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RESEARCH ARTICLE

Integrated approach for studying adaptation mechanisms in the human somatosensory cortical network

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Abstract Magnetoencephalography and independent component analysis (ICA) was utilized to study and characterize neural adaptation in the somatosensory cortical network. Repetitive punctate tactile stimuli were applied unilaterally to the dominant hand and face using a custom-built pneumatic stimulator called the TAC-Cell. ICA-based source estimation from the evoked neuromagnetic responses indicated cortical activity in the contralateral primary somatosensory cortex (SI) for face stimulation, while hand stimulation resulted in robust contralateral SI and posterior parietal cortex (PPC) activation. Activity was also observed in the secondary somatosensory cortical area (SII) with reduced amplitude and higher variability across subjects. There was a significant difference in adaptation rate between SI and higher-order somatosensory cortices for hand stimulation. Adaptation was significantly dependent on stimulus frequency and pulse index within the stimulus train for both hand and face stimulation. The peak latency of the activity was significantly dependent on stimulation site (hand vs. face) and cortical area (SI vs. PPC). The difference in the peak latency of activity in SI and PPC is presumed to reflect a hierarchical serial-processing mechanism in the somatosensory cortex.

Keywords TAC-Cell · Pneumatic stimulation · MEG · Face · Hand

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Introduction

Integration of inputs from different modalities and adaptation within cortical networks of the brain is essential for normal sensorimotor function. Adaptation is a widely observed mechanism at multiple levels of processing across all sensory channels of the nervous system (Hellweg et al. 1977; Ohzawa et al. 1982; Wilson 1998). Acting over a range of time scales, adaptation has been implicated in both shifting the sensitivity of the system to maximize the dynamic range of encoding and priming the system for responses to novel stimuli (Abbott et al. 1997; Fairhall et al. 2001; Muller et al. 1999). The sensory system adapts its input/output relation to the statistical properties of the dynamic changes in the environment, thus optimizing information transmission (Brenner et al. 2000). Despite evidence that somatosensory adaptation plays a significant role in sensory and functional motor recovery (e.g., after a cerebrovascular insult or stroke) (Staines et al. 2002), very limited information is available on adaptation patterns in different regions of the human

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somatosensory cortical network in response to controlled pneumotactile inputs.

The putative cortical network involved in somatosensory processing includes the primary somatosensory cortex (SI), secondary somatosensory cortex (SII), and somatosensory association areas like the posterior parietal cortex (PPC). SI contains four areas [Brodmann areas (BA) 3a, 3b, 1, and 2], which are densely interconnected with each other as well as with other sensorimotor areas, such as SII and PPC, the motor cortex and the supplementary motor area (Jones and Powell 1969a, b; 1970a, b). There is also a high degree of convergence and divergence of thalamocortical connections to SI (Padberg et al. 2009; Rausell et al. 1998). Numerous EEG and magnetoencephalography (MEG) studies have examined somatosensory processing mechanisms in SI using both electrical and tactile stimulation (for review, see Popescu et al. 2013). SII, located in the parietal operculum, is integral to sensorimotor function, such as sensorimotor integration (Huttunen et al. 1996), haptic size and shape perception (Hsiao 2008), guiding limb movement (Burton et al. 2002), integrating somatosensory information from both sides of the body (Manzoni et al. 1986; Ridley and Ettlinger 1976), object manipulation, and tactile learning (Binkofski et al. 1999). Notably, SII activation is enhanced during finger movements (Huttunen et al. 1996) and hand muscle contractions (Forss and Jousmaki 1998), which suggests an increase in the processing of tactile inputs during movement. Our previous MEG study (Popescu et al. 2013) using cutaneous stimulation of the hand showed that the evoked neuromagnetic activity in SII is not as consistently detected across subjects as in SI and, when present, is highly variable. PPC (BA 5 and 7) has dense interconnections with BA 1 and 2 of both ipsilateral and contralateral SI, and the thalamic association nuclei. It has been shown that BA 5 integrates complex tactile and proprioceptive information (Arezzo et al. 1981; Mountcastle et al. 1975), whereas BA 7 integrates somatosensory and visual information (Hyvarinen 1982; Sack 2009). SII and PPC have more complex receptive fields and physiological properties when compared to SI (Mountcastle 1995).

