

Using somatosensory mismatch responses as a window into somatotopic processing of tactile stimulation

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Abstract

Brain responses to tactile stimulation have often been studied through the examination of ERPs elicited to touch on the body surface. Here, we examined two factors potentially modulating the amplitude of the somatosensory mismatch negativity (sMMN) and P300 responses elicited by touch to pairs of body parts: (a) the distance between the representation of these body parts in somatosensory cortex, and (b) the physical distances between the stimulated points on the body surface. The sMMN and the P300 response were elicited by tactile stimulation in two oddball protocols. One protocol leveraged a discontinuity in cortical somatotopic organization, and involved stimulation of either the neck or the hand in relation to stimulation of the lip. The other protocol involved stimulation to the third or fifth finger in relation to the second finger. The neck-lip pairing resulted in significantly larger sMMN responses (with shorter latencies) than the hand-lip pairing, whereas the reverse was true for the amplitude of the P300. Mean sMMN amplitude and latency did not differ between finger pairings. However, larger P300 responses were elicited to stimulation of the fifth finger than the third finger. These results suggest that, for certain combinations of body parts, early automatic somatosensory mismatch responses may be influenced by distance between the cortical representations of these body parts, whereas the later P300 response may be more influenced by the distance between stimulated body parts on the body surface. Future investigations can shed more light on this novel suggestion.

KEYWORDS

body map, MMN, P300, somatosensory cortex

1 | INTRODUCTION

The cortical processing of touch to the body involves the integration of information about the location of the tactile stimulation (Heed, Buchholz, Engel, & Röder, 2015). For instance, processing of touch to the left hand needs to account for not only the fact that it is the left hand being touched, but also where the hand is in space. EEG methods have proven useful in this area of study, in part because of the high level of temporal resolution afforded by these techniques. In particular, ERPs derived from the EEG signal have been employed to study spatial and postural influences on tactile processing over the first few hundred milliseconds

after touch onset (Eimer & Forster, 2003; Heed & Röder, 2010).

In the present study, we took a novel approach to using ERP methods in the study of spatial factors in tactile processing. Studies using postural manipulations such as hand crossing often employ particular attentional demands (e.g., Eimer, Forster, & Van Velzen, 2003; Heed & Röder, 2010), although this is not the case for all studies (Ley, Steinbrg, Hanganu-Opatz, & Röder, 2015; Rigato et al., 2013). In the current study, we recorded mismatch negativity (MMN) and P300 responses to stimulation of different body parts using an oddball paradigm with no specific postural manipulations or specific attentional demands. Instead, we examined how

the relative separation of body part representations in primary somatosensory cortex, and the distance between these body locations on the body surface, influenced cortical responses to tactile stimulation over different time frames in the ERP response.

The MMN is considered to be an index of change detection that is automatic and is independent of attentional influences. The MMN response occurs in the time range of 100–200 ms over frontocentral sites and is typically elicited using an oddball paradigm in which infrequent deviant stimuli are embedded in a sequence of repetitive standard stimuli (Garrido, Kilner, Stephan, & Friston, 2009; Näätänen, Paavilainen, Rinne, & Alho, 2007). The MMN is typically elicited using paradigms that do not require participants to actively attend to (or respond to) the deviant stimuli. Because the MMN can provide information on aspects of sensory perception that are independent from attention and task performance, it has applications across various areas of research (e.g., Conboy & Kuhl, 2011; Mowszowski et al., 2012; Näätänen et al., 2012).

The P300 response to novelty (also known as the P3a) also has a frontocentral scalp distribution but occurs later than the MMN, approximately 300 ms after stimulus onset. The P300 reflects an orienting response to the violation of expected patterns of sensory stimulation and, unlike the MMN, is associated with an involuntary switch of attention toward the deviant stimulus. As such, the P300 reflects a higher level of processing of sensory novelty than the MMN (Horváth, Winkler, & Bendixen, 2008; Light, Swerdlow, & Braff, 2007; Polich, 2007). Although deviant stimuli may elicit both MMN and P300 components in the form of an “MMN/P3a complex” (Hermens et al., 2010), studies in the auditory modality have found that changes in MMN amplitude are often dissociated from changes in P300 amplitude (Horváth et al., 2008; Rinne, Särkkä, Degerman, Schröger, & Alho, 2006).

Although the MMN and P300 have been widely used to study novelty detection in the auditory modality, much less is known about these responses across other sensory modalities. The current study examines the somatosensory MMN (sMMN), which follows a similar time course (appearing at 100–200 ms) and topographic distribution (maximal at frontal-central sites) as the auditory MMN (Chen et al., 2014). The sMMN can be elicited by tactile oddball paradigms (Kekoni et al., 1997) employing irregularity in various stimulus properties, such as duration (Akatsuka et al., 2005; Butler, 2011; Spackman, Towell, & Boyd, 2010), vibrotactile frequency (Spackman, Boyd, & Towell, 2007), and spatial location (Akatsuka, Watsaka, Nakata, Kida, Hoshiyama et al., 2007; Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007; Naeije et al., 2016; Restuccia et al., 2009). Because it can be elicited without specific attentional or task requirements, there are promising applications of the sMMN in

research on the integrity and development of somatosensory processing (Chen et al., 2014; Näätänen, 2009). However, factors that influence the appearance and characteristics of the sMMN have not been systematically examined. For instance, how the degree of discrepancy between standard and deviant tactile stimuli might modulate sMMN responses remains largely unknown. In the current study, we explored the effect of the degree of spatial and cortical deviance on the sMMN by leveraging a particular kind of discrepancy that arises from the configuration of somatosensory cortex in the human brain.

Insights about possible influences on the sMMN can come from considering what is known about mismatch responses in the auditory domain, where a significant amount of research has been carried out. One primary influence on amplitude and latency of the auditory MMN is the extent of the difference between standard and deviant sounds. Specifically, auditory MMN amplitude progressively increases and peak latency decreases as the difference in frequency between the standard and deviant stimuli becomes larger (Näätänen et al., 2012; Pakarinen, Takegata, Rinne, Huotilainen, & Näätänen, 2007; Pincze, Lakatos, Rajkai, Ulbert, & Karmos, 2001). The auditory MMN is believed to primarily originate from primary and secondary auditory cortices (Garrido et al., 2009; Pincze et al., 2001), which are responsible for processing features of bottom-up sensory input and detecting sensory violation and deviance (Molholm, Martinez, Ritter, Javitt, & Foxe, 2005). There is evidence that the generators of the auditory mismatch response elicited by frequency deviance are organized tonotopically, likely reflecting the organization of primary auditory cortex (AI; Tervaniemi et al., 1999; Tiitinen et al., 1993). Numerous studies using magnetoencephalography (MEG) and fMRI have demonstrated a continuous, discrete progression of frequency sensitivity from low to high along the anterolateral to posteromedial axis of AI (e.g., Formisano et al., 2003; Talavage et al., 2004).

