

Vision of the Body Modulates Somatosensory Intracortical Inhibition

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The magnitude of somatosensory evoked potentials (SEPs) elicited by simultaneous electrical stimulation of adjacent digits is generally less than the sum of potentials evoked by stimulation of each digit individually. This under-additivity suggests suppression between representations of adjacent skin regions and may reflect a process of lateral inhibition by interneurons in somatosensory cortex. Given that simply viewing the body enhances tactile acuity and that tactile acuity depends on cortical lateral inhibition, we investigated how viewing the body modulates suppressive interactions between simultaneous afferent volleys from adjacent fingers. We recorded SEPs evoked by electrical stimulation of the right index and middle fingers, either individually or simultaneously, while participants viewed either their own hand or an object. In between trains of electrical stimuli, participants discriminated the orientation of tactile gratings applied to either finger. Consistent with previous findings, viewing the hand enhanced tactile acuity. Furthermore, viewing the hand increased the suppression of the P50 potential due to simultaneous electrical stimulation of both fingers. Moreover, the visual enhancement of tactile performance correlated across participants with the visual modulation of suppression. These results demonstrate that vision enhances somatosensation by modulating activity of inhibitory interneuronal circuits in the somatosensory cortex.

Keywords: lateral inhibition, multisensory integration, suppressive interaction, visual enhancement of touch

Introduction

The different senses do not work in isolation but interact in several ways. Most research on multisensory perception has focused on cases of “convergence” between inputs from different sensory modalities, such as individual neurons that respond to inputs from multiple modalities (Meredith and Stein 1983). A second, less investigated, form of multisensory interaction occurs when activity from one sensory modality modulates activity in another. Multisensory convergence can be considered as a largely feedforward process in which information from different sensory modalities is increasingly pooled to generate supramodal representations. In contrast, multisensory modulation involves either horizontal interactions between different sensory pathways or top-down influences on predominantly unimodal functions. Multisensory convergence and multisensory interaction co-occur in many perceptual situations. Here, we investigate the neural basis of a particular form of multisensory modulation, in a case where the contribution of feedforward convergence of multisensory input can be excluded.

Simply viewing the body improves tactile perception, relative to viewing an object in the same location, an effect

known as “visual enhancement of touch” (Kennett et al. 2001). This effect does not result simply from feedforward convergence of visual and tactile information since it occurs even when vision is entirely noninformative about touch. Explanations based on multisensory spatial attention are also insufficient since the touched body part and the object were made to appear at the same spatial location using an arrangement of mirrors. Since vision provides no information about the tactile stimulus, but only a multisensory context in which tactile information occurs, such effects cannot simply be explained as integration of tactile and visual information. Rather, viewing the body seems to provide a visual context or “set” that enhances tactile processing. This contextual interpretation is further supported by the finding that visual enhancement of touch (VET) persists for some seconds of darkness after viewing the hand (Taylor-Clarke et al. 2004).

The neuronal mechanisms underlying contextual multisensory enhancement remain unclear. Two previous studies investigated the possible locus of the VET effect. Taylor-Clarke et al. (2002) measured mechanical somatosensory evoked potentials (SEPs) in a 2-point discrimination task while viewing the arm or an object. They found that the N80 component was enhanced while viewing the arm. This component has been identified with a second wave of recurrent processing within primary somatosensory cortex (SI; Allison et al. 1992). A similar conclusion was reached by Fiorio and Haggard (2005), who found that a single transcranial magnetic stimulation (TMS) pulse over primary somatosensory cortex, during a brief dark interval between vision and touch, abolished the visual enhancement of touch. TMS over another area in the somatosensory pathway, SII, was ineffective. These neurophysiological results receive further support from the finding of Serino et al. (2009) that viewing the hand also improves tactile discrimination not only on the hand but also on the cheek. Since the overlap of hand and face representations is a peculiarity of the somatotopic organization of SI but not of other cortical tactile maps (Huang and Sereno 2007), this again suggests that the VET effect involves SI.

While these findings suggest that visual enhancement occurs within SI, the specific neuronal mechanism involved remains unclear. Several observations suggest that the mechanism is independent of the stimulated skin region but specific to the type of judgment made. Viewing the arm (Kennett et al. 2001), hand (Taylor-Clarke et al. 2004), or foot (Serino et al. 2009) all improve tactile discrimination on the viewed body part. On the other hand, while vision enhances tactile spatial discrimination, it does not affect simple detection thresholds (Harris et al. 2007). Similarly, viewing the body modulates the spatial gradient of tactile masking, producing a more highly focused spatial pattern of interference from distractors, compared with viewing an object (Haggard et al. 2007). These effects suggest that viewing the body does not produce an undifferentiated

enhancement of all somatosensory processing but specifically improves tactile spatial resolution by sharpening the spatial tuning of tactile receptive fields (RFs). These changes are consistent with a reduction of RFs size of somatosensory cortical neurons. These psychophysical findings are worth describing in some depth because they provide important insights into a potential neuronal mechanism. In particular, the VET effect seems to respect the macroscopic RF organization of SI and to modulate tactile discrimination by functional regulation of RFs size.