Our study aims to advance and assess a novel cutaneous stimulation methodology developed in our laboratory that is compatible with MEG in obtaining reliable neuromagnetic measures of evoked brain activity in an adaptation paradigm. We previously characterized adaptation in SI for face and hand stimulation (Venkatesan et al. 2010), and in SI, SII, and PPC for hand stimulation (Popescu et al. 2013) using a relatively large closed-bore (19.3 mm) pneumatic cell. In general, higher adaptation rates were found in higher-order somatosensory areas (SII and PPC) when compared to SI for hand stimulation. However, there is very limited information on the adaptation characteristics of SII and PPC to repeated stimulation of the face. There is evidence for the clinical relevance of such methodology, e.g., studying the changes in brain mechanisms in chronic pain, such as temporomandibular disorder (Alonso et al. 2010). In the present study, we conducted MEG experiments using pulsatile pneumotactile stimulation of the right lower face (at the nonglabrous oral angle), and the hand (at the glabrous surface of the distal phalanx of the right index finger) with a new TAC-Cell design that features an open bore of 6 mm to characterize the adaptation of the somatosensory cortical network. We used an independent component analysis (ICA)-based approach to derive measures of brain activity in areas of the somatosensory cortical network from the evoked neuromagnetic responses. We also aimed to test the feasibility and effectiveness of our new miniaturized second-generation open-chamber TAC-Cell design in delivering a more localized tactile input to the glabrous hand and/or lower face for studies of neural adaptation in the somatosensory cortical network (SI, SII, and PPC).

Methods

Participants

Nine healthy females [mean age = 24.2 years (SD = 3.2)] with no history of neurological disease participated in this study. Participants signed a consent form approved by the Institutional Review board of the University of Kansas after a detailed explanation of the study.

TAC-Cell

The second-generation TAC-Cell (Fig. 1a) was custom machined from acetal thermoplastic (OD = 15 mm, ID = 6 mm, $H = 6$ mm) with a 10/32″ barb fitting to allow the cell to be charged pneumatically A custom noncommutated servo motor (H2W Technologies, Inc., Santa Clarita, CA) coupled to a custom Airpel® *Anti-Stiction*® glass cylinder (Airpot Corporation, Norwalk, CT) operating under position feedback (Biocommunication Electronics, LLC, model 511 servo controller, Madison, WI), and computer control was used to dynamically modulate the internal pressure of the TAC-Cell. The computer was equipped with a 16-bit multifunction card (PCI-6052E, National Instruments, Austin, TX). Stimulus control signals were programmed with LabVIEW® software (National Instruments, v11.0) in our laboratory. These signals served as input to the servo controller and were also used to synchronously trigger neuromagnetic data acquisition by the MEG scanner.

This hardware configuration achieves synchronization between stimulus generation and MEG data acquisition. A 15-foot polyurethane line (1/4″ OD, 7/64″ ID) was used to

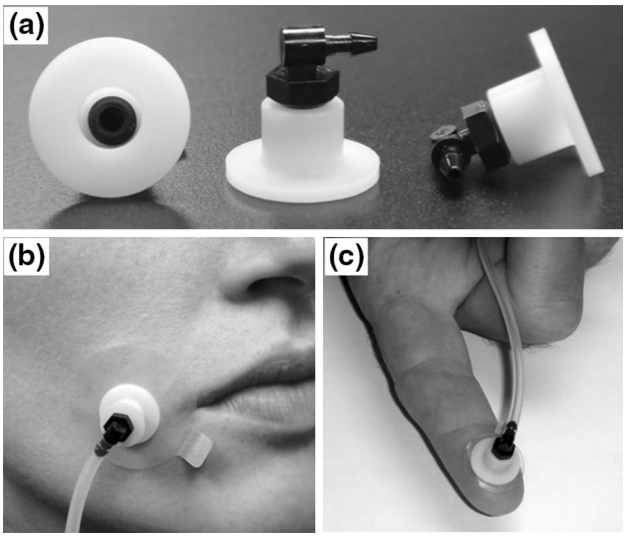

Fig. 1 **a** TAC-Cell in 3 views. Wide flange serves as the sealing surface to the skin via double-adhesive tape collars, **b** oral angle, and **c** index finger placement

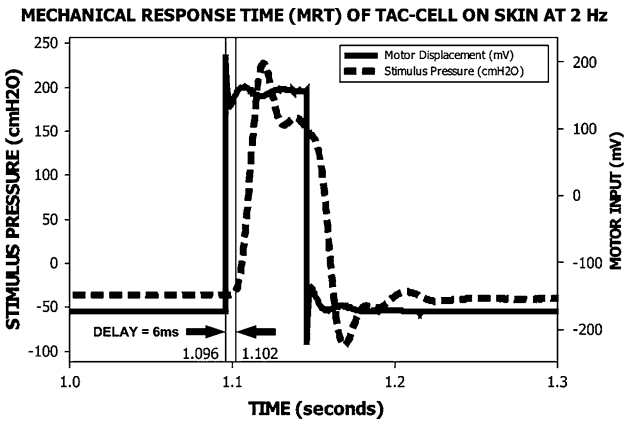

Fig. 2 Mechanical response time (MRT) calculation. Servo control voltage (*solid line*) and resultant air pressure at the TAC-Cell (*dotted line*)

conduct the pneumatic stimulus pulse (10–90 % intercept rise time = 8.5 ms) from the servo motor to the TAC-Cell placed on the participant in the MEG scanner. Mechanical response time (MRT), defined as the delay between leading edge of the pulse train voltage waveform and the corresponding TAC-stimulus displacement onset, was constant at 6 ms (Fig. 2) for all stimulus rates. The reported peak dipole strength latency values were corrected for the MRT of the TAC-Cell.