In terms of the sMMN, it is notable that primary somatosensory cortex (SI) has an organizational pattern similar to the tonotopic organization of AI, in that both show a particular topographic organization where adjacent sensory inputs encode stimulus features that are more closely related than more separated inputs (Kaas, Jain, & Qi, 2002). While AI shows a tonotopic pattern of responsivity, much of SI is organized in a somatotopic manner such that body parts that are contiguous (e.g., the leg and the hip) are located next to each other on the homuncular strip (Penfield & Boldrey, 1937). However, a notable example of discontinuity in the organization of SI is that the hands and the face have adjacent cortical representations, while the face and the neck (which are closer together on the body surface) have more separated cortical representations. We were interested in whether the sMMN response is sensitive to this specific

discontinuity, and if so, whether the influence of this discrepancy wanes in a later component of the somatosensory evoked potential, specifically the P300.

As with mismatch responses, the P300 can be elicited across various modalities (including tactile) and is also influenced by the magnitude of the deviance between frequent standards and infrequent deviant stimuli. However, the P300 tends to be more sensitive to the salience and significance of infrequent stimuli, and as such reflects a higher level of sensory processing than the MMN response (Friedman, Cycowicz, & Gaeta, 2001; Horváth et al., 2008). In contrast to the relative independence of the MMN from attentional influences, the appearance and amplitude of the P300 is influenced by the activity of frontal-parietal attention networks (Kida, Kaneda, & Nishihira, 2012; Lugo et al., 2014; Polich, 2007).

Here, we used two experimental protocols to compare sMMN and P300 responses to somatosensory deviants that differed from a standard stimulus across pairs of body locations. Given that the sMMN is generated in somatosensory cortex (Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007; Butler et al., 2011; Huang, Chatterjee, Cui, & Guha, 2005; Naeije et al., 2016; Shinozaki, Yabe, Sutoh, Hiruma, & Kaneko, 1998; Spackman et al., 2010), we hypothesized that sMMN amplitude may be influenced by the relative positioning of body parts on the cortical somatotopic map (the homuncular strip) in SI. Conversely, because of its connection of the P300 response to frontoparietal attention networks, and its sensitivity to the salience of deviant stimuli, we hypothesized that P300 amplitude would be more sensitive than the sMMN to the degree of separation on the three-dimensional (3D) body surface itself. We tested this hypothesis by contrasting sMMN responses elicited by tactile stimulation of pairs of bodily locations for which the relative proximity of representations in SI was consistent with, or varied significantly from, the degree of physical separation of these locations on the body surface.

The first protocol employed stimulation of the index finger (standard), the third finger (Deviant 1), and the fifth finger (Deviant 2), for which the relative positioning on the body surface is similar to the relative positioning in primary somatosensory cortex. We expected that the amplitudes of sMMN and P300 responses elicited by tactile stimulation to the fifth finger would be greater than for stimulation of the third finger. In the second protocol, we employed more widely spaced body locations: frequent tactile stimuli were delivered to the lip (standard stimulus) and infrequent stimuli were delivered to either the hand (Deviant 1) or the neck (Deviant 2). The use of these locations enabled us to leverage the discontinuity in the somatosensory homunculus that was mentioned above. While the lip and the neck are close together on the body surface, there is a relatively larger degree of separation between the corresponding cortical

representations of these body parts in somatosensory cortex. In contrast, the lip and the hand are more widely spaced on the body surface than the lip and neck, but have more closely spaced representations on the homuncular strip. We therefore predicted that the MMN elicited by the lip/neck contrast would have greater amplitude and shorter latency than the lip/hand contrast, but that the opposite pattern of responses would be found for the P300.

2 | METHOD

2.1 | Participants

Twenty-nine undergraduate participants received course credit in return for participation. Data from two participants were unusable due to hardware failure, resulting in a final sample of 27 participants (19 female, mean age = 19.59 years, $SD = 1.58$). Subjects were excluded from participation if they had any self-reported history of neurological disorder, were younger than 18 or older than 45 years of age, or were left-handed. The Oldfield Handedness questionnaire (Oldfield, 1971) was administered to each participant at the beginning of the study; all participants were determined to be right-handed. All participants gave their informed consent to participate in this study, which was approved by the Temple University Institutional Review Board.

2.2 | Stimuli

Tactile stimuli were delivered using an inflatable membrane (10 mm diameter) mounted in a plastic casing. The membrane was inflated by a short burst of compressed air delivered via flexible polyurethane tubing (3 m length, 3.2 mm outer diameter). The compressed air delivery was controlled by STIM stimulus presentation software in combination with a pneumatic stimulator unit (both from James Long Company) and an adjustable regulator that restricted the airflow to 60 psi. The pneumatic stimulator and regulator were located in an adjacent room to the participant. To generate each tactile stimulus, the STIM software delivered a 5-volt TTL trigger that served to open and close a solenoid in the pneumatic stimulator. The solenoid was open for 10 ms following trigger onset, with expansion of the membrane beginning 15 ms after trigger onset and peaking 20 ms later (i.e., 35 ms after trigger onset). The total duration of membrane expansion and contraction was around 100 ms, with a peak force of 2 N as measured using a custom calibration unit (James Long Company). This stimulation method has been used previously in a number of EEG and MEG studies of cortical responses to tactile stimulation (Pihko, Nevalainen, Stephen, Okada, & Lauronen, 2009; Saby, Meltzoff, & Marshall, 2015; Shen, Saby, Drew, & Marshall, 2017).

During presentation of the tactile stimuli, participants watched a video presented on a CRT monitor (40 cm viewable). Participants were seated approximately 70 cm from the monitor screen. The video consisted of approximately 30 min of footage of a wildlife documentary presented via DVD. No auditory soundtrack was presented, and subtitles were displayed in English. To mask any subtle sounds associated with delivery of the tactile stimuli, participants wore earplugs, and ambient white noise was played in the room where EEG collection was occurring.

2.3 | Design and procedure

Six blocks of tactile stimuli were presented, and participants were asked to focus on the video being shown for the duration of each block. The first three blocks involved stimulation of three fingers, and the second three blocks involved stimulation of three different body parts (lip, neck, hand).

2.3.1 | Finger stimulation

In the first block, tactile stimulation was delivered every 600 ms to either the second, third, or fifth digit of the right hand. There were a total of 1,000 trials in this block, which lasted approximately 10 min. The second digit (index finger) was designated as the standard, with 80% of the tactile stimuli (800 trials) being delivered to this digit. The third and fifth digit were designated as deviants, with each finger receiving 10% of the tactile stimuli (100 trials), respectively. The stimuli were presented in a pseudorandom order, with deviant stimuli being separated by at least two standard stimuli. The second and third blocks consisted of 1 min of stimulation to only the third and fifth digits, respectively, in order to establish a baseline waveform for these digits (see Section 2.5.2 below). Each of the second and third blocks comprised 100 total trials, with an interstimulus interval of 600 ms. In all three blocks, plastic finger clips were used to hold the inflatable membranes on each finger.

