

Vibrotactile amplitude discrimination capacity parallels magnitude changes in somatosensory cortex and follows Weber's Law

E. Francisco · V. Tannan · Z. Zhang ·
J. Holden · M. Tommerdahl

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Abstract In this study, we investigated the changes in perceptual metrics of amplitude discrimination that were observed in ten healthy human subjects with increasing intensities of stimulation. The ability to perceive differences in vibrotactile amplitude changed systematically with increasing stimulus magnitude (i.e., followed Weber's Law) in a near linear fashion ($R^2 = 0.9977$), and the linear fit determined by the amplitude discrimination task predicted the subjects' detection thresholds. Additionally, the perceptual metrics correlated well with observations from a previously reported study in which measures of SI cortical activity in non-human primates (squirrel monkeys) evoked by different amplitudes of vibrotactile stimulation were obtained (Simons et al. in *BMC Neurosci* 6:43, 2005). Stimuli were delivered simultaneously to two different skin sites (D2 and D3), enabling a method for the relatively rapid acquisition of the data. Stability and robustness of the measure, its rapid acquisition, and its apparent relationship with responses previously observed in SI cortex, led to the conclusion that deviations from the baseline values observed in the obtained perceptual metric could provide a useful indicator of cerebral cortical health.

Keywords Vibrotactile · Amplitude discrimination · Weber's Law · SI cortex · Somatosensory

Introduction

One of the fundamental questions often addressed in neuroscience is how two sensory stimuli are differentiated. Detection and integration of the differences in physical attributes of our environment is, undoubtedly, just one way in which we coordinate the processes that govern how we react and respond to external stimuli. Weber initiated a discussion on how sensory stimuli are integrated into central information processing in his 1,834 study of perceived intensity. In his experiments, he measured the difference limen (DL) of blindfolded subjects by giving them two weights of equal magnitudes (standard weight) to hold in each hand. He then proceeded to add slightly heavier weights (test weight) to one hand. The subject was asked to compare the weights in both hands and determine which was larger. Weber found that it was more difficult for the subject to determine that there was a difference in the weights when the standard weight was larger; in other words, the size of the DL was proportional to the stimulus strength and increased linearly as the initial stimulus strength increased (Goldstein 2007). Based on Weber's experiments, physicist Gustav Theodor Fechner developed the Weber–Fechner Law: $\frac{\Delta S}{S} = K$, where ΔS is the DL corresponding to the reference stimulus S , and K is a constant called Weber's Fraction. Research has shown that Weber's Fraction is usually constant for a range of stimulus intensities and can be applied to most senses, including weight, brightness, and sound frequency (Hanna et al. 1986; Gescheider et al. 1990; Stillman et al. 1993; Gescheider et al. 1996b; Gescheider et al. 1997; Scholtyssek et al. 2008).

A number of intensity related studies have been conducted in our laboratory. Most recently, we made the observation that the magnitude of the evoked optical

E. Francisco · V. Tannan · Z. Zhang · J. Holden ·
M. Tommerdahl (✉)
Department of Biomedical Engineering,
University of North Carolina,
Chapel Hill, NC 27599, USA
e-mail: Mark_Tommerdahl@med.unc.edu;
tommerda@med.unc.edu

intrinsic signal (OIS) varies in a near linear fashion in SI cortex of squirrel monkeys with the amplitude of a 25 Hz vibrotactile stimulus (Simons et al. 2005). One of the more interesting facets of that study was that while the magnitude of the centrally activated SI cortical region increased significantly with increasing amplitude, the spatial extent of the responding cortical territory did not (Simons et al. 2005). Rather, the extent of the inhibitory surround became more prominent with increasing stimulus amplitude. A similar study demonstrated that this center surround relationship was duration- as well as amplitude-dependent (Simons et al. 2007). Although this does not, in concept, seem to be a surprising revelation, it could be considered antithetical to previous hypotheses proposed about the SI cortical response to different intensities of skin stimulation—specifically, that increasing vibrotactile amplitudes would lead to an increasing spatial extent of the response in SI (Johnson 1974). Simons et al., with their subsequent stimulus duration dependent study, demonstrated and discussed how the two views are compatible (Simons et al. 2007). To summarize, brief stimuli (500 ms or less) evoke a much more spatially extensive response than longer duration stimuli, and longer duration stimuli (greater than 500 ms) more actively engage pericolumnar lateral interactions that lead to a more prominent inhibitory surround. Previous ideas about intensity perception, which were based on the increased recruitment of peripheral afferents, obviously did not incorporate the inhibitory surround and thus led to alternative ideas about the characterization of SI cortical response to increasing stimulus intensity. Nevertheless, the near linear relationship between the magnitudes of the evoked SI cortical response to supra-threshold vibrotactile stimulus amplitudes led us to posit the question as to whether or not we would observe a parallel metric perceptually. In other words, would increasing the vibrotactile amplitude of two comparison stimuli lead to a proportional increase in the DL (i.e., would Weber's Law be followed)?