Participant preparation

A whole-head MEG system (CTF Omega, Coquitlam, BC, Canada) equipped with 151 axial-gradiometer sensors was used to record the cortical response to the TAC-Cell inputs. For each participant, the MEG recording session consisted of 4 runs corresponding to the two stimulation sites (hand and face) and two stimulation rates (2 and 4 Hz). Prior to the MEG recording session, each participant was fitted with three localization coils placed at the nasion, left and right preauricular points, to determine the head position with respect to the sensor array (the head position was registered for each run separately). Two bipolar EEG channels were used to record electrooculograms (EOG) in order to identify trials affected by ocular movement artifacts and eye blinks. The TAC-Cell was placed on the face at the non-glabrous surface of right oral angle (Fig. 1b) or the hand at the glabrous surface of the right index finger (Fig. 1c) using double-adhesive collars. Stimulus site and rate was counterbalanced among participants.

Following the MEG recording session, registration landmarks were placed at the same three positions of the localizing coils. TAC-Cells were removed from the skin sites, and participants were immediately placed inside an MRI scanner in an adjacent suite to image their brain anatomy.

Stimulus paradigm

A pneumatic servo controller was used to produce pulse trains (inter-train interval of 5 s, 125 reps/train rate). Each pulse train consisted of 6-monophasic pulses (50-ms pulse width). The term *adaptation* is used throughout this study to refer to the decrease in activity in a specific brain region in response to repetitive stimulation, and it does not infer plasticity. Short-term adaptation of the cortical neuromagnetic response to TAC-Cell patterned input was assessed using a randomized block design of two pulse train rates, including 2 and 4 Hz at each skin site (finger, oral angle). The 2 and 4 Hz stimulus blocks last for approximately 16 and 14 min, respectively.

MEG data analysis

Data pre-processing

The MEG data were digitally band-pass-filtered between 1.5 and 50 Hz using a bidirectional fourth-order Butterworth filter. Trials corresponding to 1 s before and after the stimulus were visually inspected for artifacts, and those containing movement or eye-blink artifacts were discarded. The remaining trials for each experimental condition were averaged, and the DC was offset using the pre-stimulus period as baseline. No <90 trials per participant in each experimental condition were used in averaging. For an accurate source estimation of the multiple component response, the averaged datasets for each participant and condition were decomposed using a PCA-filtering ICA algorithm (Delorme and Makeig 2004). PCA filtering was

performed to reduce the data dimensionality and to facilitate segregating the contribution of each independent component (IC) to the overall magnetic field. The number of components was determined for each dataset based on a significant decrease in the singular values of the spatiotemporal data matrix.

Source reconstruction

For each dataset, the source reconstruction was performed separately for each IC in CURRY (Compumedics Neuroscan, Charlotte, NC), using a spherically symmetric volume conductor model fitted to the skull (segmented from the MRI data). The source space was defined as a regular grid of points in the brain volume (average distance between points was 5 mm). Since the independence constraint in ICA relies entirely on the amplitude distribution of the sensor data and does not include assumptions about the underlying sources, each IC can reflect the activity of single or multiple synchronous neuronal generators (Vigario et al. 2000; Hironaga and Ioannides 2007; Delorme and Makeig 2004). We expect the sources accounting for SI, SII, and PPC activities to be spatially discrete and relatively distant from each other (spatially restricted to a narrow cortical area), and the net current for each source to have relatively constant orientation with respect to the sensors. Therefore, we determine that the ICA can separate these activities as single independent components and thus provide reasonably accurate source estimation of the multiple component response. Accordingly, the ICs of interest were localized using a two-step source reconstruction algorithm. First, a current density analysis using sLORETA (Pascual-Marqui 2002) was performed to verify whether single or multiple regional generators account for each IC and to identify the corresponding spatial peaks of activity. sLORETA uses the standardization of a minimum norm inverse solution and does not require a priori information about the number of active sources. Second, a location constrained dipole analysis (with the positions of the dipoles at the spatial peaks of activity retrieved by sLORETA) was performed to obtain estimates of the direction and strength for each active brain region. The dipole fitting procedure allows characterizing the source strengths using current units rather than the statistical measures retrieved by sLORETA.