2.3.2 | Lip/neck/hand stimulation

The points of tactile stimulation in the latter half of the experimental session were the right side of the lower lip, the back of the right hand, and the right side of the neck. The same inflatable membrane stimulators were used for body stimulation as for finger stimulation. A stimulator was affixed to the participant's lower lip with an adhesive bandage, with neck stimulation delivered via a stimulator affixed by medical tape to the center of the neck area below the right ear lobe and above the right shoulder. Stimulation of the hand was delivered through a stimulator taped to the center of the back of the hand. The pattern of stimulus delivery was similar to the protocol for finger stimulation (above). In the

fourth experimental block, 800 stimuli were presented to the lip, with 100 stimuli being presented to each of the neck and hand locations. This block lasted approximately 10 min. The fifth and sixth blocks consisted of 1 min of stimulation to only the hand and neck, respectively, in order to establish a control waveform for these body locations. Each of the fifth and sixth blocks had 100 total trials, with an interstimulus interval of 600 ms.

2.4 | EEG recording

EEG was recorded from 32 electrode sites using a Lycra stretch cap (ANT Neuro, Germany) with electrodes positioned according to the International 10–20 system. The signals were collected referenced to Cz with an AFz ground, then were rereferenced offline to the average of the left and right mastoids. Vertical electrooculogram (EOG) activity was collected from electrodes placed above and below the left eye. Scalp impedances were kept under 25 k Ω , with values for most participants staying below 15 k Ω across all electrodes. All EEG and EOG signals were amplified by optically isolated, high input impedance (> 1 G Ω) bio amplifiers from SA Instrumentation (San Diego, CA) and were digitized using a 16-bit A/D converter (\pm 5 V input range) at a sampling rate of 512 Hz using Snap-Master data acquisition software (HEM Data Corp., Southfield, MI). Hardware filter settings were 0.1 Hz (high-pass) and 100 Hz (low-pass) with a 12 dB/octave roll-off. Bioamplifier gain was 4,000 for the EEG channels and 1,000 for the EOG channels.

2.5 | Data analysis

2.5.1 | Preprocessing of EEG data

Processing and initial analysis of the EEG signals were performed using the EEGLAB 13.5.4b toolbox (Delorme & Makeig, 2004) implemented in MATLAB. Epochs of 600 ms duration were extracted from the continuous EEG data, with each epoch extending from -100 ms to 500 ms relative to stimulus onset. Independent component analysis (ICA) was used to identify and remove eye movement artifacts (Hoffmann & Falkenstein, 2008). Visual inspection of the EEG signal was used to reject epochs containing other movement artifacts. The mean number of artifact-free trials per finger or body location was 91 ($SD = 8$). A one-way analysis of variance (ANOVA) showed that there was no significant difference between locations in the number of usable trials across all control and deviant conditions ($p = .572$). To prepare the data for ERP analysis, artifact-free epochs were low-pass filtered at 30 Hz before being averaged and baseline corrected relative to a 100-ms prestimulus baseline.

2.5.2 | sMMN amplitude analysis

The MMN is often quantified by subtracting the ERP response to the standard stimulus from the ERP response to the deviant stimulus as presented in the same oddball sequence. However, one potential confound of this method is that the frequent standard and infrequent deviant stimuli differ in their physical properties, and may thus elicit different ERP responses. To avoid this issue, we used the “identity MMN” method, which involves subtracting the ERP elicited to one stimulus presented as the control from the ERP elicited when the same stimulus is the deviant (deviant minus control). The MMN response obtained through this method addresses the issue of physical differences between the standard and deviant stimuli (Möttönen, Dutton, & Watkins, 2013; Pulvermüller, Shtyrov, Ilmoniemi, & Marslen-Wilson, 2006).

For the computation of sMMN amplitudes, the negative peak in the deviant-minus-control difference wave was first identified in a window of 90 ms to 190 ms at selected electrodes for each participant. For each participant, the difference wave amplitude was then averaged for a 20-ms time window extending 10 ms before and 10 ms after this negative peak. Based on previous studies (Akatsuka, Wasaka, Nakata, Kida, Hoshiyama et al., 2007; Akatsuka, Wasaka, Nakata, Kida, & Kakigi, 2007; Chen et al., 2014; Spackman et al., 2007; Strömmer, Tarkka, & Astikainen, 2014), analyses of the sMMN focused on frontal-central and central scalp regions.

The specific electrodes that were entered into the analysis of sMMN amplitudes were selected based on topographic plots of the deviant-minus-control difference waves (Figure 1). Based on these plots, the analysis of sMMN amplitude for finger stimulation involved electrodes FC1, FC2, C3, and C4. For stimulation of the other body locations (lip/neck/back of hand), the sMMN was also observed over frontal-central areas, but with a slightly more lateral distribution. For these three body locations, the analysis of sMMN amplitude involved electrodes FC5, FC6, C3, and C4. Three-way repeated measures ANOVAs were conducted separately for finger stimulation and body location stimulation using factors deviant type (third/fifth finger or neck/hand), region (frontal central/central), and hemisphere (left/right). Pairwise *t* tests with false discovery rate (FDR) correction were used in all post hoc comparisons.

2.5.3 | sMMN latency analysis

For each participant, sMMN peak latency was quantified as the latency of the most negative peak on the deviant-minus-control difference wave at C3 between 90 ms and 190 ms. Latency of the sMMN was then compared between the two deviant types for finger and body location stimulation via

separate one-way ANOVAs using the factor deviant type (third/fifth finger or neck/hand).

2.5.4 | P300 amplitude analysis

As for the computation of sMMN amplitude, P300 amplitude was derived by subtracting the ERPs for one stimulus as the control from the ERP when the same stimulus was the deviant (Zhang, Xi, Wu, Shu, & Li, 2012). Mean P300 amplitude was calculated by averaging the amplitude of the deviant-minus-control waveform in a 100-ms window surrounding the most positive value between 180 and 400 ms. Since the P300 has a central scalp distribution along the midline (Polich, 2007), three midline electrode sites were selected for statistical analysis: Fz, Cz, and Pz. Two-way repeated measures ANOVAs on P300 amplitude were conducted separately for finger stimulation and body stimulation using factors deviant type (third/fifth finger or neck/hand) and electrode (Fz/Cz/Pz). Pairwise *t* tests with FDR correction were used in all post hoc comparisons.

2.5.5 | P300 latency analysis

For each participant, P300 peak latency was quantified as the latency of the most positive peak on the deviant-minus-control difference wave at Cz between 160 ms and 400 ms. Latency values were then compared between the two deviant types for finger and body location stimulation separately via one-way ANOVAs with the factor deviant type (third/fifth finger or neck/hand).

