RESEARCH ARTICLE

Vibrotactile discriminative capacity is impacted in a digit-specific manner with concurrent unattended hand stimulation

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Abstract A number of perceptual and neurophysiological studies have investigated the effects of delivering unilateral versus bilateral tactile sensory stimulation. While a number of studies indicate that perceptual discrimination degrades with opposite-hand stimulation, there have been no reports that examined the digit specificity of cross-hemispheric interactions to discriminative capabilities. The purpose of this study was to determine whether unattended hand (UH) stimulation significantly degraded or improved amplitude discriminative capacity on the attended hand (AH) in a digit-specific manner. The methods are based on a sensory perceptual task (vibrotactile amplitude discriminative capacity on the tips of the fingers D2 and D3 of the left hand) in the absence and presence of conditioning stimuli delivered to D2 and D3 of the right hand. Non-specific equal-amplitude stimulation to D2 and D3 of the UH significantly worsened amplitude discrimination (AD) performance, while delivering unequal-amplitude stimuli to D2 and D3 of the UH worsened task performance only under the condition in which the unattended stimuli failed to appropriately match the stimulus parameters on the AH. Additionally, delivering single-site stimuli to D2 or D3 of the UH resulted in degraded performance on the AD task when the stimulus amplitude did not match the amplitude of the stimulus applied to homologous digits of the AH. The findings demonstrate that there is a reduction in performance under conditions where UH stimulation least matched stimulation applied to the AH, while there was little or no change in performance when stimulus conditions on the homologous digit(s) of the contralateral sites were similar. Results suggest that bilateral interactions influence perception in a context-dependent manner that is digit specific.

Introduction

A fundamental question which remains elusive in the field of neuroscience involves understanding the manner in which sensory information is differentiated and integrated from multiple sensory inputs. Within the somatosensory system, the functional connectivity between adjacent and near adjacent cortical ensembles that correspond to somatotopically aligned unilateral skin sites has been well studied, and a number of perceptual changes that occur in parallel with these functional interactions—often interpreted as interference stimuli—have also been demonstrated. For example, inaccuracies in spatially localizing tactile stimuli occur when interference (confounding or illusory) stimuli are delivered near tested digits or at the same skin sites (Schweizer et al. 2000; 2001; Tommerdahl et al. 2007b). However, studies of interference across the body midline, though they have demonstrated alterations in sensory percept, have not been examined at a digit-specific level. Some examples of these previously reported non-specific effects include increased detection thresholds, or worsened task performance, when an interference stimulus is located at a homologous skin site across the body midline (Levin and Benton 1973), impaired tactile localization during delivery of opposite-hand digit stimulation (Braun et al. 2005), and decreased spatial acuity on one

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hand when stimuli are delivered to the opposite hand (Tannan et al. 2005). The above-described interactions correlate well with a number of neurophysiological studies that demonstrate that the activity and contralateral hemispheric activation evoked in SI by attended hand (AH) stimulation is reduced with the introduction of a stimulus to the unattended hand (UH) on the ipsilateral hemisphere (Blankenburg et al. 2008; Eickhoff et al. 2008; Eshel et al. 2010; Gröschel et al. 2013; Iwamura et al. 2001; Jung et al. 2012; Lipton et al. 2006; Palmer et al. 2012; Premji et al. 2011; Ragert et al. 2011; Reed et al. 2012; Schäfer et al. 2012; Tommerdahl et al. 2005a, 2006; Wahl et al. 2007; Zapallow et al. 2013). Such reductions in SI cortical activity could account for the previously reported reductions in tactile sensory percept.

A semiautomated method has been previously described in a number of reports for measuring the ability of human subjects to discriminate between the amplitude of two vibrotactile stimuli delivered to the skin (i.e., amplitude discriminative capacity). These studies have shown that this metric, while stable across a wide age spectrum of healthy subjects (Zhang et al. 2011b), varies under a number of different conditions (Folger et al. 2008; Francisco et al. 2008; Nelson et al. 2012; Nguyen et al. 2013a, b; Rai et al. 2012; Tannan et al. 2007a, 2008; Tommerdahl et al. 2007a; Zhang et al. 2008, 2009, 2011a). Based on the aforementioned reports analyzing the manner in which interference stimuli degraded some aspect of sensory perceptual performance across the body midline, the goal of this study was to determine whether the locus and amplitude of UH stimulation significantly degraded or improved amplitude discriminative capacity on the AH in a digit-specific manner. Protocols were designed under the hypothesis that amplitude discriminative performance under UH stimulation would vary depending on the type of stimuli applied to the unattended hand. While a number of neurophysiological studies are consistent with the idea that perceptual discrimination on one hand would degrade with opposite-hand stimulation (Blankenburg et al. 2008; Eickhoff et al. 2008; Eshel et al. 2010; Gröschel et al. 2013; Iwamura et al. 2001; Jung et al. 2012; Lipton et al. 2006; Palmer et al. 2012; Premji et al. 2011; Ragert et al. 2011; Reed et al. 2012; Schäfer et al. 2012; Tommerdahl et al. 2005a, 2006; Wahl et al. 2007; Zapallow et al. 2013), other neurophysiological studies indicate or predict that there are digit-specific interactions across hemispheres (Fabri et al. 2005; Nihashi et al. 2005; Van der Knaap and Van der Ham 2011; Zhu et al. 2007) which could lead to alterations in discriminative performance. In order to address the question of digit specificity in bilateral interactions, protocols were designed to determine whether or not amplitude discrimination (AD) capacity on the attended hand was impacted in a digit-specific manner by unattended hand stimulation.

