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An Undergraduate Laboratory Exercise to Study Sensory Inhibition

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Sensory inhibition was first described by von Békésy as a process in which excitation of a field of sensory neurons leads to the reduction of activity of surrounding neurons and thus promotes contrast enhancement of the excited field. In the context of somatosensory cortex, the cortical neurons excited by touch or vibration will suppress excitation of neurons from surrounding receptive fields.

Using tactile stimulators both designed and fabricated at the University of North Carolina at Chapel Hill, we conducted two simple experiments in which sensory inhibition plays a role in information processing: a unilateral study in which stimuli are delivered to the digits of one hand, and a bilateral study in which stimuli are delivered to the digits of both hands. In the unilateral study, we demonstrated that threshold detection on the third digit (D3) is impacted by conditioning stimuli delivered to adjacent digits 2 (D2) and digits 4 (D4). In the bilateral study, we delivered different conditions of bilateral stimulation in order to investigate the impact that conditioning stimulation of the right hand had on amplitude discriminative capacity of the left hand. The results demonstrated that conditioning stimulation on the right hand had a significant impact on the discriminative capacity of the left hand, and this alteration in discriminative capacity was consistent with previous animal studies in which somatosensory cortical responses evoked by stimulus conditions of unilateral vs. bilateral stimulation were compared.

At the conclusion of this exercise, students will appreciate the fundamentals of sensory inhibition as well as the logistics of obtaining and analyzing data from human subjects. This study is designed to help students prepare for studying other facets of sensory processing by providing a firm foundation in the experimental methods and procedures.

Keywords: Sensory Inhibition; Ipsilateral and Bilateral Inhibition; Vibrotactile Amplitude Discrimination

INTRODUCTION

Sensory inhibition is a phenomenon in which the excitation of a neuron, evoked by sensory stimuli, inhibits or reduces the activity of other neurons. A specific form of sensory inhibition known as lateral inhibition occurs when an ensemble of cortical neurons, once excited, inhibit the activity of neighboring or surrounding neurons. The effect of this inhibition helps to sharpen the excitation profile in response to a localized stimulus. George von Békésy demonstrated lateral inhibition in the somatosensory system by mechanically stimulating points on the skin (reported in his 1967 book *Sensory Inhibition; see Figure 1)*. Subjects reported an area of sensation surrounded by a refractory area of inhibition. This perceptual finding predicts that when stimuli are delivered to the skin, the impact of transmission of that information (via projection of peripheral nerves at the stimulus site to a specific location in somatosensory cortex) is to activate specific cortical locations which not only become activated, but inhibit adjacent cortical locations. The relationship between skin and cortex is somatotopic: there is a point to point mapping of skin to cortex. In other words, the nerves in the digit tips map to neighboring places in the cortex. Thus, stimulating a digit tip will not only evoke excitatory activity in somatosensory cortex, but will, through lateral inhibitory mechanisms, result in a decrease in activity in the neighboring areas of cortex projected to from the adjacent digit tips. This, in turn, creates a “masking effect” by reducing the perceived intensity (magnitude) of a target stimulus. Stimuli in closer proximity to the test stimulus have a greater masking effect (Levin and Benton, 1973).

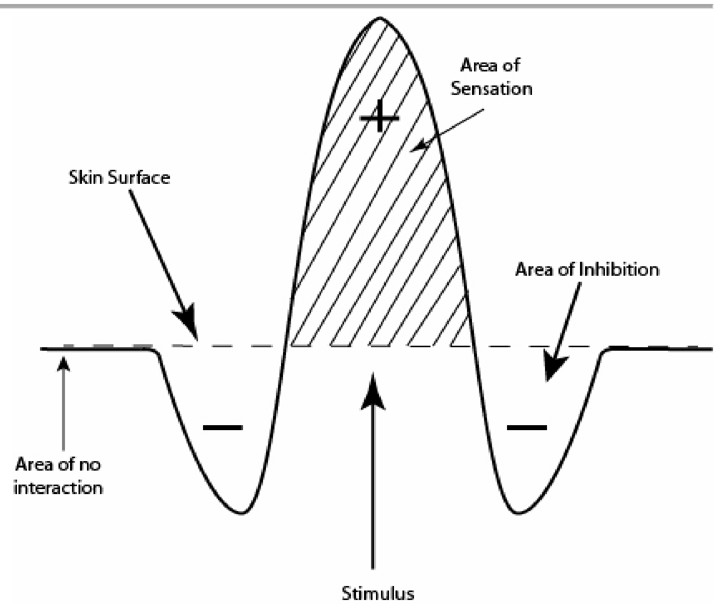

Figure 1. Model of Lateral Inhibition, modified from von Békésy's *Sensory Inhibition* (1967).

A stimulus with intensity above sensory threshold is consciously perceived (Gescheider, 1997). This minimum stimulus intensity (threshold detection) can be used in combination with different stimulus conditions to demonstrate lateral inhibition. The first of the two exercises explores this by applying different amplitudes of conditioning stimuli to the finger tips (D2 and D4) adjacent to the fingertip where threshold is being determined (D3). The test stimulus slowly increases in amplitude until it reaches the threshold, at which point the stimulus can be distinctly discriminated from the conditioning stimuli on the adjacent digits. Increasing the amplitude of the conditioning stimuli applied to digits 2 and 4 should increase the threshold level of digit 3.