3 | RESULTS

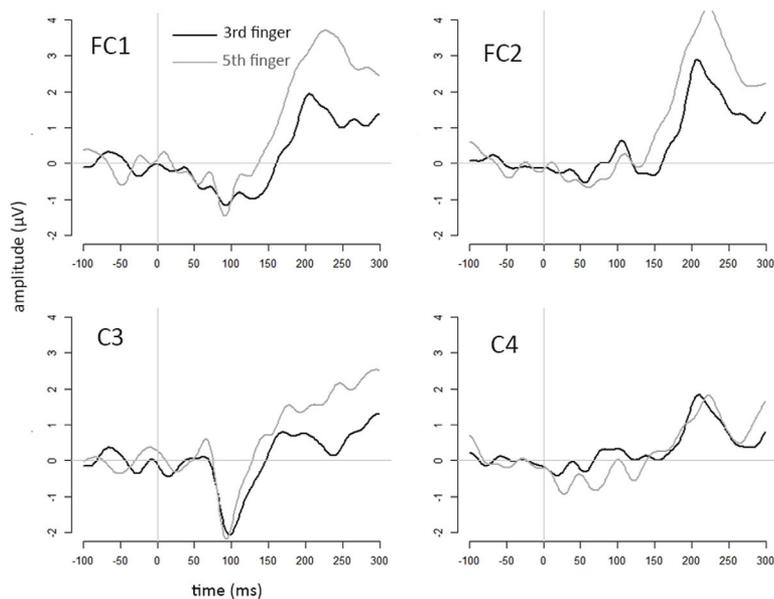
3.1 | sMMN

3.1.1 | sMMN amplitude

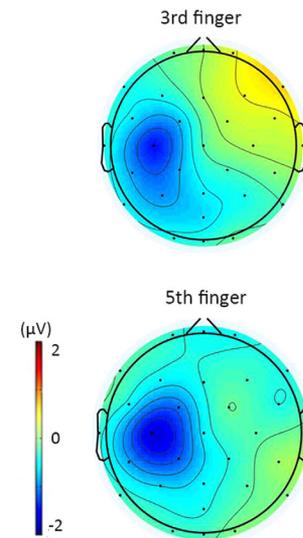
ERP waveforms and topographic maps for the responses to control and deviant stimuli are shown in Figure 2 and 3, with the difference waves and associated topographic plots being shown in Figure 1. The topographic maps in Figure 1–3 are based on mean amplitudes in a 20-ms window around the mean MMN peak for each condition at C3, where sMMN has previously been reported to be maximal in previous studies (Chen et al., 2014; Strömmer et al., 2014). The responses to the frequent standard stimuli (second finger and lip stimulation) preceding each deviant were averaged and are shown in the ERP waveforms in Figure 4.

For sMMN amplitude to finger stimulation, the main effect of hemisphere was significant, $F(1, 26) = 30.789$, $p < .001$, $\eta^2 = .079$, with amplitudes being larger (more negative) in the left than the right hemisphere. There was no significant main effect of deviant type, $F(1, 26) = 1.272$,

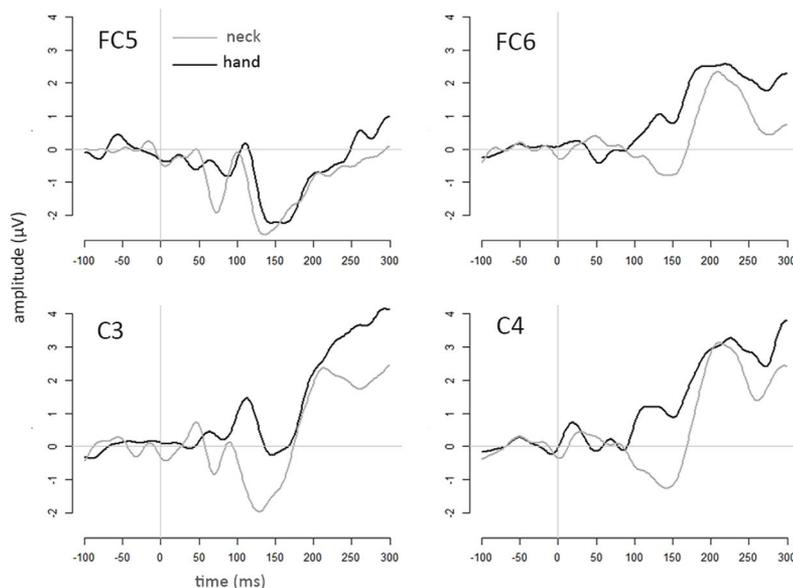
(a) Finger MMN difference wave



(c) Finger MMN topoplots



(b) Body MMN difference wave



(d) Body MMN topoplots

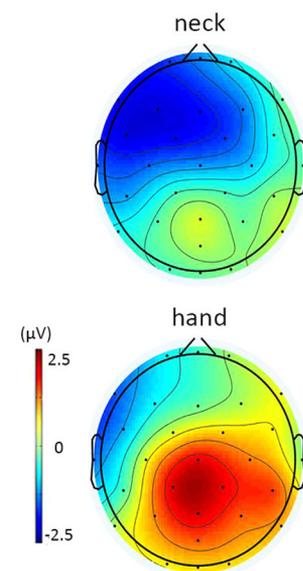


FIGURE 1 ERP waveforms of deviant-minus-control differences for (a) finger sMMN and (b) body location sMMN. (c) Topographic plots of differences between deviants and controls in a 20-ms window around the sMMN peak for finger stimulation (98 ms for third finger, 94 ms for fifth finger). (d) Topographic maps representing deviant-minus-control difference waves for the body location sMMN. The mean amplitude was computed by averaging across a 20-ms window around the sMMN peak for neck (131 ms) and hand stimuli (144 ms)

$p = .269$, $\eta^2 = .006$, or region, $F(1, 26) = 0.338$, $p = .566$, $\eta^2 = .002$, and no significant interaction between these factors.

For sMMN amplitudes at the other body locations, there was a significant main effect of deviant type, $F(1, 26) =$

22.808 , $p < .001$, $\eta^2 = .031$. The sMMN response elicited by deviant stimuli presented to the neck was significantly larger than the sMMN elicited by hand deviants. There was also a main effect of hemisphere, $F(1, 26) = 4.471$, $p = .044$, $\eta^2 = .042$, with larger (more negative) amplitudes over the