Additional intensity related, but perceptually based, studies have also been conducted in our laboratory (Tannan et al. 2007b; Tannan et al. 2008; Zhang et al. 2008). The development of novel stimulus devices that can simultaneously deliver two well controlled vibrotactile stimuli (both in terms of amplitude and frequency) has made a number of studies much more pragmatic (Tannan et al. 2007b; Tommerdahl et al. 2007a, b; Tannan et al. 2008; Tommerdahl et al. 2008a, b). For example, simultaneous delivery of two vibrotactile stimuli to different locations allows for direct comparison between the two stimuli, and problems originating from comparison of two stimuli at the same location, such as adaptive effects by the first stimulus delivered, are automatically eliminated. The decrease in overall protocol duration (to approximately 1.5 min per

standard) has made it possible to complete the multiple amplitude discrimination runs necessary for a study, such as the one described in this report, in a single 10–20 min session. In this report, the two-site amplitude discrimination protocol was executed with a number of different standard amplitudes in order to evaluate how subjects' discrimination ability changes with increasing intensity. Additionally, this data was compared with previously reported changes in SI cortical activity obtained from squirrel monkey in order to ascertain the relationship of primary sensory cortex to perceptual capacity.

Methods

Ten subjects (22–31 years in age) were studied who were naïve both to the study design and issue under investigation. The subjects consisted of seven males and three females, all right-hand dominant. The study was performed in accordance with the Declaration of Helsinki, all subjects gave their written informed consent, and procedures were reviewed and approved in advance by an institutional review board.

A two-alternative forced-choice (2AFC) tracking protocol was used to evaluate the amplitude discriminative capacity of each subject (see Fig. 1) in a manner used in a number of previous studies that have examined dual-site simultaneous vibrotactile discriminative capacity (Tannan et al. 2005, 2006, 2007a, b; Tommerdahl et al. 2007a; Zhang et al. 2008). The subject was seated with the right arm resting comfortably on a dual-site portable vibrotactile stimulator [CM-1; for full description, see: (Tannan et al. 2007a)]. Two probe tips (5 mm diameter) were positioned on the glabrous pads of digits 2 and 3 of the right hand. Digits 2 and 3 were chosen as test sites for both convenience of access (thus maximizing the test's potential in clinical applications) and because of the wealth of

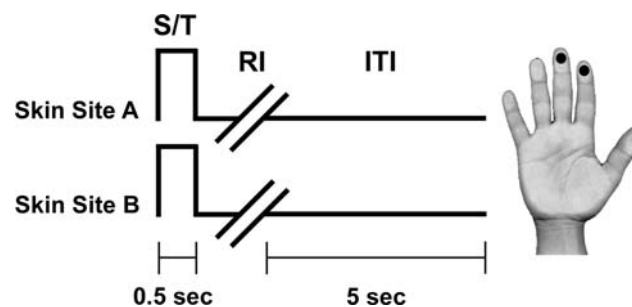


Fig 1 Schematic of the protocol used for amplitude discrimination. Two 25 Hz vibrotactile stimuli, the standard (*S*) and test (*T*), were delivered at the same time for 0.5 s. A 5 s delay [excluding subject response interval (*RI*)] was imposed before onset of the next trial. The subject was queried as to which stimulus felt more intense