Materials and methods

Participants

Twenty-seven healthy subjects ranging from 21 to 42 years of age (mean = 27.3 years, SD = 7.2 years) were recruited for the study. Because the majority of subjects (25/27 = 92.6 %) were right-handed, and because prior unpublished observations demonstrated non-significant differential effects of handedness on performance, subject handedness was not explicitly analyzed in this study. The subjects were tested during one session in which each protocol lasted no longer than 5 min. While all 27 subjects completed the first set of stimulus conditions (equal-amplitude stimuli delivered to both D2 and D3 of the unattended hand), only 11 subjects completed the protocols with the second set of conditions (unequal-amplitude stimuli delivered to both D2 and D3 of the unattended hand) and 16 subjects completed the third set of stimulus conditions (single-site stimuli delivered to D2 or D3 of the unattended hand). Subjects completed a survey on current medications and medical history prior to the experimental tests to exclude participants with any history of neurological impairment. Participants also completed a written informed consent form after a complete description of the study was explained. The experimental procedures were reviewed and approved in advance by an Institutional Review Board. Subjects were naïve to both the study design and issue under investigation.

Sensory assessments

A four-site mechanical stimulator (CM-5; Cortical Metrics Model #5), designed to optimally deliver vibrotactile stimuli to the finger tips, was used in this study. This stimulator, most recently described in Holden et al. 2011, has been utilized to assess a number of sensory information processing characteristics in various subject populations (Folger et al. 2008; Francisco et al. 2008, 2011; Nelson et al. 2012; Nguyen et al. 2013a, b; Rai et al. 2012; Tannan et al. 2005, 2007a, b; Tannan et al. 2008; Tommerdahl et al. 2007a, b; Zhang et al. 2009, 2011a, b). Typically, one stimulator is interfaced with a personal computer via an internal data acquisition box (DAQ), which is connected to the computer with a universal serial bus (USB) cable. Software developed in house with Microsoft's.NET Framework v3.5 allows for a wide range of stimulus conditions to be delivered independently and simultaneously to each of the four probes that contact the digit tips. The stimulator is mounted on a drum that rotates and allows for independent positioning of each probe tip to best fit the hand of the individual. For a full technical description, see Holden et al. (2011).

Fig. 1 Cortical metrics (CM-5) stimulator. Left and right hands were positioned on two separate head units for the bilateral protocols. The device cabling was modified to simultaneously deliver coordinated stimuli to pairs of digits on two hands (*left*, attended; *right*, unattended)
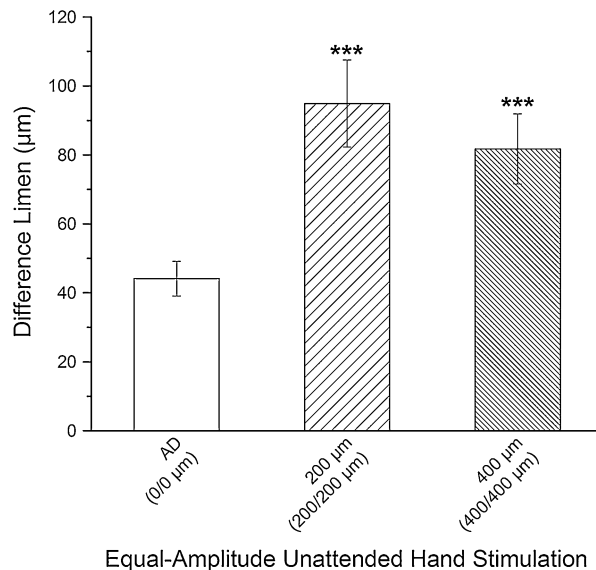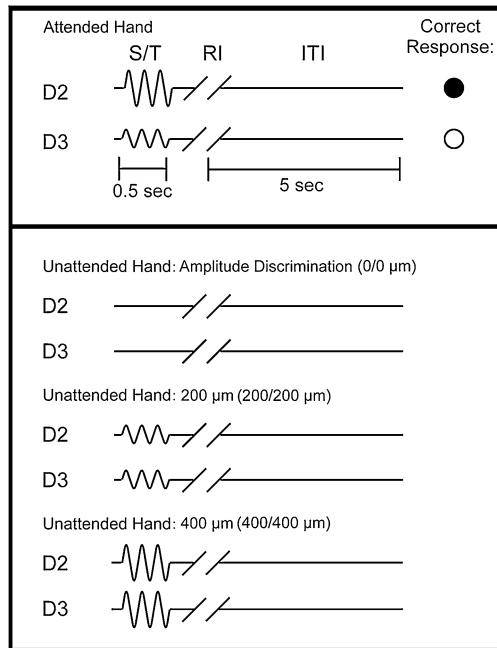

Fig. 2 Equal-amplitude stimulation to the unattended hand. The UH received simultaneous stimulation of equal amplitude under one of three conditions: no stimulation, 200, or 400 μm. In the represented case, unattended hand stimulation is applied to D2 and D3 (standard/test μm, S/T) where D2 of the AH receives the test stimulus and D3 receives the standard stimulus. Equal-amplitude conditioning stimulation at 200 μm and at 400 μm resulted in significantly higher average DLs compared to that for the simple amplitude discrimination task (no stimulation of UH) ($n = 27$; ***$p < 0.001$)

In order to deliver stimuli simultaneously to two hands, the device cabling was modified so that two stimulators were mounted on two separate hand rests. This configuration allowed for coordinated stimulation of pairs of digits on each hand (Fig. 1). During the experimental session, the subjects were seated comfortably in a chair with their left and right forearms situated on ergonomic armrests attached to the two head units of the vibrotactile stimulators. Plastic probes from the stimulators made contact with the glabrous tips of the second (index, D2) and third (middle, D3) digits of the left and right hands. Visual cueing, indicating when the experimental stimuli were being delivered as well as when subjects were to respond, was provided via the computer monitor during each of the experimental runs. Subjects were instructed to verbally indicate which digit on the left, attended hand (L-AH) the higher stimulus amplitude was applied. The test

administrator then recorded the response by using a wireless mouse directly connected to the computer.