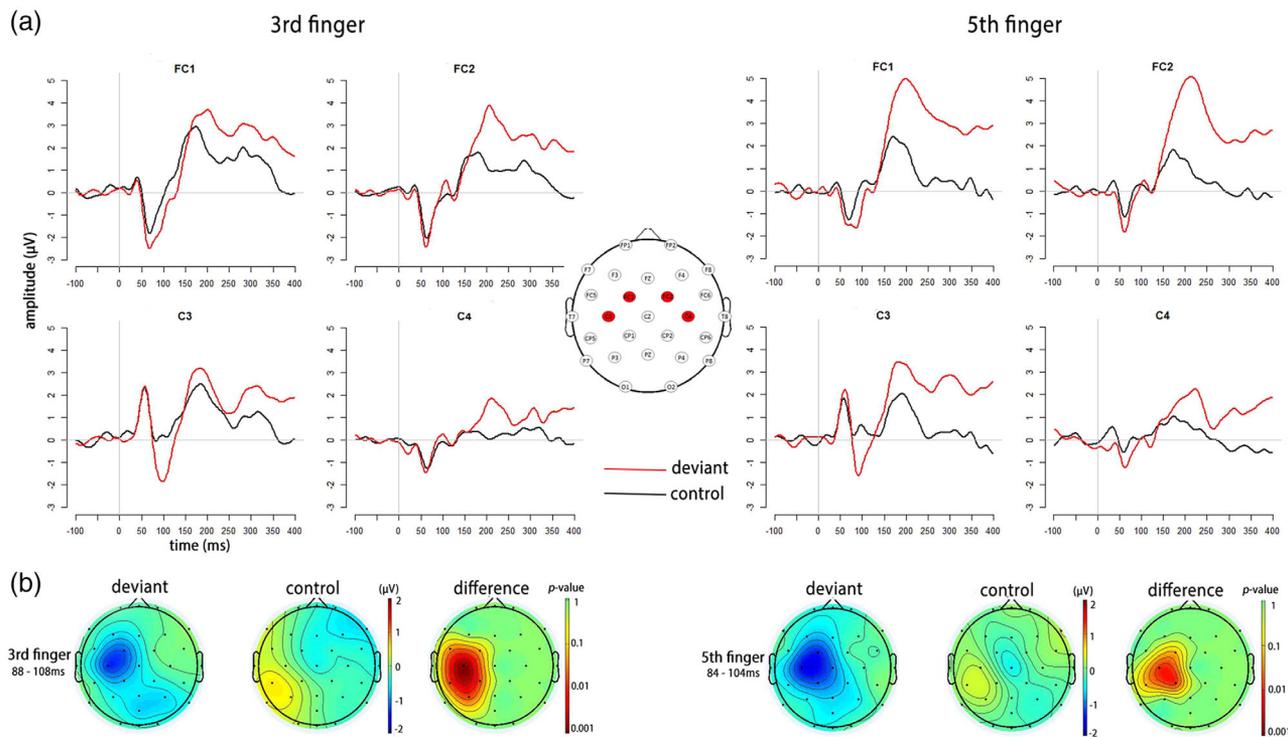


FIGURE 2 Finger sMMN. (a) Grand-averaged ERP waveforms at FC1, FC2, C3, and C4 in response to third finger (left) and fifth finger (right) stimuli presented as frequent controls (black) and as infrequent deviants (red) embedded in repeated second finger stimuli. (b) Topographic plots of mean sMMN amplitude of a 20-ms interval around the sMMN peaks for third finger (98 ms) and fifth finger (94 ms). The third topographic map shows the locations where the amplitude differed significantly between control and deviant stimuli ($p < .05$, with FDR correction)

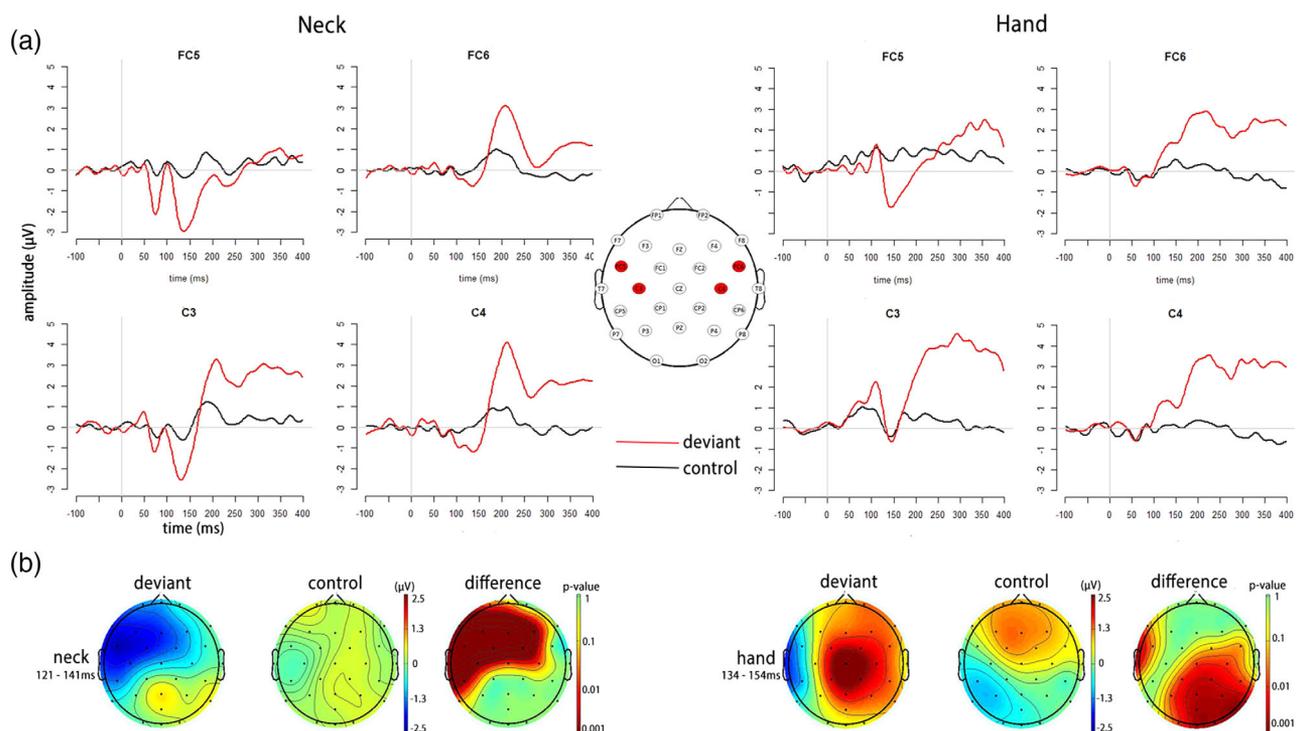
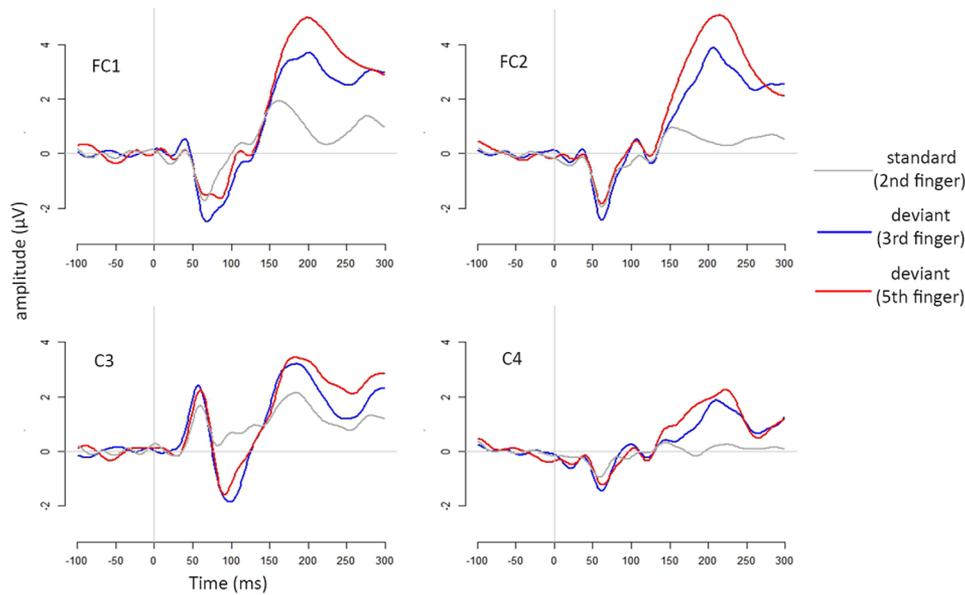