Given evidence that VET operates by reducing the size of tactile RFs, one attractive hypothesis is that viewing the body shrinks tactile RFs in SI by increasing lateral inhibition. Lateral inhibition is a neuronal mechanism that is widespread in sensory cortical areas and has a major role in spatial acuity. Briefly, a local network of inhibitory interneurons connects adjacent cortical neurons so that firing of one cortical neuron tends to lead to inhibition of its neighbors. This arrangement enhances responses to small spatially detailed stimuli since these do not trigger the lateral inhibition from neighboring RFs that are triggered by larger stimuli. As a result, increases in lateral inhibition tend to increase spatial acuity. This general principle has been confirmed by neurophysiological studies of RFs of SI neurons. Many SI neurons have inhibitory regions adjacent to a central excitatory area (DiCarlo et al. 1998). This organization is controlled by γ -aminobutyric acid (GABA)ergic inhibitory interneurons within SI since administration of GABA antagonists such as bicuculline produces a dramatic enlargement of the RF. Thus, under normal circumstances, lateral inhibition reduces the RF to a small central subsection of the skin region that sends excitatory inputs to the neuron (Dykes et al. 1984). This modulation of the RF serves to improve detection of fine tactile details such as points and edges (Brown et al. 2004). Psychophysical measures of tactile spatial perception, such as 2-point discrimination and grating orientation, thus depend strongly on intracortical inhibitory function. Therefore, the capacity to modulate the local interneuronal network that provides lateral inhibition may be an important means to flexibly enhance perception. However, direct evidence for such modulation is lacking.

In the somatosensory system, suppressive interactions between adjacent stimuli are thought to be an index of intracortical inhibitory function. Several studies have shown that the somatosensory evoked response elicited by 2 stimuli applied simultaneously to adjacent skin regions, or to different nerves, is reduced relative to the sum of responses evoked by stimulating each skin region or nerve independently (Gandevia et al. 1983; Hsieh et al. 1995; Ishibashi et al. 2000). This suppression phenomenon is thought to depend on the presence of inhibitory interneuronal connections between cortical neurons, for 3 reasons. First, suppression follows the somatotopic RF organization. Suppressive interactions are stronger when simultaneously stimulating the digital nerves of fingers II and III compared with II and V (Ishibashi et al. 2000). Second, analysis of somatosensory evoked field components showed suppressive interaction in several structures along the somatosensory pathway, with stronger interactions in the cortex than in brainstem or thalamus (Hsieh et al. 1995). Third, somatosensory interactions can vary with the functional state of the sensorimotor system (Haavik Taylor and Murphy 2007).

Conclusive evidence linking suppressive interaction, interneuronal inhibitory networks, and acuity would require intervention studies, for example, using GABA antagonists, which have not yet been conducted. However, studies in

rodents demonstrate the contribution of GABAergic interneurons to suppression. Recordings from neurons in the primary somatosensory forepaw representation in anesthetized raccoons showed that administration of a specific GABA_B receptor antagonist, CGP 55845, produces significant enlargement of RFs (Chowdhury and Rasmusson 2002). A similar effect was observed using administration of bicuculline methiodide, a GABA_A receptor antagonist (Tremere et al. 2001). Conversely, the GABA_B receptor agonist baclofen reduced RF size in most somatosensory neurons studied and enhanced the ON-centre/OFF-surround organization of somatosensory RFs (Kaneko and Hicks 1990; Chowdhury and Rasmusson 2002). Thus, both GABA_A and GABA_B play a major role in regulating RF boundaries by suppressing neuronal responses.

In this study, we tested the hypothesis that vision of the body enhances touch by modulating somatosensory intracortical inhibition. We combined a tactile spatial discrimination task with an electroencephalography (EEG) measure of intracortical suppression, while participants looked directly either at their own hand or at an object. We measured suppression of SEPs elicited by simultaneous electrical stimulation of adjacent fingers as an index of the state of cortical networks underlying lateral inhibition. We predicted that viewing the body would lead to an increase in somatosensory intracortical inhibition, and hence, to an increase in the suppressive interaction between SEPs for adjacent skin regions. Furthermore, this increased inhibition should be associated with improved tactile acuity.

Materials and Methods

Participants

Fifteen naive paid healthy volunteers (age 20–35, mean 25.5, 8 females) participated in the experiment. All participants were right-handed as assessed by the Edinburgh Inventory (Oldfield 1971; M: 83.7, range: 11.1–100). They reported normal or corrected-to-normal vision and no abnormalities of touch. Procedures were approved by the University College London (UCL) research ethics committee and were in accordance with the principles of the Declaration of Helsinki.