neurophysiological information that exists for that somatotopic region of cortex in primates. Visual cueing was provided with a computer monitor during the experimental run. Specifically, an on-screen light panel was used to indicate to the subject when the stimulus was on and when the subject was to respond. The subject was not given performance feedback or knowledge of the results during the data acquisition until all sessions were completed. At the start of each run, the two probe tips were driven towards the skin until each tip registered a force of 0.1 g, as determined by a closed-loop algorithm in the CM-1 stimulator feedback system. The tips were then further indented into the skin by 500 μm to insure good contact with the skin. An audiometer was used to ensure that no auditory cues were emitted from the stimulator during delivery of the range of stimuli used in this study. All vibrotactile stimuli used in this study were delivered at the frequency of 25 Hz flutter.

Amplitude discrimination was tracked for nine conditions of standard stimulus amplitude, each condition tracked in a separate experimental run: 50, 100, 200, 300, 400, 500, 600, 700 and 800 μm . During an experimental run, a vibrotactile test stimulus was delivered simultaneously with a vibrotactile standard stimulus (the standard amplitude remained constant throughout the run). The loci of the test and standard stimuli were randomly selected on a trial-by-trial basis. Stimulus duration was 0.5 s, followed by subject response (subject was queried to select the skin site that received the most intense stimulus) and a 5 s delay before onset of the next trial. The test stimulus amplitude was always greater than that of the standard stimulus.

Each experimental run consisted of 20 trials total. In the initial ten trials, the amplitude of the test stimulus was modified based on the subject's response to the preceding trial—accomplished using a 1-up/1-down algorithm. This approach was selected because it enabled rapid determination (“tracking”) of each subject's minimally detectable difference in the amplitudes of two-site skin flutter stimulation (Tannan et al. 2007a). The difference between the amplitudes of the test and standard stimuli delivered on each of these initial ten trials was adjusted on the basis of the subject's response in the preceding trial (the discrepancy in amplitude was decreased if the subject response in the preceding trial was correct; it was increased if the response was incorrect). After the initial ten trials were completed, test stimulus amplitude was modified using a 2-up/1-down algorithm—in these trials two correct/one incorrect subject response(s) resulted in a decrement/increment, respectively, in the amplitude difference between the test and standard stimuli. The subjects' DLs were calculated by averaging the amplitude of the test stimulus in the last five trials of each run and comparing

this to the standard used in each test. The step size for each condition was 5% of the standard amplitude. This value was chosen in order to maximize resolution of the method as well as to standardize the relative step size for each run. A series of training trials, each consisting of a pair of stimuli differing in amplitude by 100 μm (200 vs. 100 μm), were conducted prior to the first run. These amplitudes were chosen to provide only minimal challenge to the subjects performing the discrimination task during training. The subject was provided with feedback only during training trials and was allowed to continue on to the first run after answering correctly five times in a row. Each subject participated in a single experimental session that consisted of nine separate runs of different standard amplitude conditions (randomized in order). A single session, including actual testing time and short breaks between each run, took 30–45 min. A modified 2AFC protocol was also used to evaluate the detection threshold of each subject. For this procedure, amplitude discrimination was performed for 60 trials using a 3-up/1-down algorithm, due to the lower signal-to-noise ratio at this low-amplitude testing level. In this condition, the standard amplitude was held constant at 0 μm , thereby testing the ability of the subject to simply detect the presence of the 25 Hz stimulus.

Results

A 2AFC tracking protocol was used to determine subjects' capacities to discriminate between the amplitudes of two simultaneously delivered vibrotactile stimuli and to directly compare subjects' discriminative capacities under different conditions of standard amplitude [protocol previously described in (Tannan et al. 2007b, 2008; Zhang et al. 2008); also see Methods]. To summarize, a tracking protocol was employed in which two stimuli were delivered simultaneously in one trial. The subject was queried as to which stimulus was more intense, and the difference between the two subsequent stimuli of the next trial was increased or decreased based on subject response. The DL for each subject was determined by averaging the tracking values obtained from the last five trials of each experimental run.