Statistical analysis

Analysis of variance (ANOVA) was performed for SI activity with peak dipole strengths and latencies as dependent variables. Stimulus pulse index number (1–6), stimulus frequency (2, 4 Hz), and stimulation site (Face SI, Hand SI) were used as the independent variables. A separate ANOVA was performed for the hand stimulation condition to assess the dependence of the peak dipole strength and latencies on stimulus pulse index number (1–6), stimulus frequency (2, 4 Hz), and the response components (Hand SI, Hand PPC). Post hoc pairwise comparisons were performed using the Tukey method at 95 % confidence. This analysis allowed us to examine how these variables and their interactions influence peak dipole strength adaptation and their response latencies. Statistical analysis for this study was performed using IBM SPSS Statistics software (*v. 20*).

Results

Source locations

Hand stimulation resulted in the activation of the contralateral SI and PPC areas (Figs. 3, 4, 6), while face stimulation evoked a response only in the contralateral SI cortex (Figs. 4, 5). The results of source estimation (i.e., current density reconstruction using sLORETA) are shown for each of the ICs that correspond to SI and PPC response components for hand stimulation (Fig. 3), and SI components for face stimulation (Fig. 4). The activity maps shown on the cortical surface at the peak latency of the first pulse in the train (for 2 Hz stimulation frequency) are clipped at 80 % of the spatial maximum for each source. Consistent with our previous studies, where multiple digits or both lip vermilions were stimulated (Popescu et al. 2013; Venkatesan et al. 2010), the SII response was variable in latency and inconsistent across subjects for both stimulation conditions. In addition, the PPC activity could not be identified for face stimulation, and when present in the hand stimulation condition, the suppression of SII response was similar to the one observed in our earlier study (Popescu et al. 2013) that used the larger TAC-Cells. The results of

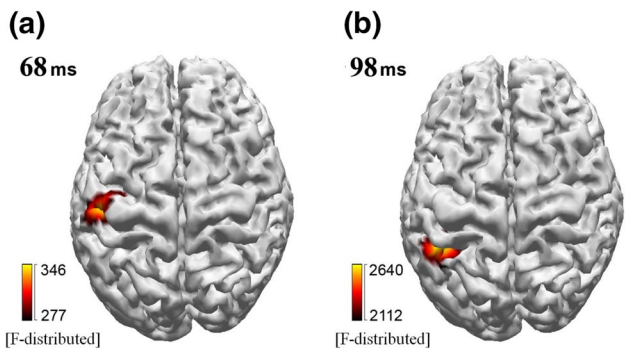

Fig. 3 Results of current density reconstruction are shown for SI (**a**) and PPC (**b**) for the hand stimulation condition (*superior view*) (SI = primary somatosensory cortex, PPC = posterior parietal cortex)

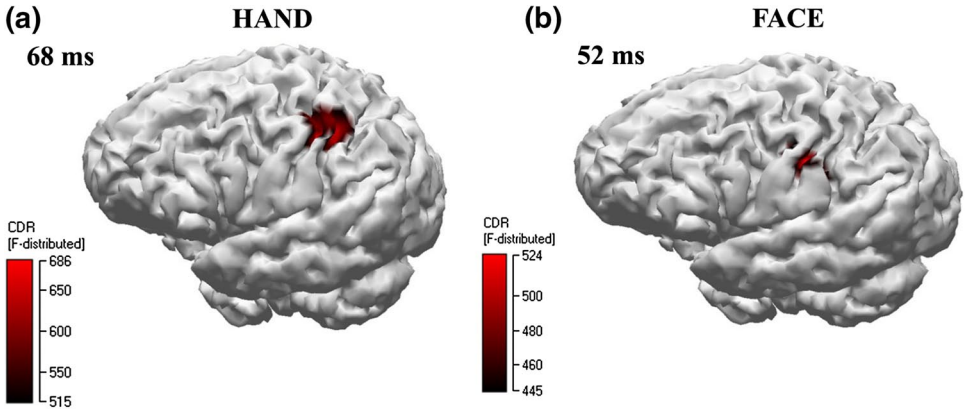

Fig. 4 Results of current density analysis at the peak latency of the SI response for the hand (**a**) and face (**b**) stimulation conditions (*lateral view*) (SI = primary somatosensory cortex)