Stimuli and Procedure

Participants sat at a table with their right arm resting palm-up on a cushion, arranged so that the participants had a clear view of their hand. Electrical stimulation was delivered via a pair of ring electrodes placed over the distal phalanges of the right index and middle fingers with a cathode 1 cm proximal to the anode, at a rate of 2 Hz. Stimulation was delivered with a neurophysiological stimulator (a Digitimer stimulator was used for 6 participants and a custom Stanmore stimulator, Medical Physics Department, UCL, for the others) as a square-wave pulse current, for 0.2 ms, at an intensity 1.4 times higher than individual sensory threshold (see later). In different blocks, the index finger, the middle finger, or both were stimulated. There were 450 stimuli delivered in each experimental block.

There were 2 visual conditions: viewing one's own hand or viewing an object. In the view hand condition, participants were asked to focus their visual attention and gaze directly at the fingers of their stimulated right hand. In the view object condition, at the beginning of the block, a box was moved over the hand, and participants were asked to focus their visual attention and gaze on a wooden block (ca. hand-sized) fixed to the surface of the box. Blocks randomly alternated between view hand and view object conditions.

To measure effects of vision on tactile acuity, participants made judgments of the orientation of square-wave gratings (Van Boven and Johnson 1994) applied to the tip of either the right index or middle finger. The finger touched varied between blocks. The gratings were applied periodically between the shocks. In each block, 30 gratings were manually applied by the experimenter, half running along, and

half across, the long axis of the finger. The experimenter held the grating in readiness directly above the fingertip. As soon as the train of shocks stopped, the experimenter received a visual signal to deliver the tactile stimulation. Thus, tactile stimulation and electric shocks always occurred at different interleaved times. The number of electrical stimulations between touches was randomly varied (10 or 20) to make the timing of touch unpredictable, thereby forcing participants to maintain tactile attention continuously.

Care was taken to ensure that viewing the gratings did not provide any information about the tactile task. The outer visible edge of the tactile grating stimuli was wrapped in plastic so that no visual information about grating orientation was available. Furthermore, in the view object condition, a second grating was held above the object and pressed down on the object at the same time as the to-be-judged grating was presented to the participant's finger. Thus, the temporal and attentional cues provided by seeing the approach of the tactile grating were equivalent in the 2 visual conditions. Participants made unsped verbal judgments of grating orientation.

Participants completed 12 blocks, each representing a different combination of visual condition (view hand, view object), stimulated finger (index, middle, both), and touched finger (index, middle) (see Fig. 1). Since we were interested in visual modulation of SEPs and tactile acuity, regardless of which finger has been touched, our main analysis averaged across all blocks in which the same finger was stimulated, regardless of which finger was touched.

Electrophysiological Recordings

A SynAmp amplifiers system and Scan 4.3 software (Neuroscan) were used to record EEG data. Sixteen scalp electrodes were recorded (FP1, FP2, F3, F4, C5, C3, Cz, C4, C6, CP5, CP3, CPz, CP4, CP6, O1, O2), according to the 10-20 System. The reference electrode was AFz and the ground electrode was placed on the chin. Electrode impedances were kept below 5 K Ω . The left and right mastoids were also recorded. Horizontal electroculogram (EOG) was recorded from bipolar electrodes placed on the outer canthi of each eye, and vertical EOG was recorded from bipolar electrodes placed above and below the right eye. EEG signals were amplified and digitized at 1 KHz.

EEG data were analyzed with EEGLAB (Delorme and Makeig 2004). Data were re-referenced to the average of the mastoids. Epochs of 250 ms were extracted from the raw EEG data from 50 ms before each shock to 200 ms after electric shock onset. For each epoch, signal between 2 and 13 ms after electric shock onset was linearly

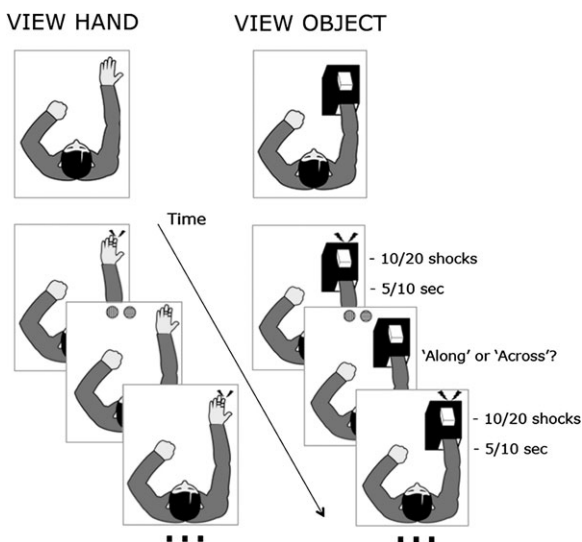


Figure 1. Experimental paradigm. All participants performed 12 blocks, lasting ~5 min each, while EEG activity was recorded. In between electrical stimulations of fingers, participants were asked to judge the orientation of gratings applied to the tip of their right index or middle finger. Visual conditions, electrically stimulated fingers, and touched fingers were blocked and counterbalanced.

interpolated in order to remove electrical artifact. Data were then digitally low-pass filtered at 70 Hz. Trials with eyeblinks (any of FP1 and FP2, HEOG left and right, VEOG up and down exceeding $\pm 80 \mu\text{V}$) or with voltage exceeding $\pm 120 \mu\text{V}$ at any channel between -50 and 200 ms relative to each shock were eliminated. The mean percentage of trials rejected was 9% (standard deviation 10%). Inspection of the grand averages was used to identify components of the evoked response. The values of peak potentials for each component were then calculated by identifying maxima/minima in individual subject averages in each condition in the time window appropriate for each component seen in the grand average.