FIGURE 3 Body location sMMN. (a) Grand-averaged ERP waveforms at FC5, FC6, C3, and C4 in response to neck (left) and hand (right) stimuli presented as frequent controls (black) and infrequent deviants (red) among frequent lip stimuli. (b) Topographic plots of mean sMMN amplitude of a 20-ms window around the sMMN peak for neck (131 ms) and hand stimuli (144 ms) presented as deviants during repeated lip stimulation. The third topographic map shows the locations where the amplitude differed significantly between control and deviant stimuli ($p < .05$, with FDR correction)

(a) Finger MMN



(b) Body location MMN

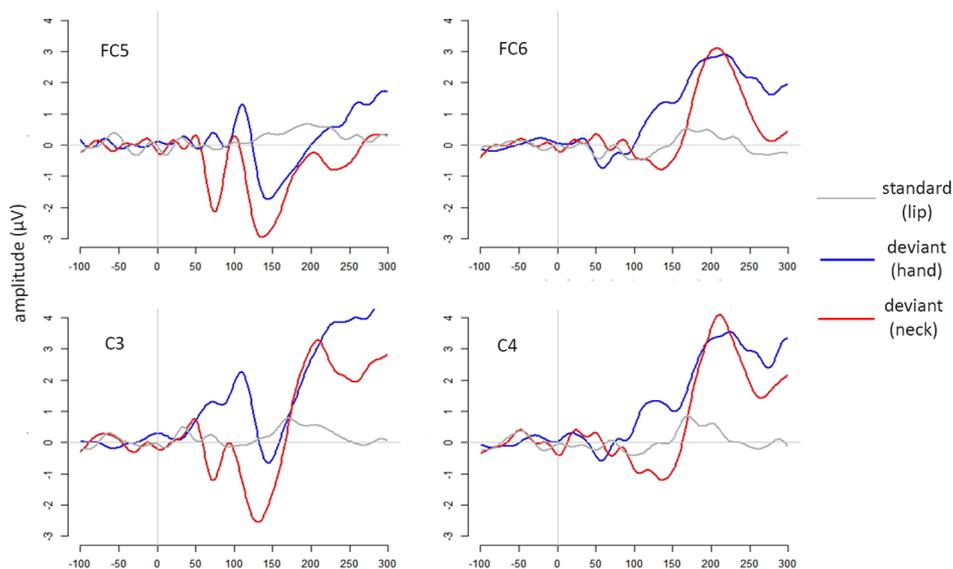


FIGURE 4 MMN waveforms of deviants and standards (second finger for the finger sMMN, and lip for body location sMMN)

left hemisphere than the right. There was no significant main effect of region, $F(1, 26) = 2.433$, $p = .131$, $\eta^2 = .006$, and no significant interaction between the factors.

3.1.2 | sMMN latency

For finger stimulation, there was no significant difference in sMMN latency between fifth finger deviants ($M = 98$ ms) and third finger deviants (mean = 94 ms; $F(1, 26) = 0.236$, $p = .631$, $\eta^2 = .004$) conditions. For stimulation of the other body locations, sMMN latency was significantly shorter for

neck deviants ($M = 121$ ms) than for hand deviants ($M = 144$ ms; $F(1, 26) = 7.689$, $p = .01$, $\eta^2 = .056$).

3.2 | P300

3.2.1 | P300 amplitude

Grand-averaged waveforms at electrode Fz, Cz, and Pz are shown in Figure 5. The topographic maps showing the scalp distribution of differences between each deviant type and its corresponding control stimulus are shown in Figure 6. For