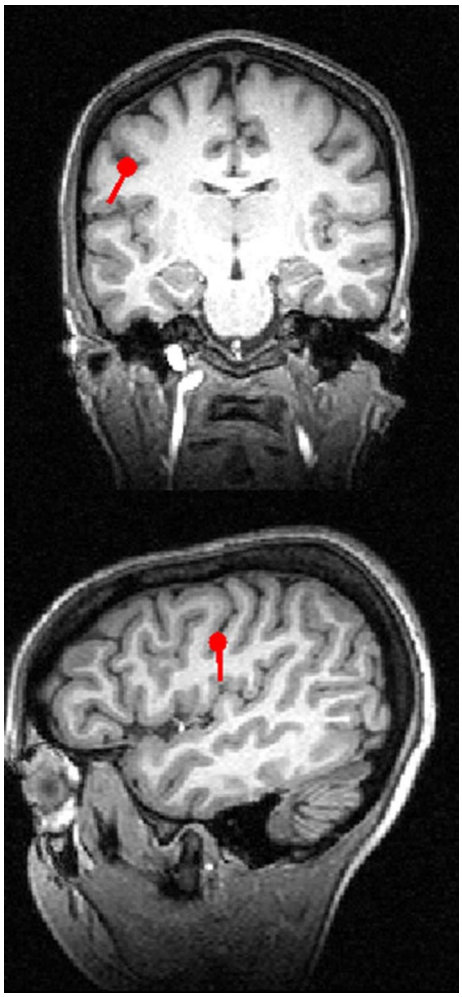

Fig. 5 Dipole locations are shown in orthogonal axial and sagittal MRI slices for the SI during face stimulation (SI = primary somatosensory cortex)

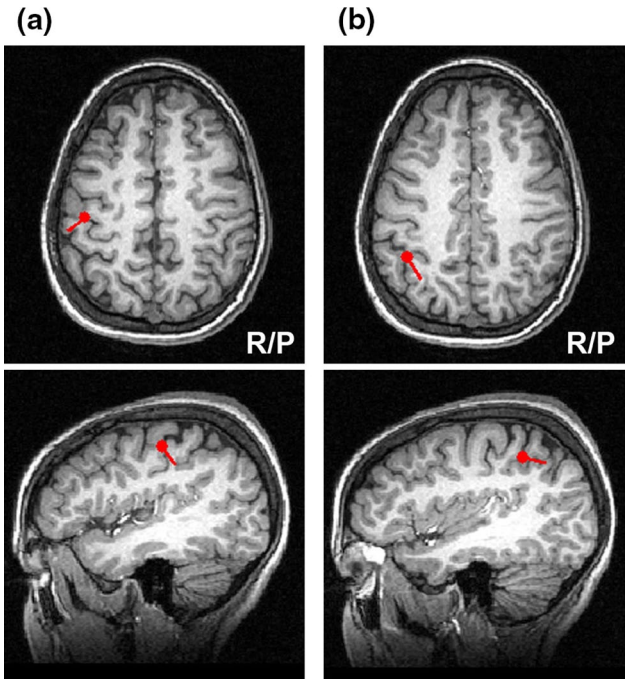

Fig. 6 Dipole locations are shown in orthogonal axial and sagittal MRI slices for the SI (**a**) and PPC (**b**) activation during hand stimulation [SI = primary somatosensory cortex, PPC = posterior parietal cortex]

source reconstruction (i.e., sLORETA-constrained dipole fitting) are exemplified in Figs. 5 and 6 on T1-weighted MRI orthogonal images. For the early (first) response component, dipoles were localized in the anterior wall of the postcentral gyrus, consistent with generators in the proximal neuronal populations of SI areas 3b and 1. Dipoles for the second response component observed for hand stimulation were localized in regions of the postcentral sulcus, posterior, and slightly medial with respect to the SI source. The results are in agreement (Table 1) with the somatotopic organization of the primary somatosensory cortex with the face SI source (mean $\Delta x = -38$ mm, SD = 7 mm; mean $\Delta y = -5$ mm, SD = 5 mm; mean $\Delta z = 73$ mm, SD = 9 mm) represented more toward the base of the postcentral gyrus, i.e., more laterally, anteriorly, and inferiorly than the Hand SI (mean $\Delta x = -41$ mm, SD = 5 mm;

Table 1 Face SI, Hand SI, and PPC source locations and latencies

Source	Location (mm)			Peak latency (ms)
	x (right–left)	*y* (posterior–anterior)	*z* (inferior–superior)	
Face SI	−38 ± 7	5 ± 5	73 ± 9	52 ± 6
Hand SI	−41 ± 5	1 ± 8	84 ± 6	66 ± 5
Hand PPC	−37 ± 6	−3 ± 12	86 ± 7	96 ± 7

Mean ± SDs across subjects are expressed in a Cartesian system of coordinates based on external landmarks on the scalp, with the *x*-axis going from left to right through preauricular points, *y*-axis from the back of the head to nasion, and *z*-axis pointing toward the vertex