Results

Behavioral Results

Judgments of grating orientation were significantly above chance both when viewing the hand (75% correct; $t_{14} = 15.61$, $P < 0.0001$) and the object (70% correct; $t_{14} = 11.22$, $P < 0.0001$). More importantly, the difference between these conditions was significant, with performance being better when viewing the hand than when viewing the object ($t_{14} = 3.91$; $P < 0.01$, 2-tailed; Fig. 2). This result replicates the visual enhancement of touch reported previously (Kennett et al. 2001; Taylor-Clarke et al. 2002).

We also used signal detection theory to investigate separately any visual modulation of tactile sensitivity (d') and response criterion (c) (Wickens 2002). For this purpose, the "across" response was arbitrarily designated as the to-be-detected target. d' was higher when viewing the hand (1.48) than when viewing the object (1.16) ($t_{14} = 4.16$; $P < 0.01$), indicating heightened sensitivity. In contrast, c scores did not show any significant difference between the 2 visual conditions (view hand = -0.14; view object = -0.01; $P = \text{NS}$). These findings suggest that viewing the hand enhanced tactile sensitivity without affecting response biases.

Electrophysiological Results

Inspection of scalp topographic maps showed broadly consistent components across contralateral central and parietal leads (Fig. 3A,B).

Figure 3A,B shows grand mean SEPs from C3, C5, CP3, and CP5 channels.

Two clear somatosensory components are identifiable from the grand averages. These are a P50 in the 40-70 ms time window and an N140 in the 120-150 ms time window. Consistent with other studies using comparable electrocutaneous stimuli

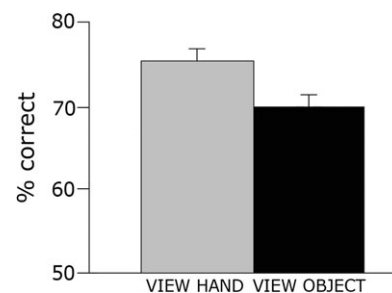


Figure 2. Behavioral results for the grating orientation task. Accuracy in discriminating the "across" or "along" orientation of gratings applied to the tip of the right index or middle finger was higher when participants looked at their own hand than when they looked at an object. Error bars show standard error across participants.