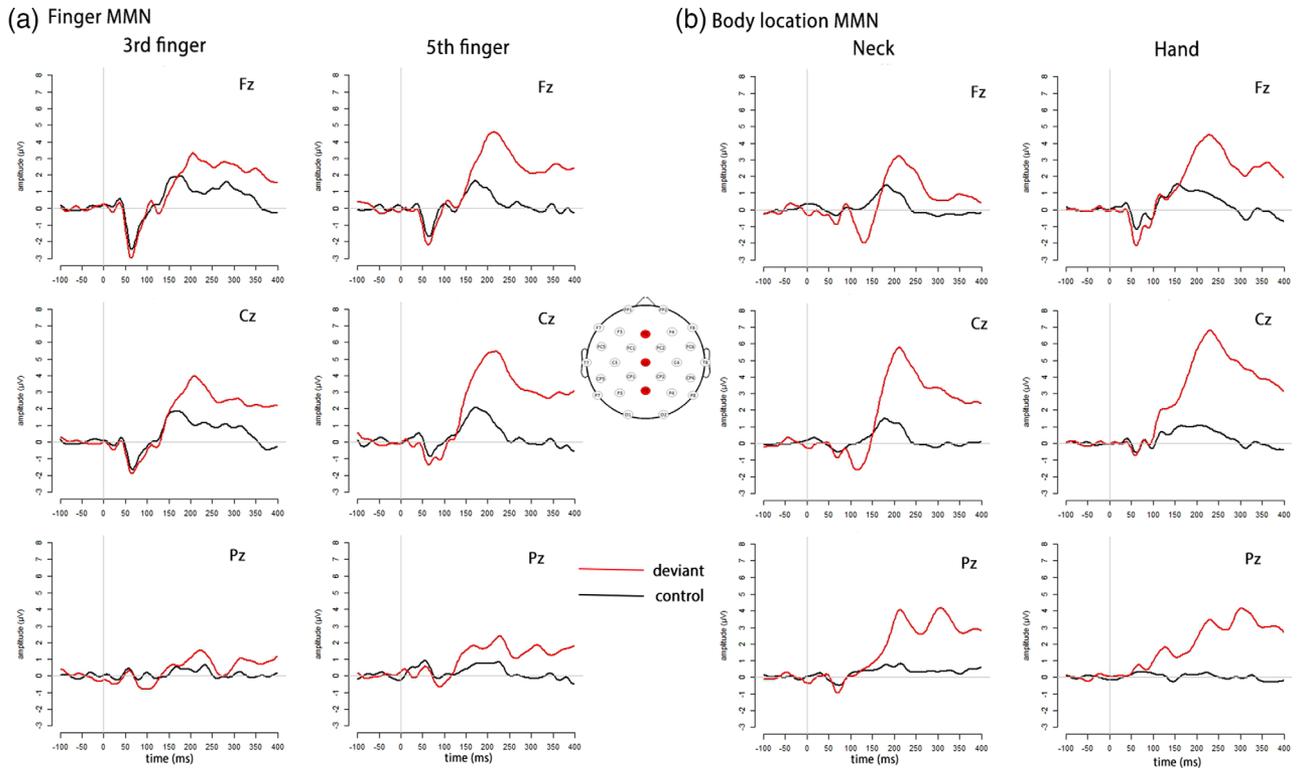


FIGURE 5 P300 waveforms. Grand-averaged ERP waveforms at Fz, Cz, and Pz in response to tactile stimuli presented as infrequent deviants (red) and frequent controls (black)

finger stimulation, there was a significant main effect of deviant type, $F(1, 26) = 4.599$, $p = .041$, $\eta^2 = .041$, with P300 for fifth finger deviants being larger than for third finger deviants. There was also a significant main effect of electrode, $F(1, 52) = 6.597$, $p = .011$, $\eta^2 = .065$. Pairwise t tests using FDR correction showed that P300 amplitude at Cz was significantly greater than at Pz and Fz (Cz > Fz, $p = .002$, Fz > Pz, $p = .014$). There was no significant interaction between deviant type and electrode.

For stimulation of the other body locations, there was a significant main effect of deviant type, $F(1, 26) = 4.922$, $p = .035$, $\eta^2 = .039$, with greater P300 amplitude for hand deviants than for neck deviants. There was also a significant main effect of electrode, $F(1, 52) = 29.391$, $p < .001$, $\eta^2 = .105$. Pairwise t tests with FDR correction showed that P300 amplitude was largest at Cz (Cz > Fz, $p < .001$; Fz > Pz, $p = .008$). No significant interaction was found between factors.

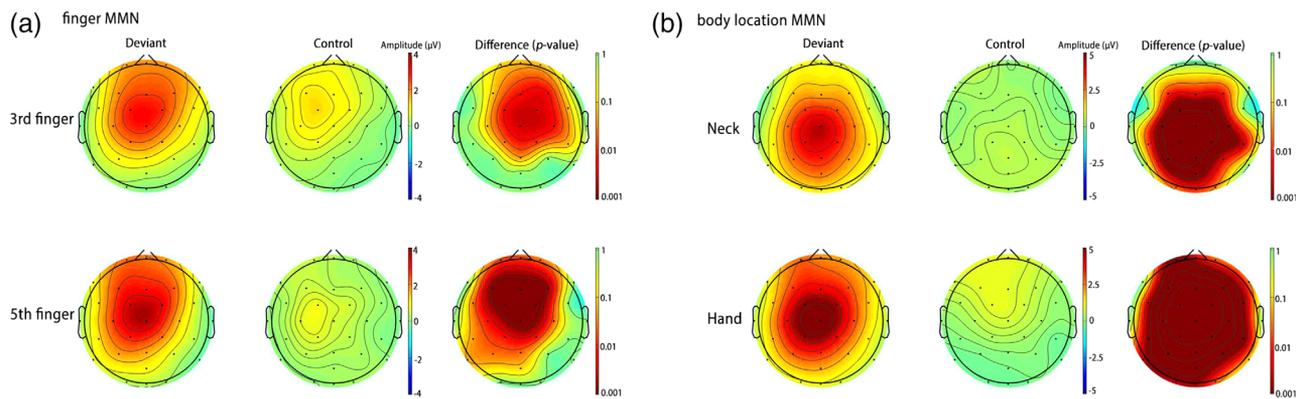


FIGURE 6 (a) Mean P300 amplitude (200–300 ms) for third finger (upper) and fifth finger (lower) presented as infrequent deviants among frequent index finger stimulation. Right column shows the topographic locations where the amplitude differs significantly between control and deviant stimuli ($p < .05$, with FDR correction). (b) Mean P300 amplitude (200–300 ms) for neck (upper) and hand stimuli (lower) presented as deviants during frequent lip stimulation

3.2.2 | P300 latency

For finger stimulation, mean P300 latency for fifth finger deviants (264 ms) was shorter than for third finger deviants ($M = 295$ ms), but the difference was not statistically significant, $F(1, 26) = 2.744$, $p = .109$, $\eta^2 = .044$. For stimulation of the other body locations, mean P300 latency was significantly shorter for neck deviants ($M = 252$ ms) than for hand deviants ($M = 286$ ms) $F(1, 26) = 7.645$, $p = .01$, $\eta^2 = .079$.

4 | DISCUSSION

Previous studies have successfully employed oddball paradigms to elicit sMMN responses to tactile stimulation of different points on the back of the hand (Akatsuka, Wasaka, Nakata, Kida, Hoshiyama et al., 2007) and to different fingers (Spackman et al., 2010; Strömmer et al., 2014). These studies have shown that stimulating different locations on the skin can evoke somatosensory mismatch responses, but how and whether the extent of spatial differences between stimulation points might modulate sMMN amplitude and latency has not previously been investigated. In the current study, we compared the influence of two spatial factors on sMMN amplitude: the relative positions of these body parts in the somatotopic organization of primary somatosensory cortex and the distance between two stimulated body parts on the 3D body surface.

Given what is known about time course and cortical generators of somatosensory mismatch responses, we hypothesized that the sMMN would be more sensitive to the relative positioning of the body parts in somatosensory cortex than to their physical distance on the body surface. In contrast, we predicted that the later P300 response would be less sensitive to cortical somatotopy: we hypothesized that the amplitude of the P300 would be larger for pairs of stimuli that were further apart on the body surface, regardless of the distance between the representations of these body parts in somatosensory cortex. We reasoned that the stimulation of two body parts that are further apart on the body surface presents a more perceptually salient contrast than the stimulation of body parts that are closer together, and therefore would elicit a larger P300 response.

Somatosensory MMN responses were elicited for all stimulated locations in a time window between 90 and 190 ms following onset of the tactile pulses. The sMMN was strongest over contralateral frontal-central regions, which is consistent with previous studies (Spackman et al., 2007; Strömmer et al., 2014). The P300 was also apparent in the ERP responses to the tactile deviants, appearing as a positive potential over frontal-central and central electrode sites in a window of around 200 to 400 ms after the onset of tactile stimulation.