Amplitude discrimination

This procedure has been described in a number of previous reports (Folger et al. 2008; Francisco et al. 2008; Nelson et al. 2012; Nguyen et al. 2013a, b; Puts et al. 2013; Rai et al. 2012; Tannan et al. 2007a, 2008; Tommerdahl et al. 2007a; Zhang et al. 2008, 2009, 2011a). For all AD tasks, the device delivered simultaneous stimuli to D2 and D3 of the L-AH (Figs. 2, 3, 4, attended hand). The AD task measured the AD capacity of the AH in the absence of UH stimulation (Fig. 2, unattended hand: AD). The stimuli applied to the left digits D2 and D3 consisted of a test stimulus (ranging 400–205 μm) that was applied to one digit and a standard
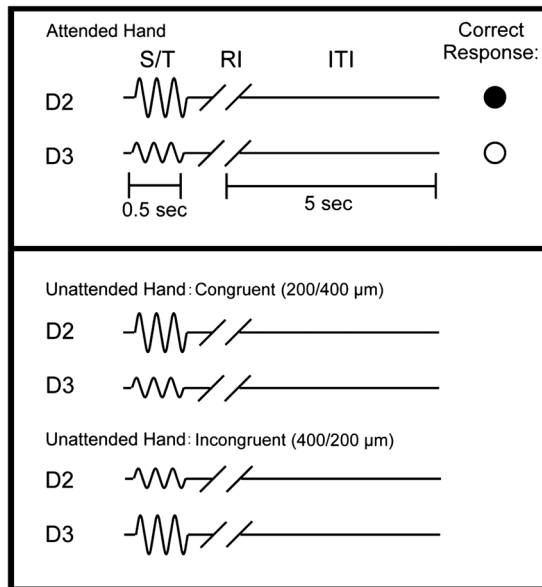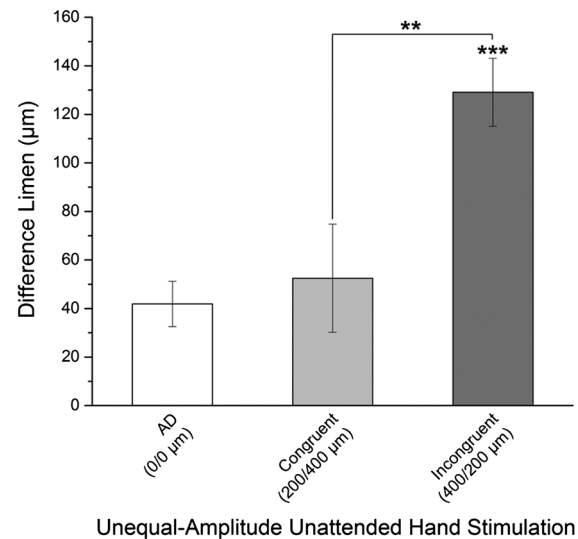
Fig. 3 Unequal-amplitude stimulation to the unattended hand. The UH received simultaneous stimulation of unequal amplitudes. In the represented case, UH stimulation is applied to D2 and D3 (standard/test μm, S/T) where D2 of the AH receives the test stimulus and D3 receives the standard stimulus. In this case, D2 > D3 on the AH; thus, D2 > D3 for the congruent condition and D3 > D2 for the incongruent condition on the UH. Only incongruent stimulation resulted in a significantly higher average DL compared to that for the simple amplitude discrimination task ($n = 11$; ***$p < 0.001$)
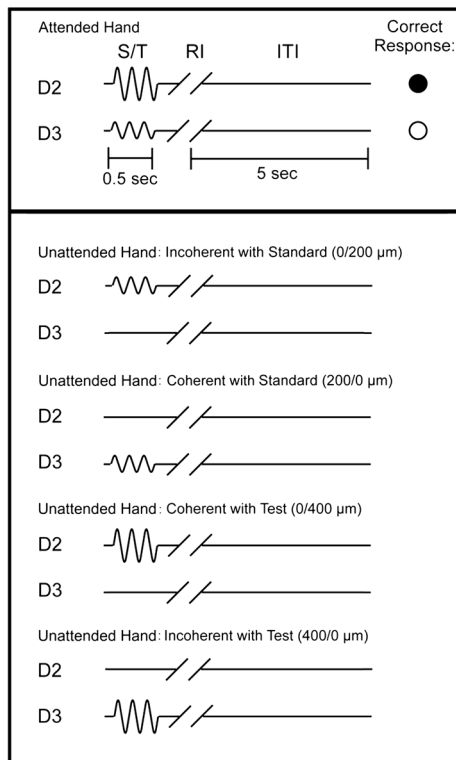