Across-subject DLs for each of the standard values are summarized in Fig. 2. Subject performance was highly consistent, and the results demonstrated that subjects performed much better, on an absolute scale, when the standard stimulus was smaller [e.g., compare the DL obtained with a 50 μm standard ($14.8 \pm 1.26 \mu\text{m}$) to the DL obtained with an 800 μm standard ($101.6 \pm 1.72 \mu\text{m}$)]. A linear least-squares fit was applied to the data, and an R^2 value of ~ 0.998 was obtained for the linear regression, demonstrating a remarkably strong correlation between DL

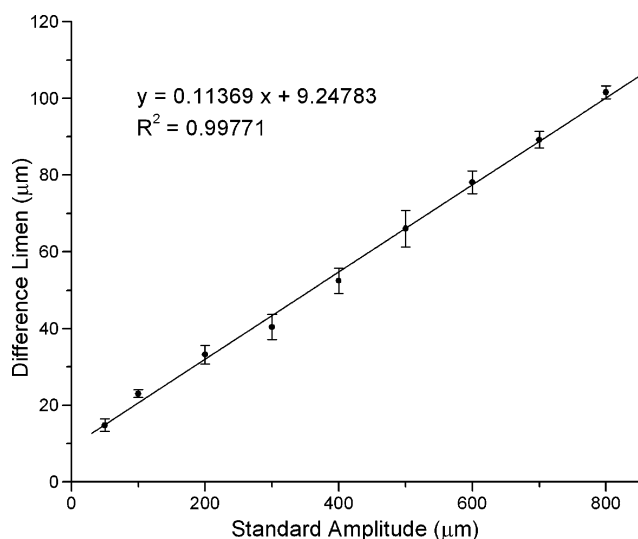


Fig 2 Averaged difference limen values of the ten subjects at various standard amplitudes (with s.e. bars). The plotted linear regression has a correlation coefficient of 0.99771, and the y -intercept (predicted detection threshold) is approximately 9.25 μm

and standard amplitude and thereby verifying the application of Weber's Law for this particular task. Extrapolation of the linear fit (shown in Fig. 2) to the y -intercept yields the prediction that the detection threshold—or in other words, the ability to correctly discriminate between a vibrotactile test stimulus and a 0 μm “standard” stimulus—should be $\sim 9.25 \mu\text{m}$. Under the condition of 0 μm standard stimulus amplitude, a modified amplitude discrimination protocol was used (which required a much larger number of trials—see “Methods”) and detection thresholds were directly obtained and averaged across all subjects. Subjects were consistently able to detect stimuli at amplitudes of $9.21 \pm 1.76 \mu\text{m}$, and an independent two subject t -test verifies that there is not a statistically significant difference between the actual average detection threshold and the predicted measure derived from the linear fit to the amplitude discrimination DLs obtained with this protocol ($t = 0.029$, D.F. = 15, $P = 0.977$).

In order to ascertain whether or not $\Delta S/S$ was constant (i.e., whether or not the Weber–Fechner Law held true) DLs, averaged across all subjects, were re-plotted as a percent of the corresponding standard amplitude from which they were obtained (see Fig. 3). The data suggest that DLs are proportionally higher at lower amplitudes (i.e., standard amplitude $< 300 \mu\text{m}$), then level off for higher standard amplitudes ($\geq 300 \mu\text{m}$) at a percent difference of approximately 13%. Thus, the non-linearity of this data demonstrates a deviation from the Weber–Fechner law in the region tested below 300 μm , suggesting that the Weber–Fechner Law holds true only for the amplitude discrimination tasks with the relatively higher standards.