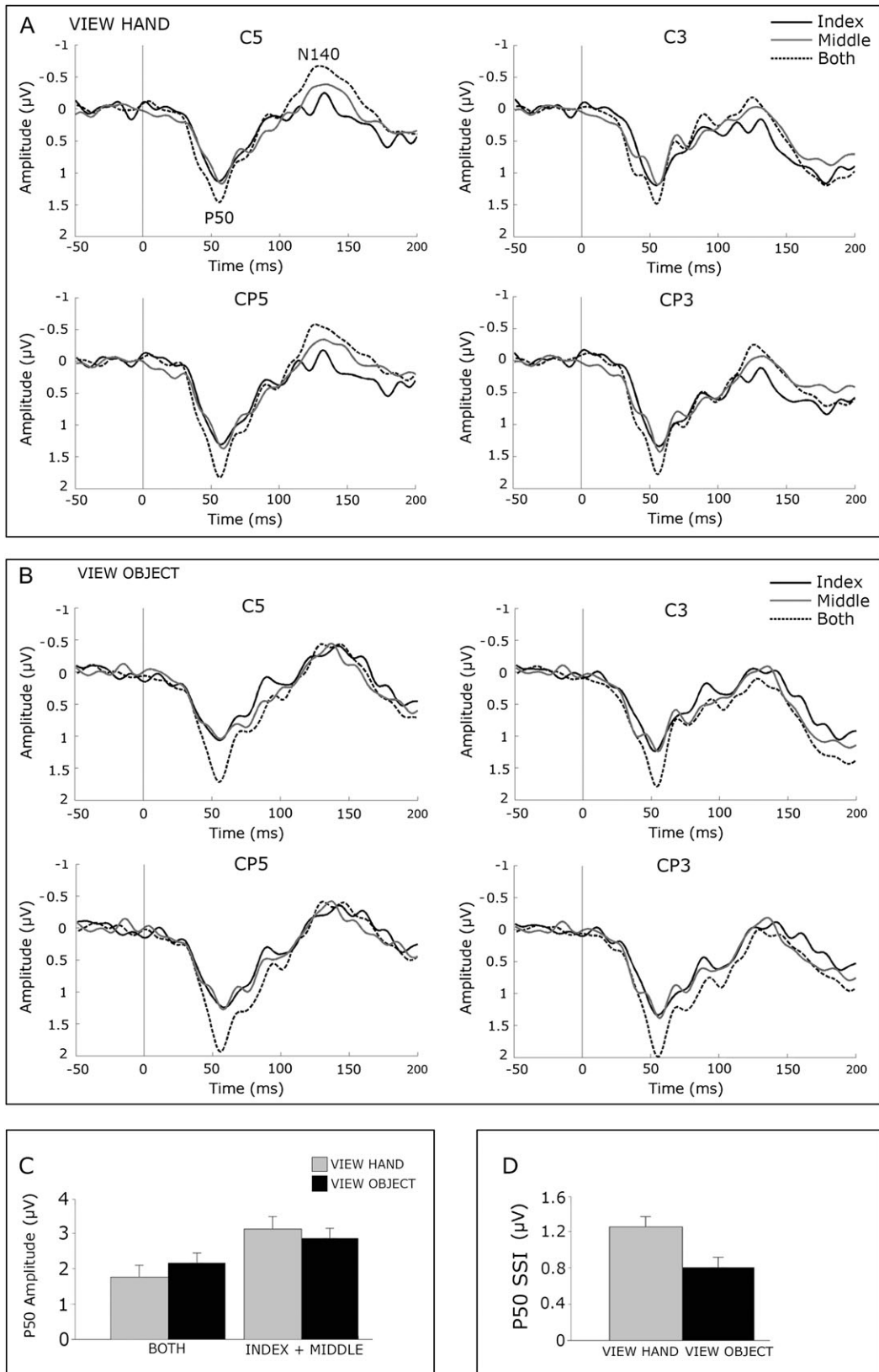


Figure 3. Visual modulation of SEPs. (A) Grand average SEPs, recorded from C3, C5, CP3, CP5 electrodes, in the view hand condition. (B) Grand average SEPs, recorded from C3, C5, CP3, CP5 electrodes, in the view object condition. (C) Results from a 2-by-2 ANOVA on the average of C3, C5, CP3, and CP5 P50 components, with factors of view (hand vs. object) and stimulation (both vs. summed index and middle). Note suppression when both fingers are stimulated, relative to sum of individual stimulations. (D) The SSI was defined as the difference between the arithmetic sum of potentials evoked by 2 individually stimulated fingers and the potential evoked by simultaneous stimulation of the 2 fingers. SSI in the P50 component is stronger when participants look at their own hand compared with when viewing an object.

(Schubert et al. 2008), components earlier than the P50 were not apparent in our grand averages. The absence of earlier components may reflect the relatively weak stimuli used.

Suppression is defined as the amplitude reduction for combined stimulation compared with the sum of the amplitudes for individual finger stimulation. To investigate suppression quantitatively, we first summed the amplitudes for individual index and middle finger stimulation. This effectively provides a prediction of the amplitude for combined stimulation under a hypothesis of no somatosensory suppression (i.e., perfect additivity). We then performed a 2-by-2 analysis of variance (ANOVA) with factors of view (hand vs. object) and stimulation (both vs. summed index and middle) (Fig. 3C). For P50 peak amplitudes, a main effect of stimulation ($F_{1,14} = 80.2$; $P < 0.001$) confirmed the suppression effect since peak amplitudes following simultaneously stimulating 2 fingers were significantly smaller than the sum of activations from stimulation of each finger individually. Duncan post hoc comparisons confirmed a suppression effect in both viewing conditions (both $P < 0.001$). There was no main effect of view ($F_{1,14} = 0.06$; $P = 0.79$). However, vision did significantly influence the magnitude of suppression ($F_{1,14} = 10.9$; $P < 0.01$), with greater suppression when viewing the hand compared with the object. We compared the effects of vision for each form of stimulation. This showed that vision of the hand reduced P50 peak amplitude compared with vision of the object ($P < 0.05$) for combined stimulation, while no effect was found for summed individual stimulations ($P > 0.05$).

An overview of this pattern of ANOVA interaction was provided by calculating a ‘‘Somatosensory Suppression Index’’ (SSI), defined as the difference in amplitude between the arithmetic sum of potentials evoked by 2 individually stimulated fingers and the potentials evoked by simultaneous stimulation of 2 fingers. The SSI was calculated with the following equation:

$$\text{SSI} = \text{Index alone} + \text{Middle alone} - \text{Combined}$$

Higher values of SSI indicate stronger suppression within the somatosensory system. A 2-tailed t -test revealed greater SSI in the view hand condition than in the view object condition ($t_{14} = 3.31$; $P < 0.01$; Fig. 3D), confirming the ANOVA interaction. While previous studies expressed this difference as a proportion of the summed individual stimulations, by calculating an interaction ratio (Hsieh et al. 1995), we found that this produced unstable and nonnormally distributed results due to occasional small peak amplitudes in the denominator.