Fig. 4 Single-site stimulation to the unattended hand. The UH received simultaneous stimulation of unequal amplitudes. In the represented case, UH stimulation is applied to D2 or D3 (standard/test μm, S/T) where D2 of the AH receives the test stimulus and D3 receives the standard stimulus. In this case, D2 > D3 on the AH; thus, D2 receives coherent stimulation at 200 μm and D3 receives coherent stimulation at 400 μm on the UH. Only the incoherent stimuli resulted in significantly higher average DLs compared to that for the simple amplitude discrimination task ($n = 16$; **$p < 0.01$, ***$p < 0.001$)
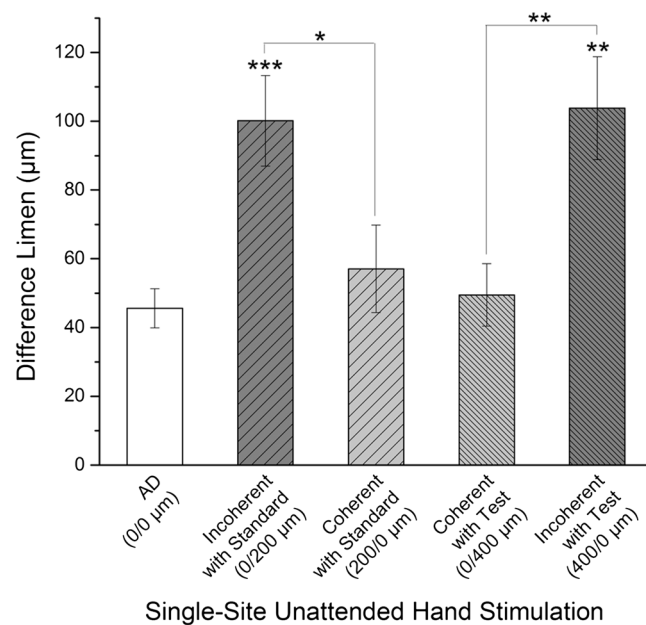
stimulus fixed at 200 μm that was applied to the other digit. The amplitude of the test stimulus was always greater than that of the standard stimulus, but the loci of the stimuli (D2 versus D3) were selected in a pseudorandom manner between the paired digits on a trial-by-trial basis. Both the standard and test stimuli for the AH were applied at a frequency of 25 Hz. For all protocols, the subject responded (response interval, RI) to a 0.5 s delivery of the standard/test (S/T) stimuli with an inter-test interval (ITI) of 5 s.

Amplitude discriminative capacity is defined as the minimal difference in amplitudes of two mechanical sinusoidal vibratory stimuli for which an individual can successfully identify the stimulus stronger in magnitude. Discrimination capacity was assessed using a two-alternative forced-choice (2AFC) tracking protocol (see "Tracking paradigm"). Following each stimulus, subjects were prompted to select the digit where the stimulation felt perceptually larger. After a 5 s delay, the stimulus amplitude was modified until completion of the 20 trials of the test based on the previous response of the subjects. The rationale for implementing these algorithms was to initially expedite determination of vibrotactile discriminative range.

Tracking paradigm

A modified von Békésy tracking algorithm (Cornsweet 1962) was used to determine amplitude discriminative thresholds on the AH. The adaptive 2AFC tracking method has been described and implemented in a number of previous studies (Folger et al. 2008; Francisco et al. 2008; Tannan et al. 2007a, 2008; Tommerdahl et al. 2007a, b; Zhang et al. 2009, 2011a, b) where the difference between the amplitudes of the test and standard stimuli was adjusted on the basis of the previous response. Correct responses resulted in lowering of the magnitude of the test stimulus while incorrect response raised the amplitude of the test stimulus on subsequent trials. A 1-up/1-down algorithm was implemented during the first ten trials, and a 2-up/1-down algorithm was implemented during the remaining ten trials. Each run consisted of twenty trials in which subjects were able to track down to the smallest test amplitude that they could consistently differentiate from the standard amplitude, which is also called the discrimination threshold (difference limen; DL). The same approach has been taken using other sensory modalities (e.g., auditory stimuli: Pienkowski and Hagerman 2009).

For each run, while the standard stimulus was maintained at the amplitude 200 μm, the test stimulus was initially delivered at twice the standard amplitude (400 μm) and had the potential to track down to a magnitude of 205 μm. The test amplitude was increased or decreased by a step size of 20 μm, or 10 % of the standard stimulus amplitude. The amplitude of the test stimulus was always greater than that of the standard stimulus. These settings allowed the

test stimulus amplitude strength to be applied well above the discrimination threshold, but low enough for subjects to track down to their discrimination thresholds within the 20 trials that were administered during the run. Previous reports have demonstrated that most subjects reach their discrimination threshold within 10 to 15 trials (Francisco et al. 2008; Tannan et al. 2007b). Stimulus frequency remained at 25 Hz for both the standard and test stimuli for the duration of assessment. As the AD task was performed, this tracking paradigm was used for the right AH only.

Protocols were typically interleaved with one another in a pseudorandomized manner in order to assess the effects of unattended hand stimulation on the same AD task. This interleaved tracking algorithm was termed as "dual staircase" whereby two protocols were run simultaneously, but discriminative thresholds were tracked independently according to the adaptive (2AFC) tracking method. AD tasks in the absence of unattended hand stimulation were interleaved with those in the presence of equal-amplitude unattended hand stimulation while congruent conditions were interleaved with incongruent conditions (for both the unequal-amplitude and single-site unattended hand stimulations) resulting in 40 total trials for the five protocols (20 trials per test, two tests interleaved).