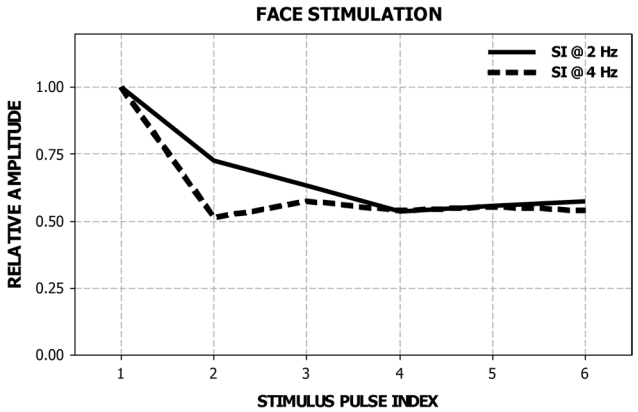

Fig. 7 Peak dipole strength adaptation in SI for face stimulation [SI = primary somatosensory cortex]

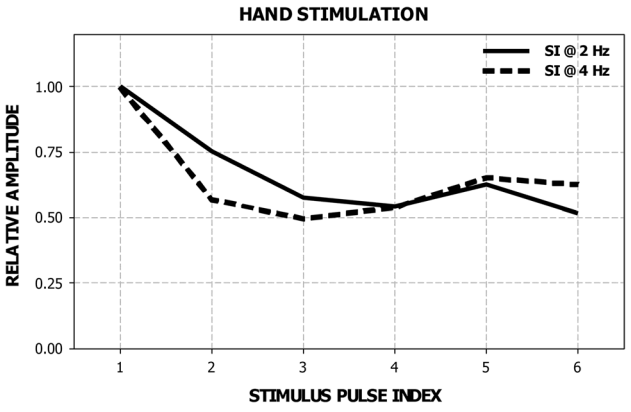

Fig. 8 Peak dipole strength adaptation in SI for hand stimulation [SI = primary somatosensory cortex]

mean $\Delta y = 1$ mm, SD = 8 mm; mean $\Delta z = 84$ mm, SD = 6 mm). The PPC component for hand stimulation was more medial (mean $\Delta x = 3$ mm, SD = 5 mm), more posterior ($\Delta y = -4$ mm, SD = 10 mm), and more superior ($\Delta z = 2$ mm, SD = 3 mm) with respect to the Hand SI, consistent with our previous study (Popescu et al. 2013).

Peak response amplitude

Inter-subject variability in the absolute response amplitude for the SI and PPC sources can be caused by neuroanatomical differences or physical factors like variability in the orientation of current sources relative to local radial direction, and they were eliminated by normalizing the peak dipole strength with the corresponding peak amplitude of the first response in the train. Figures 7, 8 and 9 show the mean normalized peak amplitudes for each pulse index number as a function of stimulus frequency, stimulus site, and the response component for face and hand stimulation, respectively. In general, the relative peak dipole strengths of SI and PPC (for hand stimulation) attenuate rapidly after the first stimulus pulse index number for both hand and face stimulation (Figs. 7, 8, 9). Maximum attenuation in peak response amplitude generally occurs in the response corresponding to the second pulse index. Further decay is

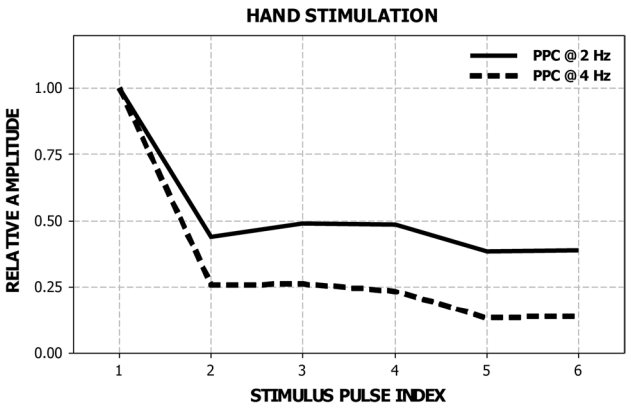

Fig. 9 Peak dipole strength adaptation in PPC for hand stimulation [PPC = posterior parietal cortex]

observed for the subsequent pulse index numbers but the observed attenuation is comparatively smaller. The PPC responses exhibit a more pronounced decay of the peak dipole amplitude when compared to SI responses for both 2 and 4 Hz (Figs. 8, 9). An ANOVA was performed on the peak response amplitude (dependent variable) for each SI response component (Face SI, Hand SI), stimulation frequency, and stimulus pulse index numbers. Significant

main effects of stimulus frequency [$F(1,161) = 4.09$, $p < 0.05$)], stimulus pulse index [$F(5,161) = 8.07$, $p < 0.001$)], and response component [$F(1,161) = 4.07$, $p < 0.05$)] were observed. No significant interaction effects were observed. All comparisons had an effect size (R^2) of 0.57. An ANOVA was performed on the peak response amplitude (dependent variable) for each response component recorded during hand stimulation (Hand SI, Hand PPC), stimulation frequency, and stimulus pulse index numbers. Significant main effects of stimulus pulse index [$F(5,167) = 13.25$, $p < 0.001$)], and response component [$F(1,167) = 30.18$, $p < 0.001$)] were observed. No significant interaction effects were observed. All comparisons had an effect size (R^2) of 0.41. Post hoc Tukey comparison tests showed a significant difference in the peak response amplitude only for pulse index 1 when compared to pulse index numbers 2–6 ($p < 0.05$) for all stimulation frequencies and response components. There were no significant differences in peak response amplitudes between the other pulse index numbers (2–6).