Similar analysis of N140 peak amplitude provided no evidence for suppressive interactions at this later stage of tactile processing. The 2-by-2 repeated measure ANOVA revealed a no-significant main effect of stimulation ($F_{1,14} = 2.12$; $P = 0.16$) and a no-significant main effect of view ($F_{1,14} = 1.76$; $P = 0.20$). Although the interaction view \times stimulation was significant ($F_{1,14} = 4.69$; $P < 0.05$), post hoc comparisons showed that this was due to enhanced N140 peak amplitude for summed individual stimulations while viewing the object compared with the other 3 conditions ($P < 0.05$ for all comparisons). In particular, no significant difference was found between combined and summed individual stimulations, in the view hand condition ($P > 0.05$), suggesting inconsistent or no suppression. Visual modulation of suppression for the N140 component was therefore weak or absent. Indeed, 2-tailed t -test revealed a greater

SSI in the view object condition than in the view hand condition ($t_{14} = 2.16$; $P < 0.05$) due to the enhancement of N140 peak amplitude for summed individual stimulations when viewing the object, as previously shown by ANOVA.

To investigate the relation between psychophysical and electrophysiological measures, we predicted an association between visual enhancement of touch effect (expressed as the difference between accuracy in view hand condition and accuracy in view object condition) and visual modulation of P50 suppression (expressed as difference between SSI in view hand condition and in view object condition). Correlating the psychophysical and electrophysiological effects across participants revealed that the visual enhancement of touch was reliably associated with the visual modulation of suppression for the P50 component ($r = 0.55$; $P < 0.05$; Fig. 4). In contrast, VET was not correlated with difference between visual conditions in P50 amplitudes when stimulating either the index or middle finger alone (respectively, $r = 0.18$ and $r = 0.38$; both $P > 0.16$) nor for stimulating both fingers together ($r = 0.005$; $P = 0.98$). To further investigate the specificity of the relation between perceptual and neurophysiological effects, we performed a single multiple regression to predict each participant’s visual enhancement of touch from their P50 SSI, index-only P50, middle-only P50 and P50 for combined stimulation. SSI was a significant predictor of VET ($t_{14} = 2.27$; $P < 0.05$), while no other predictors reached significance (all $P > 0.05$).

Finally, we investigated how our results might relate to tactile spatial attention (Gillmeister et al. 2010). Specifically, we compared the P50 component of SEPs evoked by individual stimulation of the finger touched on each block (which we considered to be the attended finger) with SEPs evoked from stimulation of the untouched and therefore unattended finger. A 2-by-2 ANOVA of P50 peak amplitude with factors of view (hand vs. object) and tactile attention (attended finger vs. unattended finger) revealed no significant main effects of view ($F_{1,14} = 0.96$; $P = 0.33$) or tactile attention ($F_{1,14} = 0.77$; $P = 0.39$) and no interaction ($F_{1,14} = 0.009$; $P = 0.92$).

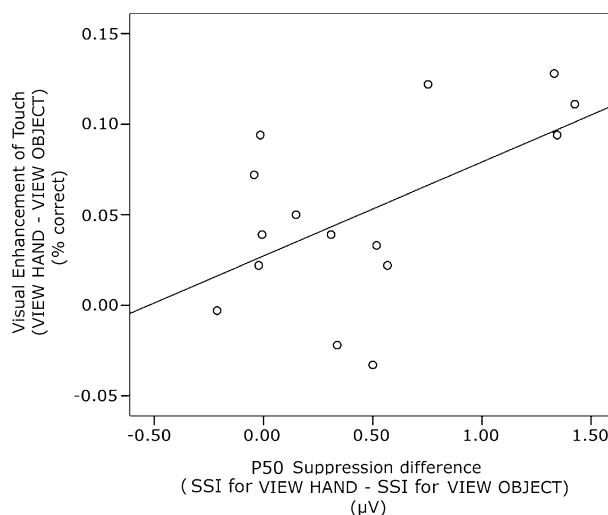


Figure 4. The visual enhancement of tactile performance, expressed as the difference between accuracy in view hand condition and accuracy in view object condition, correlates across participants with the visual modulation of suppression, expressed as the difference between SSI in view hand condition and SSI in view object condition.

Discussion

Viewing the body modulates somatosensory intracortical inhibition. The suppression of SEPs produced by simultaneous stimulation of the adjacent index and middle fingers was significantly increased when participants looked at their hand compared with an object. Consistent with previous results (Kennett et al. 2001), viewing the hand also enhanced tactile spatial acuity. Moreover, the visual enhancement of touch correlated across participants with the visual modulation of suppression, suggesting a functional relation between these effects. We suggest that vision of the body, even when noninformative, enhances the spatial sensitivity of touch by increasing inhibition in SI. This increased inhibition produces both a shrinking of tactile RFs, implying improved acuity, and stronger suppressive interactions between SEPs for adjacent skin regions. Both results are consistent with the hypothesis that viewing the body increases activation in the system of GABAergic interneurons that give rise to the RF organization of the somatosensory cortex (Dykes et al. 1984).