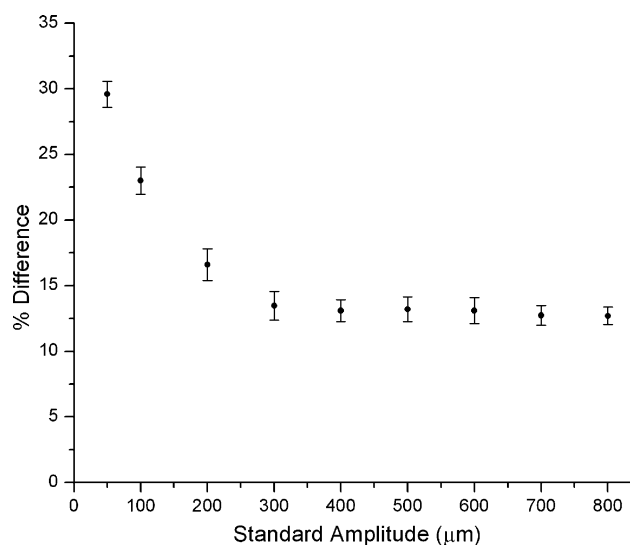


Fig 3 Difference limen values of the ten subjects plotted as percent different from the corresponding standard amplitude, for each standard amplitude (with s.e. bars)

In a previous study that investigated the SI response to different amplitudes of vibrotactile stimulation (at the same frequency as this study) utilizing the technique of OIS imaging in non-human primates, we found that an increase in the amplitude of the stimulus corresponded with the increase in absorbance evoked within the region of SI cortex that receives its input from the stimulated skin field (Simons et al. 2005, 2007). The relationship between the maximal change in absorbance and stimulus amplitude was characterized by a near-linear function within the range of amplitudes studied (50–400 μm). Measurement of the spatial extent of the activated SI region, on the other hand, showed that higher amplitudes of stimulation did not produce a more extensive region of SI activation. Instead, as the amplitude was increased, average peak absorbance within an $\sim 2 \text{ mm}$ diameter SI region increased with the amplitude of stimulation, and the region of surrounding cortex underwent a prominent decrease (frequently to levels well below background) in absorbance. In order to directly compare the two principle findings of that study—the relationship of absorbance evoked by different amplitudes of stimulation and the apparent lack of correspondence of the spatial extent with amplitude of stimulation—we directly compared the DLs obtained from the results of this report with those two entities. The results from those comparisons are shown in Fig. 4 and demonstrate that there is a very strong correlation ($R^2 = 0.9971$) between the DLs obtained at each standard amplitude and the neural activity evoked at each amplitude. On the other hand, a much weaker (not significant) correlation was observed between the spatial extent of the cortical response and the DLs obtained at the same amplitudes ($R^2 = 0.4542$).

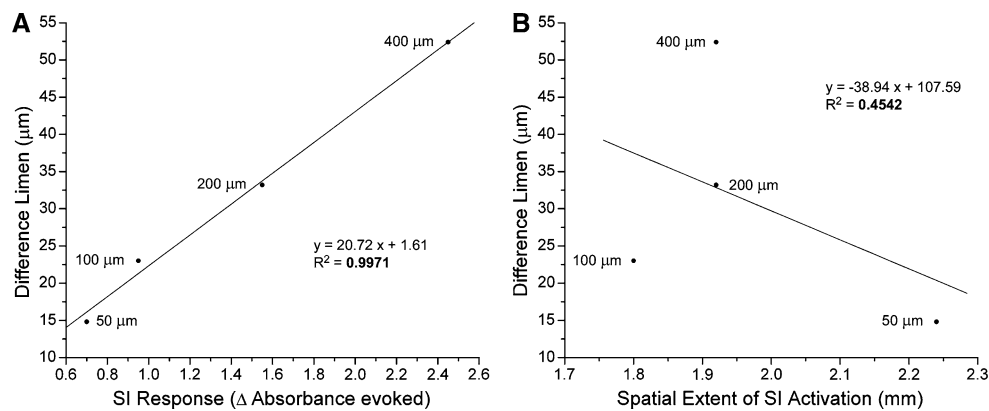


Fig 4 Panel A. Correlation between the DLs, obtained from this study, and the maximal change in absorbance in *SI*, previously reported (Simons et al. 2005). As the standard amplitude increases, both DL and *SI* response increase in a linearly proportional manner

($R^2 = 0.9971$). Panel B. Correlation between the DLs and the spatial extent of *SI* activation. As the standard amplitude was increased, no correlation was observed ($R^2 = 0.4542$)