Amplitude discrimination in the presence of equal-amplitude unattended hand stimulation

After the determination of amplitude discriminative capacity in the absence of stimulation to the unattended hand, the same task was assessed in the presence of equal-amplitude vibrotactile conditioning stimuli delivered to the unattended hand (Fig. 2, unattended hand). For the left (attended) hand (AH), stimulus parameters for AD in the presence of unattended hand stimulation were the same as in the AD task in the absence of unattended hand stimulation (200 μm standard). For the right (unattended) hand (UH), two stimulus conditions were tested. The stimuli delivered to the UH were either 200 or 400 μm at 25 Hz (Fig. 2, unattended hand: 200, 400 μm). The amplitudes of stimulation were chosen for the unattended hand to match the maximum initial test stimulus amplitude (400 μm) and the fixed standard stimulus amplitude (200 μm) of the attended hand. A frequency of 25 Hz was used for the UH to match the frequency of the test and standard stimuli of the AH. The parameters of the stimuli on D2 and D3 of the right hand (UH) were equal and held constant in frequency and amplitude. For instance, a 200 μm stimulus was applied to both D2 and D3 of the right hand (UH) throughout the duration of the test (Fig. 2, unattended hand: 200 μm). The AH and UH were simultaneously stimulated, and subjects were instructed to verbally indicate which digit on the left hand (AH) the higher stimulus amplitude was applied. The test administrator then recorded the response by using the response device.

Amplitude discrimination in the presence
of unequal-amplitude (congruent or incongruent)
unattended hand stimulation

The following test conditions assessed amplitude discriminative capacity in the presence of unequal-amplitude unattended hand stimulation (Fig. 3, unattended hand). For the left (attended) hand (AH), stimulus parameters for AD in the presence of unattended hand stimulation were the same as in the AD task in the absence of unattended hand stimulation. For the right (unattended) hand (UH), stimulus amplitudes on the paired digits on the right hand (UH) were unequal (Fig. 3, unattended hand: congruent, incongruent). Similar to the stimulus parameters for the digits of the left hand (AH), one digit (D2 or D3) of the right hand received a stimulus of higher amplitude than the other digit (either 400 or 200 μm; both at 25 Hz). The amplitudes were chosen for the UH to match the maximum test stimulus amplitude (400 μm) and the fixed standard stimulus amplitude (200 μm) of the AH. As a result, considering unequal-amplitude stimulation of adjacent digits on the UH, "congruent" conditions refer to the higher amplitudes of UH vibrotactile stimulation being applied to the same homologous spatial location as the (larger) test stimulus on the AH (i.e., stimulated the same contralateral digit), while "incongruent" conditions refer to the higher magnitude of UH stimulation being delivered to the same homologous spatial location as the (smaller) standard stimulus on the AH. The terminology for congruency was utilized under the notion that the larger test and smaller standard stimulus amplitudes delivered to the digits of the attended hand matched the larger "test" and smaller (or null) "standard" stimulus amplitudes concurrently applied to the contralateral digits/location of the unattended hand. In this particular case, for the congruent condition, the stimuli of greater amplitude occurred on the same digit on both hands [i.e., when the amplitude of $D2_{AH} > D3_{AH}$ on the left hand (AH), then $D2_{UH} > D3_{UH}$ on the right hand (UH)]. For the incongruent condition, the stimuli of greater amplitude occurred on different digits on both hands [i.e., when the amplitude of $D2_{AH} > D3_{AH}$ on the left hand (AH), then $D3_{UH} > D2_{UH}$ on the right hand (UH)].

Amplitude discrimination in the presence of single-site
(coherent or incoherent) unattended hand stimulation
at different amplitudes

Single-site test conditions further assessed amplitude discriminative capacity in the presence of coherent (stimulus matching by locus and amplitude) and incoherent (stimulus mismatching by locus and amplitude) unattended hand stimulation of individual digits at different amplitudes (Fig. 4, unattended hand: coherent/incoherent with standard/test). Similar to the AD task in the presence of unequal-amplitude unattended hand stimulation, the same tests were

repeated for concurrent single-site stimulation on either D2 or D3 of the unattended hand at either 200 μm or 400 μm. During these conditions, the right hand (UH) received one stimulus on either D2 or D3 at a magnitude of either 200 or 400 μm. Subsequently, in the case of the 200-μm single-site stimulation, the vibration was applied on the same digit either as the test stimulus (incoherent condition) on the AH [i.e., when the amplitude of $D2_{AH} > D3_{AH}$ on the left hand (AH), then $D2_{UH}$ was stimulated at 200 μm on the right hand (UH)], or as the standard stimulus (coherent condition) on the AH [i.e., when the amplitude of $D2_{AH} > D3_{AH}$ on the left hand (AH), then $D3_{UH}$ was stimulated at 200 μm on the right hand (UH)]. The same task was repeated for the 400-μm condition where the coherent condition involved stimulating the contralateral test site and where the incoherent condition involved stimulating the contralateral standard site of the unattended hand (Fig. 4; unattended hand: coherent/incoherent at 400 μm).

Data analysis

The discriminative thresholds, or DLs, of each subject were calculated by averaging the amplitudes of the last five trials recorded in the tasks and then subtracting the standard amplitude of 200 μm. Unilateral AD thresholds, which were interleaved with tests in the presence of equal-amplitude UH stimulation, were averaged over multiple tests and both conditions (200 and 400 μm) to obtain mean DLs with which unilateral thresholds could be compared. An increase in DL compared to baseline performance indicates a worsening of AD capacity while a relative decrease in threshold suggests improvement. The DL of the population was computed as the average DL across subjects.