Peak response latency

To test for the presence of stimulation rate- and SI-dependent adaptation effects on the response latency, an ANOVA was performed, with stimulation frequency, SI response component, and pulse index number as independent variables, and the peak response latency as dependent variable. Results indicate significant main effects of the response component [$F(1,161) = 222.44$, $p < 0.001$)] with an effect size (R^2) of 0.64. ANOVA tests for stimulation rate, and hand stimulation response component (Hand SI, Hand PPC) dependent adaptation effects indicate a significant main effect of the response component [$F(1,167) = 910.62$, $p < 0.001$)] with an effect size (R^2) of 0.87. There was no pulse index number-specific adaptation of the SI, or PPC response latencies. Peak response latencies for each individual component for face and hand stimulation are summarized in Table 1. Mean peak response latencies for each individual response component (Face SI, Hand SI, and Hand PPC) are shown in Fig. 10.

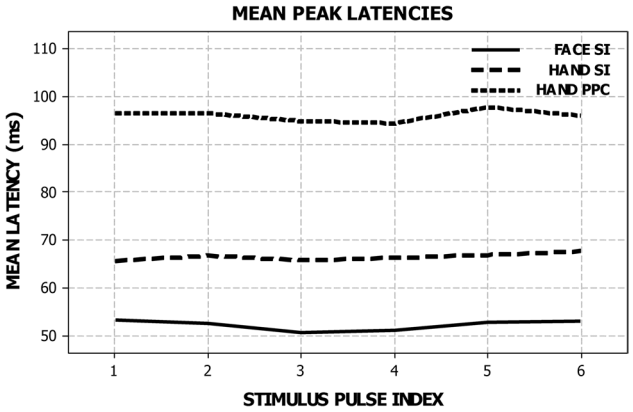

Fig. 10 Comparison of peak latencies for the primary somatosensory cortex (SI) and posterior parietal cortex (PPC) activation during face and hand stimulation

Discussion

Electrical stimulation of the peripheral afferent nerves can result in a highly replicable cortical response. However, stimulation using this modality bypasses the sensory receptors of the skin, entrains undifferentiated afferents, and generates "*unnatural*" interactions at subcortical and cortical levels (Willis and Coggeshall 1991). Mechanical stimulation of the facial region in the MEG environment presents technical challenges due to electrical interference produced by devices like piezoelectric crystals, linear motors and actuators, or the added challenge of signal spread, calibration and tedious setup associated with air-puff stimuli.

The MEG/MRI compatible TAC-Cell developed in our laboratory was highly effective in activating the somatosensory cortex in healthy adult participants (Venkatesan et al. 2010). The newer, small-bore TAC-Cell used in the present study is highly efficient in producing a controlled, punctate, inaudible stimulus and has the capability to displace the skin at a specified site to produce an adequate cortical response. Repetitive patterned pneumatic stimulation of the hand and face using the miniature TAC-Cells evoked responses in SI and somatosensory association areas like PPC (only for hand stimulation). This allowed for a comparison of the characteristics of cortical adaptation in multiple levels of the somatosensory cortical network.

Evoked regional brain activity

Many experimental studies have shown that the PPC plays a role in multimodal stimulus integration, e.g., audiotactile processing (Gobbele et al. 2003), and during visual-manual exploration tasks like grasp, self-feeding behaviors, and coordinated motor tasks that involve the hands (Fogassi et al. 2005; Hinkley et al. 2009; Hyvarinen 1982). Activity in the PPC has also been observed during median nerve stimulation (Forss et al. 1994), as well as vibrotactile (Bardouille and Ross 2008) and pneumotactile (Popescu et al. 2013) stimulation of the hand. No study to date has shown that the PPC is activated during repetitive passive tactile stimulation of the face. Somatotopic representation of the hand and foot has been observed in the PPC, with the hand area being closer to SI when compared to the foot (Hoshiyama et al. 1997). In the same study, lip stimulation showed

no consistent activity in the PPC, leading to the speculation that the lip area might not be represented in the PPC. The absence of PPC response during TAC-Cell stimulation of the face seems to corroborate the idea of the absence of face representation in the PPC. In an earlier study (Alonso et al. 2010), consistent activation of the postcentral gyrus (SI) and parietal operculum (SII) was observed in response innocuous tactile stimulus delivered to the face, and distinct changes in SI and SII activity were identified and compared between healthy adults and patients with chronic pain. Activation was less reliable across subjects in other regions of the brain, such as the supramarginal gyrus and angular gyrus in the parietal lobe, which supports our findings of inconsistent activity in PPC. The characteristics of the stimulus (e.g., stimulus size and shape, static vs. dynamic stimulus patterns) may play an important role in this regard too, as the PPC has been shown to integrate activity from multiple concurrent sensory inputs (e.g., adjacent but distinct cutaneous areas).