The first part of the experimental protocol involved the stimulation of three different fingers, and as such did not involve a dissociation between the relative distances between the stimulated points on the body surface and the relative positioning of the representations of these points in somatosensory cortex. Consistent with our hypothesis that stimulating locations further apart on the body surface would result in larger P300 responses, the contrast between the second and fifth fingers resulted in significantly larger P300 responses than the contrast between the second and third fingers. However, the amplitude and latency of the sMMN were not significantly different across these two contrasts. The similarity in mismatch responses between the two deviant fingers suggests that the sMMN measured via low-density EEG recordings may have limited spatial resolution for closely spaced body parts. Another contributing factor may be the overlap of digit representations in the somatosensory cortex. Investigations of the somatotopic organization of digit representations at the cortical level have revealed overlap in the statistical parametric maps between fingers, both with fMRI (Maldjian, Gottschalk, Patel, & Detre, 1999; Sanchez-Panchuelo, Francis, Bowtell, & Sculpeck, 2010; Schweisfurth, Frahm, & Schweizer, 2014) and MEG (Baumgartner, Doppelbauer, & Sutherling, 1991). This prior work also suggests a degree of individual variability in this overlap, with some participants showing more clearly defined cortical representations for each digit, while others exhibiting a higher degree of overlap in digit representations.

The second part of the experimental protocol employed tactile stimulation of locations on the body that were more separated than the fingers that were stimulated in the first part of the experiment. Specifically, lip stimulation was used as the standard stimulus, with neck and hand stimulation being used as the deviant conditions. Significantly greater sMMN amplitude and shorter sMMN latencies were observed for stimulation of the neck in relation to lip stimulation, compared with stimulation of the hand in relation to lip stimulation. This suggests that, for body parts with greater separation than different fingers, the relative separation in cortical somatotopy exerts a stronger influence on sMMN amplitude than does the degree of physical separation on the 3D body surface. We speculate that the greater sMMN for the lip/neck contrast than for the lip/hand contrast is related to the relative positioning of the cortical representations of these body parts, such that the distance between the cortical representations of lip and neck is greater than the distance between lip and hand representations. This is consistent with our hypothesis that since the dominant generators of MMN responses are located in somatosensory cortex (Huang et al., 2005), the somatotopic organization of this cortical region should influence the patterning of the sMMN response to stimulation of different body parts.

For the P300 response, greater amplitude was observed for the lip/hand contrast than for the lip/neck contrast. This is consistent with our expectations given that the P300 component reflects the activity of frontal-parietal attentional networks that detect particularly salient levels of stimulus change. In this respect, we suggest that the P300 appears to be less sensitive to cortical somatotopy and may be more reflective of tactile processing in relation to the actual 3D human body in space.

Our findings also add a novel aspect to work showing a dissociation between MMN and P300 responses in other modalities (Horváth et al., 2008). The current results are also consistent with the suggestion that the sMMN may index an early bottom-up stage of novelty processing that involves the somatotopic organization of SI. Research using other experimental paradigms has suggested that tactile stimulation is initially processed in relation to cortical somatotopy, followed by a shift toward processing of the stimulation relative to other frames of reference (Azañón & Soto-Faraco, 2008; Engel, Maye, Kurthen, & König, 2013). Much of this work has examined the time course differences in the evoked response to somatosensory stimulation in response to postural manipulations such as hand crossing. This work has shown that the earliest components (<100 ms) are unaffected by postural modulations, with the effects of hand crossing becoming apparent at around 150 ms after tactile stimulation onset (Heed & Azañón, 2014; Rigato et al., 2013). These findings suggest various avenues for further investigation of sMMN and P300 responses to tactile stimulation. Specifically, one modification of our procedure that would be of interest is to use postural manipulations to alter the distance between body parts in external space (e.g., by recording EEG while the hand is held close to the mouth). Such manipulations would help clarify whether distance between bodily locations in space—and not just distances on the 3D body surface—may influence electrophysiological responses to novelty as recorded during tactile oddball paradigms.

Various theoretical interpretations of the MMN response have been proposed, including explanations involving predictive encoding (Garrido et al., 2009) and sensory memory (Näätänen, 1992; Näätänen & Winkler, 1999). Another potential explanation concerns stimulus-specific adaptation, according to which the MMN is a result of sensory neurons adapting to highly repetitive stimulation while at the same time retaining their responsiveness to deviant stimulus features (May & Tiitinen, 2010; Musall, Haiss, Weber, & von der Behrens, 2015; Nelken & Ulanovsky, 2007). Future investigations can examine whether stimulus repetition has the same attenuating or refractory effect on hand and neck sensory evoked potentials. In the auditory domain, methods have been established to control for refractory effects on MMN responses (e.g., Jacobsen & Schröger, 2001; Schröger & Wolff, 1996), but whether these methods can be applied

in the somatosensory domain needs further research. In addition, although we were able to control for possible perceptual differences between neck and hand stimulation by subtracting the ERPs of the physically identical control stimuli from the deviants, differences in perceived intensity or tactile sensitivity between the neck and hand regions could still have influenced sMMN and P300 amplitudes at these locations. Studies comparing sensory evoked potentials elicited by stimulation of these body locations (using longer interstimulus intervals and nonoddball paradigms) can shed light on this issue.

The findings from the current study suggest that the sMMN may be useful in the study of tactile processing, particularly for investigating the representation of the body in somatosensory cortex. Specifically, the tactile oddball paradigm used in the current study could be applied to investigate various influences on somatotopic body representations, such as motor experience (Bütefisch, Davis, & Wise, 2000; Candia, Wienbruch, & Elbert, 2003) and functional category boundaries between body parts (Knight, Longo, & Bremner, 2014). The sMMN may also prove useful for understanding disorders characterized by altered somatosensory discrimination, including cerebellar lesions (Chen et al., 2014; Restuccia, Marca, Valeriani, Leggio, & Molinari, 2007), coordination disorders (Sigmundsson, Hansen, & Talcott, 2003), and autism (Näätänen, 2009; Penn, 2006). The present study was conducted in typical adults, but because the elicitation of sMMN does not depend on participants' attention allocation and task performance, tactile oddball paradigms are potentially useful in contexts in which participants cannot be instructed to pay attention or give clear behavioral responses. Building on work in older children (Restuccia et al., 2009), the sMMN could be a useful tool in studying the development of body representations in infants (Saby et al., 2015), including the development of tactile remapping (Rigato et al., 2013). Future work employing the sMMN may shed further light on the development, plasticity, and maintenance of neural body maps (Marshall & Meltzoff, 2015).

In summary, the findings from the current study suggest novel avenues for examining somatosensory novelty processing, and provide a connection to an extensive body of literature on mismatch and P300 responses in other modalities. While further work is needed to clarify the characteristics and meaning of sMMN and P300 responses elicited by tactile oddball tasks, the present data suggest intriguing possibilities for follow-up investigations that can further draw from and inform current theorizing about the mechanisms and time course of somatosensory processing in the human brain.

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