Discussion

In this study, a dual-site vibrotactile amplitude discrimination protocol was used to determine the DL for a number of standard amplitudes. The DLs were found to increase in a near-linear fashion with an increase in standard amplitude, thus adhering to Weber's Law for the stimulus range employed in this study (50–800 μm). Extrapolation of the linear least squares fit of the data (DL vs. standard amplitude) yielded a prediction—at the y intercept—of the detection threshold. An independent method of threshold observation demonstrated that the same group of subjects had a detection threshold very close to the one predicted ($9.21 \pm 1.76 \mu\text{m}$ detected vs. $9.25 \mu\text{m}$ predicted), and both values are consistent with those reported by other investigations (Gescheider et al. 1996b, 1997; Hollins and Sigurdsson 1998; Gescheider et al. 2004). Previously reported relationships of *SI* cortical activity (in squirrel monkey) evoked by different stimulus amplitudes were proportional to changes observed in the perceptual metrics obtained in this study with different standard amplitudes.

One of Ken Johnson's principle contributions to the field of somatosensory neurophysiology was his emphasis on the description of linearity between subjective experience and the underlying neural activity on which it is based. In essence, he concluded that "all the available evidence points to linearity as the basic law of psychophysics" (Johnson et al. 2002). The results of this paper fully support his statement, as not only was there a linearity demonstrated in the perceptual metrics, but the perceptual metrics obtained in this study co-vary with the *SI* cortical response (from non-human primates) in a fashion that strongly suggests that the magnitude of the neural activity evoked in *SI* could be essential to the neural code of intensity discrimination. Although *SI* is considered primary sensory

cortex, it has, nevertheless, been observed to reflect other aspects of perception exceedingly well. Chen and colleagues observed evoked *SI* activity between the somatotopic representations of two digit tips when the two digits were simultaneously stimulated—an apparent parallel to the perceptual illusory effects generated by the same dual site stimulus (Chen et al. 2003).

A number of other somatosensory studies suggest that the increase in stimulus intensity could be proportional to an increase in the evoked *SI* cortical activity. Most closely related to our *SI* cortical study—briefly summarized in the results section—was a study by Chen and colleagues who used the OIS to demonstrate that a proportionally greater (larger magnitude) response is evoked in *SI* of squirrel monkeys as the amplitude (as measured by force) of a skin stimulus is increased (Chen et al. 2003). Several studies examined the global *SI* response using non-invasive imaging techniques in humans such as functional Magnetic Resonance Imaging (fMRI) (Arthurs et al. 2000; Backes et al. 2000; Nelson et al. 2004) and MagnetoEncephalography (MEG) (Iguchi et al. 2002; Torquati et al. 2002). In general, results from these non-invasive studies indicated that increases in stimulus intensity are accompanied by increases in the intensity of the evoked signal as well as increases in the activated volume of *SI* cortex. As a result, these studies predicted that amplitude might be coded not only by the average firing rates of individual *SI* neurons, but also by the total aggregate of responding neurons. These population based studies seemed to confirm prior predictions of the *SI* neuronal population response based on reconstructions from afferent recordings (Werner and Mountcastle 1965; Johnson 1974; Connor et al. 1990; Whitsel et al. 2000; Guclu and Bolanowski 2002) and single unit cortical recordings (Mountcastle et al. 1963; Simons 1978).

Could the neural code for intensity be as simple as the above-described relationship suggests? One aspect that has not been addressed in this study is the effect that stimulus duration could potentially have on the results. A longer stimulus duration would result in both improvements perceptually, such as those that occur with adapting stimulation (Goble and Hollins 1993, 1994; Gescheider et al. 1996b, 1999; Tannan et al. 2007b) as well as changes in the SI cortical response. One of the most notable changes in SI cortical response with increasing vibrotactile stimulus duration is the increased funneling that leads to the development of a surround (Llinas and Sugimori 1980; Tommerdahl et al. 2002; Chiu et al. 2005; Simons et al. 2005). The surround appears to spatially constrain the responding cortical region (Simons et al. 2007), and within the spatially constrained area of evoked cortical activity, spatially non-homogenous patterns of response develop which are amplitude dependent (Chiu et al. 2005; Tommerdahl et al. 2005a). Such stimulus dependent patterns have been observed in other cortical studies as well (Bruno et al. 2003) that strongly suggest that minicolumnar patterns of response play a role in cortical information processing (Tommerdahl et al. 1987; McCasland and Woolsey 1988; Tommerdahl et al. 1993; Favorov and Kelly 1996; Chiu et al. 2005; Tommerdahl et al. 2005a).