Paired t tests were used to evaluate the difference in the performance of each of the subjects across different conditions. Data are presented as means and standard errors of the mean. A probability (p value) of <0.05 was considered to be a statistically significant difference. The analytical methods implemented for population averages and within-subject normalization were similar to those described in previous reports (Nguyen et al. 2013b; Simons et al. 2007; Tannan et al. 2005; Tommerdahl et al. 2005b, c, 2008).

Results

Non-specific stimulation to D2 and D3 of the unattended
hand significantly worsens amplitude discrimination
performance

All subjects completed the AD and equal-amplitude unattended hand stimulation conditions. The average difference limen (DL) obtained across subjects for the

amplitude discrimination task (no stimulation of UH) was 44.1 ± 5.0 μm (Fig. 2: AD; $n = 27$). This baseline metric of amplitude discriminative capacity was subsequently used to analyze any impact of non-specific unattended hand stimulation on the task. For the 200-μm condition, the average DL increased to 94.9 ± 12.6 μm (Fig. 2: 200 μm; $n = 27$; ***$p = 0.0003$), whereas in the 400-μm condition, the mean DL increased to 81.7 ± 10.2 μm (Fig. 2: 400 μm; $n = 27$; ***$p = 0.0006$). Both conditions of 200- and 400-μm equal-amplitude stimulation of D2 and D3 on the UH resulted in significant increases in discriminative thresholds. The majority of subjects showed increases in DLs compared to their mean amplitude discrimination in the presence of 200-μm ($23/27 = 85.2$ %) and 400-μm ($18/27 = 66.7$ %) equal-amplitude unattended hand conditioning stimulation.

Delivering unequal-amplitude incongruent stimuli to D2 and D3 of the unattended hand results in worsened performance on the amplitude discrimination task

Of the 27 subjects, 11 completed the unequal-amplitude unattended hand stimulation condition. The average difference limen (DL) obtained for these subjects for the amplitude discrimination task without UH stimulation was 41.9 ± 9.3 μm (Fig. 3: AD; $n = 11$). In the presence of congruent stimulation to the digits of the unattended hand, the mean DLs (Fig. 3: congruent; $n = 11$; 52.5 ± 22.3 μm; $p = 0.68$) were not statistically significant from the baseline metric. However, performance in the incongruent assessment had demonstrated a significant reduction of discriminative capacity (Fig. 3: incongruent; $n = 11$; 129.1 ± 14.0 μm; ***$p = 0.0003$). In summary, application of incongruent stimuli results in increased DLs while that of congruent stimuli results in no change in thresholds when compared to baseline metrics. The data also demonstrate a significant difference between the congruent and incongruent conditions (**$p = 0.002$). The majority of subjects ($10/11 = 90.9$ %) had lower DLs on the task when the unattended hand stimulation was congruent than when it was incongruent.

Delivering single-site incoherent stimuli to D2 or D3 of the unattended hand results in worsened performance on the amplitude discrimination task

Of the 27 subjects, 16 completed the single-site unattended hand stimulation condition. The average difference limen (DL) obtained for these subjects for the amplitude discrimination task was 45.6 ± 5.7 μm (Fig. 4: AD; $n = 16$). For single-site unattended hand stimulation at 200 μm, incoherent stimulation on the same finger as the standard stimulus (Fig. 4: incoherent with standard; 100.1 ± 13.1 μm;

$n = 16$; ***$p = 0.0005$) was significantly different from the baseline metric while that of the coherent stimulation on the same finger as the standard stimulus (Fig. 4: coherent with standard; 57.1 ± 12.8 μm; $n = 16$; $p = 0.39$) was not. There was a significant difference between these coherent and incoherent conditions at 200 μm (*$p = 0.04$). For the 400-μm single-site unattended hand stimulation, the coherent stimulation (Fig. 4: coherent with test; 49.5 ± 9.1 μm; $n = 16$; $p = 0.62$) was not statistically significant from the DL in the amplitude discrimination whereas the discriminative threshold for the incoherent condition (Fig. 4: incoherent with test; 103.8 ± 15.0 μm; $n = 16$; ***$p = 0.003$) was. Similarly, there was a significant difference between these coherent and incoherent conditions at 400 μm (**$p = 0.005$). Subjects generally had lower discriminative thresholds during coherent conditions when the 200-μm unattended hand stimulus was applied to the same site at the standard stimulus on the AH ($10/16 = 62.5$ %) and when the 400-μm unattended hand stimulus was applied to the same site as the test stimulus on the AH ($12/16 = 75.0$ %).

Discussion

The amplitude discriminative capacity of the attended (left) hand was compared with several other conditions in which stimuli were delivered to the unattended (right) hand. The findings demonstrate that there is a reduction in performance under some of these conditions where UH stimulation least matched stimulation applied to the AH, while there was little or no change in performance when stimulus conditions delivered to the homologous digit(s) of the contralateral sites were similar. Table 1 summarizes these results.