Previous studies reported attenuated sensory responses when 2 stimuli either of different modalities (Cheron and Borenstein 1987; Jones et al. 1992) or within a single sensory modality (Gandevia et al. 1983) were applied simultaneously to adjacent skin regions. For example, suppressive interactions between simultaneous cutaneous afferent volleys were elicited by electrical stimulation of different fingers (Gandevia et al. 1983). More recently, Okajima et al. (1991) demonstrated that suppressive interactions can also result from stimulation of nonadjacent skin regions, such as the left and right median nerves. Suppression of sensory inputs has been observed in several locations along the sensory afferent pathway, including the cuneate nucleus, the thalamus, and the somatosensory cortex, with the greatest interaction occurring in the cortex (Hsieh et al. 1995). This finding is consistent with the general observation that suppressive interactions may be relevant to the specific cortical mechanism of lateral inhibition that underlies tactile spatial perception.

Contribution of Primary Somatosensory Cortex

In line with previous results, we found suppressive effects at around 50 ms (Biermann et al. 1998; Ishibashi et al. 2000), whereas suppression of later components was unaffected by inhibitory interactions. As previously suggested, P50 might be generated in the primary somatosensory cortex (Allison et al. 1989; Ishibashi et al. 2000), whereas the later component we observed, N140, might be generated bilaterally in regions of the frontal lobes (Allison et al. 1992). As a consequence, we suggest that our findings reflect visual modulation of early activity in SI. The visual enhancement of touch was previously localized to SI on the basis both of amplitude modulations of N80 component evoked by touch itself (Taylor-Clarke et al. 2002) and also of abolition of VET by SI TMS delivered just prior to touch (Fiorio and Haggard 2005). In the present study, SEPs were recorded to task-irrelevant electrical stimuli rather than to to-be-judged tactile stimuli. Nevertheless, inspection of different somatosensory components showed clear evidence that viewing the body modulates somatosensory processing in early cortical areas. Multisensory effects in early cortex have also been reported for interactions between other sensory modalities (Macaluso 2006).

Previous neurophysiological findings suggested that suppressive somatosensory interactions depended on lateral

inhibitory interneurons and involved GABAergic intracortical circuits (Laskin and Spencer 1979a, 1979b). Most of these studies assumed a fixed level of inhibitory connectivity. However, more recent studies showed plasticity of lateral inhibition mechanism, which would be required by any role in multisensory modulation data. For example, cortical maps show high input-dependent plasticity, including profound and rapid reorganization in response to altered afferent inputs. In particular, surgical amputation of a digit lead to cortical neurons having RFs on that digit rapidly developing RFs on adjacent skin regions (Merzenich et al. 1984; Calford and Tweedale 1991). This was attributed to unmasking of latent afferent drive from the adjacent skin regions. Normally, the latent input would have been suppressed by lateral inhibitory connections from the amputated digit. Removal of the afferent input postamputation effectively removed the normal effects of lateral inhibition.

Our data suggest that lateral inhibitory mechanisms are not solely driven by afferent input in a feedforward manner. Rather, the strength of lateral inhibition in somatosensory cortex appears to be modulated by visual context, specifically vision of the body. We hypothesize that areas in occipital cortex, or in multisensory parietal cortex, house a representation of the body, driven in this case by viewing the hand. Our results suggest that this representation can modulate the strength of somatosensory lateral inhibition by top-down projections.

The effects of multisensory interactions on unisensory cortical processing have already been shown for different sensory modalities (Sathian and Stilla 2010). However, it remains unclear how such multisensory interactions can alter activations in primary sensory areas and change the way that primary areas respond to unisensory inputs. Our results suggest, for the first time, that top-down regulation of lateral inhibition may be the mechanism underlying such multisensory modulation. The same mechanism might underlie other modulatory effects in perceptual systems, such as within-modality top-down attentional modulation of early perceptual processing (Noudoost et al. 2010).

Potential Contribution of Tactile Spatial Attention

Attention is known to modulate early sensory processing. For example, directing attention to a specific finger alters processing in SI, sharpening the contrast between representations of attended and unattended fingers (Braun et al. 2002). This effect could result from an enhancement of cortical lateral inhibition (Iguchi et al. 2001; Braun et al. 2002). Moreover, recent findings have demonstrated that attentional modulation can change as a function of the visual context in which touch occurs. Gillmeister et al. (2010) showed that attending to one finger rather than another modulates the P45 and N80 SEP components: stimulating the attended finger increased amplitudes relative to stimulating an unattended finger. However, when the hand was visible, this attentional modulation was suppressed. The functional significance of this result, however, and its relation to the VET effect remain unclear.

Our design offered an opportunity to investigate the same effect. Since we delivered touches to the index and middle finger in separate blocks, we assumed that tactile attention was directed to whichever finger was touched on that block. The results of Gillmeister et al. (2010) would predict that P50 differences between attended and unattended finger should be smaller in the view hand condition than in the view object

condition. Moreover, this attenuation of individual potentials in the view hand condition would mean that the difference between combined potentials and the sum of individual potentials would be larger in the view hand than in the object condition. Therefore, our suppression results could be a by-product of attentional modulations of individual potentials. However, we did not find any effect in our data analogous to that reported by Gillmeister et al. (2010). P50s on the attended and unattended finger did not differ significantly, and there was no interaction between attention and view. Therefore, we consider it unlikely that our suppression results are a by-product of view-specific attentional effects.

