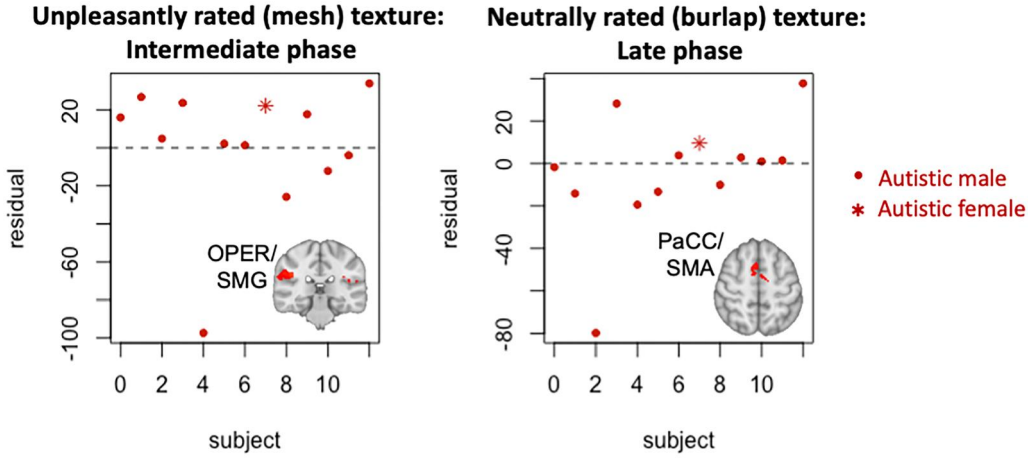

Figure A1. Residual plots for blood oxygenation level-dependent (BOLD) response percent signal change in significant autism group clusters, for texture phases with significant autism group responses. Plots include the n = 13 autism group participants, plotting general linear model residual (y-axis) within the cluster mask (inset brain) by subject order (x-axis, arbitrary). Male participants are plotted in red dots; the female participant is plotted with a red asterisk. The female participant did not have outlying values for either of these contrast results.