A number of studies support both structural and functional associations between homologous regions across cortical hemispheres. Bilateral somatosensory integration is primarily mediated by callosal fibers which are involved in interconnections among the left and right cerebral hemispheres. These complex connections allow for interhemispheric modulation of information processing (Fabri et al. 2005; Van der Knaap and Van der Ham 2011). Animal models have revealed neuronal mechanisms involved in interhemispheric inhibition (Palmer et al. 2012; Wahl et al. 2007), and human imaging studies have also revealed that stimulation of one hand leads to significant activation in the contralateral somatosensory cortex while inhibiting homologous regions in the ipsilateral somatosensory cortex (Gröschel et al. 2013; Jung et al. 2012; Lipton et al. 2006; Palmer et al. 2012; Premji et al. 2011; Reed et al. 2012; Schäfer et al. 2012; Tommerdahl et al. 2005a, 2006; Wahl et al. 2007; Zapallow et al. 2013). Many of these studies

Table 1 Summary of protocols and results

	Attended hand stimulation (S/T μm)	Unattended hand stimulation (S/T μm)	Threshold (μm)
Amplitude discrimination	200/[205–400] μm	0/0 μm	44.1 ± 5.0
Equal amplitude			
200 μm	200/[205–400] μm	200/200 μm	94.9 ± 12.6***
400 μm	200/[205–400] μm	400/400 μm	81.7 ± 10.2***
Unequal amplitude			
Congruent	200/[205–400] μm	200/400 μm	52.5 ± 22.3
Incongruent	200/[205–400] μm	400/200 μm	129.1 ± 14.0***
Single site			
Incoherent with standard	200/[205–400] μm	0/200 μm	100.1 ± 13.1***
Coherent with standard	200/[205–400] μm	200/0 μm	57.1 ± 12.8
Coherent with test	200/[205–400] μm	0/400 μm	49.5 ± 9.1
Incoherent with test	200/[205–400] μm	400/0 μm	103.8 ± 15.0**

Sensory tasks are outlined by defining the stimuli delivered to the UH during the amplitude discrimination task on the AH

AH stimulation indicates the range of amplitudes delivered to the test site throughout the 2AFC tracking method

UH stimulation standard and test (S/T) sites correspond to the homologous sites of applied stimulation on the S/T sites on the AH

** $p < 0.01$, *** $p < 0.001$

claim that the secondary somatosensory cortex is primarily responsible for interhemispheric information transfer, but recent studies show that bilateral processing may occur in early stages of processing in the caudal portion of the postcentral gyrus (Blankenburg et al. 2008; Eickhoff et al. 2008; Eshel et al. 2010; Iwamura et al. 2001; Ragert et al. 2011). Because of the evidence supporting interhemispheric modulation of information, amplitude discrimination capacity on an AH was expected to be impacted with application of UH stimulation.

The results indicate that amplitude discrimination capacity is significantly worsened with equal-amplitude stimulation regardless of the amplitude applied to D2 and D3 on the UH. In these cases, the UH stimulation suggests interhemispheric modulation of the stimulated digits of the AH subsequently resulting in worsened performance on the amplitude discrimination task. While this change in performance may be due to inhibitory modulation from stimulation of the UH (Gröschel et al. 2013; Jung et al. 2012; Lipton et al. 2006; Palmer et al. 2012; Premji et al. 2011; Reed et al. 2012; Schäfer et al. 2012; Tommerdahl et al. 2005a, 2006; Wahl et al. 2007; Zapallow et al. 2013), perceptual differences may alternatively be due to a combination of inhibitory and/or excitatory mechanisms (Nihashi et al. 2005; Zhu et al. 2007). Increasing the amplitude of the UH stimulation failed to significantly alter discrimination performance in comparison with the lower amplitude condition. Subsequent tests with more specific types of UH stimulation were performed to further reveal potential mechanisms (interhemispheric inhibition and/or excitation of homologous sites) involved in the attenuated performance.

Unequal-amplitude UH stimulation differentially impacts amplitude discrimination capacity. In particular, the results suggest that incongruent stimulation results in a deterioration of amplitude discrimination performance, while the congruent condition indicates that similar patterns of stimulation on homologous sites across hemispheres do not significantly affect discriminative capacity. However, the decrease in amplitude discriminative capacity in the incongruent condition suggests that one of the several potential mechanisms may be involved in perceptual modulation, and thus degraded performance. The results implied that UH stimulation may modulate sensory perception on the opposite hand via long-range interhemispheric connections. The magnitude of the UH stimuli may either potentiate or suppress AH perception depending on the particular pattern and loci of stimulation applied to the AH. For example, incongruent stimulation may reduce perceptual contrast due to increased activation of the locus where the standard stimulus is applied on the AH. In this case, the standard stimulus would be perceived as more intense, and therefore, the performance on the task may subsequently worsen. Alternatively, decreased activation of the locus where the test stimulus is applied on the AH may also worsen discriminative capacity in the same manner; the test stimulus would be perceived as less intense and performance degrades. Lastly, there may be more complex mechanisms involved due to the lateral inhibitory mechanisms that exist among the UH itself. The UH percept may induce a perceptual rivalry which evokes tactile illusions and thus context-dependent differential performance on the amplitude discrimination task in the presence of unequal-amplitude UH stimulation.

In order to study the effects of unequal-amplitude digit stimulation in the absence of potential lateral inhibitory mechanisms in the UH, single-site stimulations were applied to observe whether there were any similar differential effects on amplitude discrimination performance. The results from the single-site UH stimulation at individual digits (D2 or D3) also resulted in differential performance on the amplitude discrimination task. Subjects performed worse when the pattern of stimulation on the UH least matched that applied to the homologous site on the AH. In other words, when similar patterns of stimuli are applied to homologous sites, amplitude discrimination capacity is not significantly affected. This conclusion is based on the results which show that subjects generally perform worse in the incoherent conditions than in the coherent ones. Repetitive vibrotactile stimulation leads to distinct and stimulus parameter-specific patterns of evoked activity in SI cortex (Chiu et al. 2005), and if these patterns are perceptually relevant, then stimulus amplitude specificity could contribute to differential performance on the AH. From the data in this study, it appears that what stimulus is delivered on the UH has an impact on task performance of the AH. The implications of this finding are that bimanual manipulations and explorations of objects are optimized when both homologous digits receive the same or similar input. Whether or not this similarity paradigm exists only for one parameter—in this study, amplitude—remains to be tested, and future studies will investigate this interesting possibility.