There could be potential clinical implications from this study. Since the results suggest a strong correlation with SI cortical activity and the capacity for amplitude discrimination at multiple amplitudes, we would predict that a systemic cortical alteration, in which cortical activity deviates from the norm, would change a subject's capacity for amplitude discrimination. For example, the function determined by the relationship between the DL versus standard amplitude (such as plotted in Fig. 2) could be impacted significantly in a neurologically compromised individual, and this function could be determined relatively rapidly by deriving it from two or three DLs obtained from larger amplitude (>300 μm) standards.

Based on the data plotted in Fig. 3, it appears that subjects are much more accurate at higher standards, most likely due to the higher signal-to-noise ratio (with "noise" determined by the baseline values of neural activity that are correlated with subthreshold perceptual values). If this is, in fact, the case, then the data presented in Fig. 3 would present a fairly strong argument against obtaining and interpreting threshold and/or near-threshold measures, as accuracy clearly decreases with the magnitude of the stimuli. In other words, accurate threshold detection measures necessitate much longer protocols (in the case of this study, three times as long) than does deriving amplitude discrimination capacity at multiple supra-threshold standards. Additionally, the multiple DLs obtained from studies such as this one can be used to determine a

functional relationship; threshold detection, on the other hand, yields only one measure, and it is difficult to derive a systemic function from a single point. Although numerous studies have successfully shown differences in thresholds for different neurologically compromised subject populations (Gescheider et al. 1996a; Goble et al. 1996; Hollins et al. 1996; Kosek et al. 1996; Rocheron et al. 2002; Guclu et al. 2007; Ofek and Defrin 2007; Wiacek et al. 2007; Alary et al. 2008), relatively fewer studies have emphasized the amplitude discriminative capacities of those subject populations (Gescheider et al. 1996a; Hollins et al. 1996; Rocheron et al. 2002; Wiacek et al. 2007), most likely due to the difficulty of implementing such a study in a clinical or clinical research setting. The increased efficiency and performance that is associated with dual-site simultaneous delivery of tactile stimuli makes it much more feasible to rapidly perform amplitude discrimination studies of the type described in this report (Tannan et al. 2007a) and potentially implement in a clinical setting. Moreover, a growing number of similar studies are demonstrating significant cerebral cortical differences between a number of different subject populations (Tommerdahl et al. 2007a; Folger et al. 2008; Tannan et al. 2008; Tommerdahl et al. 2008a). Related to the issue of resolution is that an exponential growth of brain imaging (fMRI, EEG, MEG) studies have yet to reveal significant differences that parallel those observed in studies which obtain perceptual metrics such as those in this report. Furthermore, it is highly unlikely that such brain imaging studies will be capable of detecting differences in the responses evoked by stimuli which vary in intensity by as little as 10–20%. Given the cost—both in time and in monetary expense—it may serve diagnosticians well to take a closer look at the perceptual measures that strongly reflect cortical activity and are sensitive to systemic cortical alterations.

Although some strong correlations were observed in this study, there are questions that observations of this study raise that remain to be resolved. One of the most prominent questions stems from the observation that the weaker stimuli studied (50, 100, 200 μm) had proportionally larger DLs than the stronger stimuli. At the stronger stimulus conditions, the DLs maintained a fairly constant value in proportion to the standard stimulus. While our current interpretation of this is that it could simply be a signal-to-noise issue, we cannot rule out other stimulus-dependent mechanisms. For example, the studies of Chen and colleagues (Chen et al. 2003) would suggest that stimuli delivered to adjacent digit tips, particularly when the stimuli are near equal in strength, would result in mutual inhibition of the cortical responses evoked by the two stimuli. In this scenario, the DLs observed in the weaker standard stimulus range would be more significantly impacted. Decreases in the evoked SI cortical response

have been observed in a number of stimulus conditions (Tommerdahl et al. 2005b, 2006), and the impact of such stimuli on perceptual metrics such as those reported in this study are currently being explored.

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