One possible explanation for the lack of attentional P50 modulations in our experiment is the relatively weak modulation of attention. In particular, we did not explicitly instruct participants to attend to a particular finger. Rather, we assume that the consistent tactile stimulation of one finger in each block drew tactile attention to that finger and away from the untouched finger. However, our data do not allow any formal test of how strong this modulation of attention was in our participants.

Relevance to Other Somatosensory Modalities

Vision of the body has other somatosensory effects, notably a reduction in acute pain. We recently found that vision of the body is analgesic (Longo et al. 2009), leading to clear reductions in the acute pain generated by an infrared laser and also in the amplitude of laser evoked potentials. Intriguingly, several pieces of evidence suggest that intracortical inhibition may also suppress pain. GABA agonist drugs are effective treatments for several types of chronic central pain (Canavero and Bonicalzi 1998). Similarly, patients with complex regional pain syndrome show reduced intracortical inhibition as measured by paired-pulse TMS (Schwenkreis et al. 2003). Finally, repetitive TMS to primary motor cortex, which is known to increase intracortical inhibition, also reduces chronic pain (Lefaucheur et al. 2006). Thus, the finding that viewing the body increases intracortical inhibition in the somatosensory cortex provides a potential common mechanism underlying both increased tactile spatial acuity (Kennett et al. 2001) and analgesia (Longo et al. 2009). Differences in the spatial arrangement of a common interneuronal mechanism might explain why viewing the body produces pain suppression in the nociceptive system and spatial enhancement in the tactile system.

Convergence and Modulation

In the introduction, we described 2 classes of multisensory interactions, convergence and modulation. Multisensory convergence involves bringing together information from distinct sensory streams. The most striking examples involve single neurons that respond to inputs from 2 or more modalities, for example, in the superior colliculus (Meredith and Stein 1983), putamen (Graziano and Gross 1993), premotor cortex (Graziano et al. 1994), and posterior parietal cortex (Avillac et al. 2007). This convergence may serve for sensitive detection of events (Stein and Meredith 1993) or for generating a single supramodal object percept (Ernst and Banks 2002). Convergence is also required to construct general representations and processes that are independent of specific sensory inputs, such as peripersonal space (Ladavas and Farne 2004), or spatial attention (Driver and Spence 1998).

Multisensory modulation, in contrast, involves activity from one sensory channel modulating activity in another sensory channel. Examples include intersensory substitutions, such as ventriloquism (Bertelson et al. 2000; Shams et al. 2000), signals from one modality biasing perception in another modality (Shams et al. 2000), and synesthetic cross-talk (Bargary et al. 2009). Importantly, whereas integration and convergence can be considered as purely feedforward processes in which sensory information is increasingly pooled across several source modalities, modulation involves either horizontal influence between different sensory pathways or descending influence of a multimodal representation on lower level unimodal functions.

In many cases, convergence and modulation will co-occur. For example, both cortical (Avillac et al. 2007) and subcortical (Stein et al. 1993) areas contain multimodal cells that respond to inputs in 2 (or more) modalities. Moreover, the response to a stimulus in each modality also depends on the other modality. For example, the response to combined tactile and visual stimulation may exceed the sum of responses to either visual stimulation or tactile stimulation alone. In this case, the presence of a response to either modality is evidence of integration, while the nonlinearity of the bimodal response is evidence of intersensory modulation. The fact that both integration and modulation co-occur in such cases makes it difficult to separate the processes of multisensory integration from those of multisensory modulation. Furthermore, the widespread co-occurrence of integration and modulation has made the modulation component hard to characterize. In our study, vision of the body provides a continuous context, rather than a time-locked afferent signal describing a specific sensory event. Therefore, our experimental paradigm may serve to isolate the multisensory modulation component, as distinct from multisensory convergence.

To conclude, we have identified a novel mechanism for multisensory modulation. Most previous multisensory studies focused on convergence of different sensory inputs to provide a multisensory representation. Indeed, the representation of the body activated by viewing the hand may depend on precisely this form of multisensory integration. We now additionally show that multisensory interactions can involve top-down feedback projections from such representations to primary sensory cortex. These projections have the functional role of enhancing perception, in this case enhancing tactile acuity by boosting the gain of a network of inhibitory interneuronal connections within primary somatosensory cortex. This mechanism, already known to underlie plastic reorganization of perceptual systems, is therefore also involved in rapid, functional multisensory enhancement. Previous studies suggested that the key function of multisensory convergence was sensitive detection, orienting, and alerting (Stein and Meredith 1993). We have suggested that the key function of multisensory modulation is the enhancement of perceptual detail, such as acuity.

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Notes

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