The critical questions that remain to be addressed are how and where the modulation of the perceptual metric on the attended hand occurs. Prior neurophysiological studies have shown that vibrotactile stimulation of the digits—as delivered in this study—result in an SI evoked response with single-site stimulation, and a positive response is evoked in both the contralateral and the ipsilateral hemispheres (Tommerdahl et al. 2005a, 2006). However, when a second stimulus is introduced to the homologous skin site on the opposite side of the body, the responses evoked by the two stimuli are not summed. In other words, while positive responses are evoked by independently delivered contralateral or ipsilateral stimuli, the combined response evoked by both stimuli in unison is reduced significantly—the sum is much less than computational sum of the individually evoked responses of the two stimuli. Combining those observations with those of the current study suggests that in some cases, magnitude of the evoked SI response does not necessarily correlate with task performance; if stimuli do not match, then perhaps some other factor—such as synchronization of cortical ensembles—plays a role in stimulus identification. One of the impacts of the change in stimulus conditions can be observed in SI, although how much influence SII has on the evoked response of SI via

these types of stimulus conditions would be difficult to assess. However, in this report, we did observe digit specificity in the influence that different patterns of stimulation of the UH had on task performance, and this observation suggests a strong SI influence since SII receptive fields are much larger than those in SI). Both SI and SII play a role in the cortical network response that modulates the performance on tasks such as the ones deployed in this study, and ascertaining the independent roles of those cortical areas could only be teased out with additional experimentation, as the current literature simply does not provide sufficient information to address the questions posed by this study.

In summary, the stimulus conditions where amplitude discrimination capacity is not significantly affected are when the unattended hand stimulations more closely matched the stimuli applied to the attended hand. The results of the three parts of the study suggest potential mechanisms involved in interhemispheric interactions. For instance, when stimuli are applied to the same homologous locus on both hands, if the stimulus magnitude on the UH is greater than that on the AH, the percept of the AH stimulation suggests an increase in intensity (excitatory). On the other hand, if the stimulus amplitude on the UH is less than that applied to the AH, that percept is thought to decrease in intensity (inhibitory). These interactions are both dependent on the locus and amplitude of stimulation applied to both hands. The findings suggest that each bilateral interaction is a context-dependent feature of the cortical network. Inhibitory and excitatory cortical circuits are dependent on each other in order to appropriately form balanced networks of activity (see Zhang and Sun 2011c for review). However, alterations in these networks can cause shifts in network balance (Heiss et al. 2008; Hull et al. 2009; Klingner et al. 2012). Interhemispheric interactions have been shown in studies where stimulus input evoked excitatory cortical responses to the contralateral hemisphere (Nihashi et al. 2005; Zhu et al. 2007), but there are also implications of inhibitory responses (Hlushchuk and Hari 2006; Lipton et al. 2006). Future neurophysiological studies will be required to determine the mechanisms involved in the digit-specific interactions demonstrated in this report.

Conclusion

For the past several years, we have been developing protocols that utilize "illusory confounding stimuli" that alter the perception of a sensory stimulus. These confounds are hypothetic, mechanistic, or process-based. For example, delivery of a repetitive vibrotactile conditioning stimulus to one of two skin sites before an amplitude discrimination task, such as described in this report, results in degradation of performance in healthy subjects (Nguyen et al. 2013a, b;

Tannan et al. 2007a, b, 2008; Zhang et al. 2009, 2011a, b). The impact of repetitive vibrotactile stimulation on the evoked SI cortical response is well documented; the evoked response of SI is reduced after a conditioning stimulus (for review, see Tommerdahl et al. 2010). However, a number of neurologically compromised subjects have demonstrated that this conditioning stimulus does not impact their performance. In other words, some subject populations (e.g., individuals with autism, alcoholism, multiple types of chronic pain, concussion) do not adapt to the conditioning stimulus, and for this reason, they actually outperform healthy subjects on the postconditioning amplitude discriminative task (Folger et al. 2008; Nguyen et al. 2013a, b; Tannan et al. 2008; Tommerdahl et al. 2010; Zhang et al. 2011a) because the illusory conditioning stimulus has little or no impact.

The significance of the finding in this report is that a relatively simple protocol, such as amplitude discrimination in the presence and absence of a confounding conditioning stimulus delivered to the UH, could potentially be used to determine deficits in the connectivity across hemispheres. Thus, individuals with atrophied or damaged callosal connectivity would be predicted to outperform healthy individuals on a metric that compares amplitude discrimination capacity in the presence and absence of conditioning stimuli delivered to the UH. Deficiencies in callosal connectivity have been demonstrated in a number of neurological disorders (e.g., aging deficits: Voineskos et al. 2010; Zahr et al. 2009; autism: Barnea-Goraly et al. 2004; Hardan et al. 2009; schizophrenia: Swayze et al. 1990; Degreef et al. 1992; Lewis et al. 1988; Tibbo et al. 1998; Wolf et al. 2008; attention deficit disorder: Hynd et al. 1991). Detection of these deficits utilizing simple and straightforward sensory testing methods could provide an efficient means for determining callosal abnormalities, but direct validation of this idea with parallel imaging studies needs to be conducted. Such studies are planned for the near future and we anticipate that differences in performance in perceptual tasks that integrate information across the body midline will parallel callosal health.

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