In contrast, bilateral evoked responses in the ventrolateral somatosensory association areas (SII) were not clearly identifiable during face or hand stimulation. Suppression of SII activity during hand stimulation was observed in a prior study (Popescu et al. 2013) using the TAC-Cell. Significant SII activation was not observed in a similar study that used a pneumatic device to deliver a vibrotactile stimulus to the index finger (Bardouille and Ross 2008). The nature of the somatosensory stimulus required to activate SII has not fully been understood. Electrical stimulation represents a more unnatural mode of stimulation when compared to delivering a punctate mechanical stimulus using the TAC-Cell. Electrical stimulation results in bilateral SII activity (Forss et al. 1994), but recruits many undifferentiated fibers, and increases the probability of evoking a response. The large, bilateral receptive fields in SII respond more vigorously to a moving stimulus than a stationary stimulus (Bodegard et al. 2001; Disbrow et al. 2000). A consistent cortical response is observed in the SII when a larger area of the skin is stimulated (e.g., via a rotating brush), or when the task involves sensorimotor integration (e.g., tactile discrimination of roughness, shape, or texture, object manipulation). Repeated stimulation of a small, focal area on the face or finger using a passive stimulator like the TAC-Cell might not be adequate to induce a consistent SII response.

Response amplitudes

The magnitude of attenuation of SI and PPC response depends on the stimulus frequency and pulse index with attenuation being most prominent at higher frequencies for both hand and face stimulation. PPC response amplitudes exhibit a higher sensitivity to repeated stimulation of the hand. This may be due to hierarchy in the SI–PPC network, and the associative areas inheriting the adaptation in SI, and appears consistent with the hypothesis that PPC is involved in higher-order stimulus processing and has a more complex multisensory receptive field.

Response latencies

The significant difference between the latencies of peak dipole strengths of hand and face SI, and hand PPC is attributable to the difference in axon length and distance from the mechanosensory nerve terminals in the lip and hand to their central targets in SI. A short delay in the PPC response reveals the hierarchy in the serial-processing mechanism that exists in the somatosensory cortical network. These results may also reflect the role of the somatosensory association areas in sensorimotor integration. Rapid processing and integration of tactile and proprioceptive data from afferent receptors and muscle spindles is essential for continuous relay of this information to the related motor areas (Lederman and Klatzky 1987).

Study limitations

Variability in brain activity is present both intra-train, i.e., from pulse to pulse, and inter-train. Averaging across trains mitigates the inter-train variability by spatially smoothing the field distribution. Intra-train, the signal-to-noise ratio differs from pulse to pulse, and thus is expected to affect the source amplitude estimation for each pulse individually. However, we performed dipole fitting on the signals reconstructed from a single IC, and the field distribution does not change with time, and implicitly with pulse index.

Conclusion

This study reveals that repeated stimulation of either the face or hand with the same stimulus pattern was effective in inducing adaptation in SI responses. Peak SII responses were highly attenuated for both hand and face stimulation. A more complex stimulus pattern or stimulation of a larger target area might be required to activate SII in a consistent manner, as detectable SII peak responses to repeated confined cutaneous tactile stimuli were not observed in earlier studies (Bardouille and Ross 2008; Popescu et al. 2010). Difference in short-term adaptation patterns and peak response amplitudes of the hand and face may be related to differences in mechanoreceptor typing and musculature between these regions. The peak amplitude of SI and PPC response depends on the stimulus frequency and pulse index for both hand and face stimulation. Absence of PPC response during face

stimulation leads us to speculate that the face area might not be represented in the PPC. We anticipate that our feasibility study on the integration of our innovative TAC-Cell stimulator and novel MEG data analysis approach will support future research and clinical investigations, e.g., studies of plasticity in specific pathologies, such as chronic pain or sensorimotor rehabilitation associated with cerebrovascular stroke.

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Conflict of interest Drs. Barlow and Venkatesan are the inventors of the TAC-Cell, which is registered and licensed by the University of Kansas to Epic Medical Concepts and Innovations, Incorporated (Olathe, KS, USA). There are no additional conflicts of interest with any of the commercial manufacturers listed in this research paper.

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