Can sensory inhibition play a role in information processing across the body midline? It has been demonstrated that stimulation on one hand will negatively impact the sensory performance of the other hand. For example, stimulating the left hand has shown a decrease in the ability to perceive the location and intensity of a stimulus on the right hand. This has been proposed to be due to suprathreshold stimulation on one hand affecting the thresholds of the opposite (Braun et al., 2005). Other reports have demonstrated a decrease in spatial acuity when the opposing hand was simultaneously stimulated (Tannan et al., 2005). These reductions in performance are consistent with findings from animal research that examined the evoked cortical activity that occurred with stimulating one vs. two hands (Tommerdahl et al., 2006).

The second exercise is designed to study information processing across the midline. This is accomplished by delivering conditioning stimulation on the right hand while simultaneously measuring amplitude discriminative capacity on the left hand. The fundamental hypothesis being tested is that a conditioning stimulus on the right hand will reduce the stimulus evoked activity in the somatosensory cortical region that is engaged in the amplitude discrimination task via callosal connections. In order to obtain the necessary observations to address this question, performance on a unilateral amplitude discrimination task will be observed in the presence and absence of a conditioning stimulus on the opposite hand. The amplitude discrimination task consists of delivering a standard and a test sinusoidal vibrotactile stimulus simultaneously to digits 2 and 3 of the left hand, after which the subject determines which stimulus is larger in magnitude. This protocol has been used in a number of previous studies that have demonstrated that the metric is a robust measure across healthy populations (Francisco et al., 2008; Zhang et al., 2011). Students will use the Cortical Metrics Stimulator (CM-4; Cortical Metrics LLC; Holden et al., 2011a) for both exercises.

LEARNING OBJECTIVES

Upon completion of the experiment, students should be able to:

1. Define and understand sensory inhibition and its applications to tactile stimuli.
2. Explain the basic fundamental mechanisms of somatosensory testing, such as threshold detection and amplitude discrimination.
3. Understand the relationship between the physical intensity of a stimulus and perceived intensity.
4. Conduct other sensory perceptual experiments to predict and observe interactions across the body midline.
5. Gain familiarity with the operation procedures of the Cortical Metrics Stimulator as well as be able to conduct future experiments involving sensory data collection and analysis.

MATERIALS

A four-point vibrotactile stimulator (CM4; Cortical Metrics Model #4; see Figure 1) was used to conduct the first experiment. Typically, there is one stimulator 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 probe tips that come in contact with the subject's digit tips. The stimulator is mounted on a drum that rotates and allows for independent positioning of each probe tip to best fit an individual's hand. For a full technical description see Holden et al., 2011a. In the second bilateral experiment, the device cabling was modified so that two stimulator head units, one per hand, were connected to one system. This configuration allowed for stimulation of two digits on each hand (see Figures 2 and 3). Software for the device is included with the system. Protocols were downloaded and the setup for the experiment is fully automated.

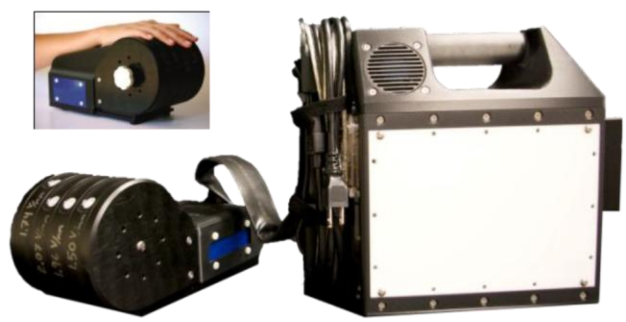

Figure 2. Cortical Metrics (CM-4) Stimulator. INSET: Subject's hand properly positioned on the head unit of the stimulator.

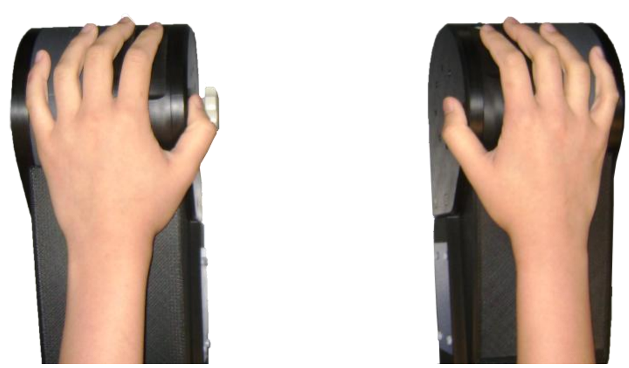

Figure 3. Overhead view of hand positioning in Bilateral setup.

PROCEDURES

Subjects

Ten healthy control subjects were recruited into the study. Subjects were naïve to both the study design and issue under investigation.

Unilateral Sensory Threshold Detection

During the experimental session, the subjects were seated comfortably in a chair with their left arm situated on an ergonomic armrest attached to the head unit of the vibrotactile stimulator. Probe tips from the stimulator made contact with the glabrous skin of the second (index, D2), third (middle, D3), and fourth (ring, D4) digits of the left hand. Subjects placed their right hand on a two-button response device (wireless mouse), which was directly connected to the computer. Visual cueing was provided through the computer monitor during each of the experimental runs. The cues indicated when the experimental stimuli were being delivered as well as when subjects were to respond. Participants were instructed to maintain fingertip contact with the probe tips throughout the duration of the experiment.

Vibrotactile flutter stimulation (25 Hz) was simultaneously applied to D2, D3, and D4 of the left hand. Conditioning stimulation occurred on D2 and D4 at constant amplitudes of either 15, 50, 100, or 200 µm. The test stimulus was delivered to D3, where the amplitude of the stimulus initially began at 0 µm and increased at a rate of 2 µm/s. The slow increase rate of the amplitude of the test stimulus allowed for reaction time of the subject to play a relatively small role in the assessment of the subject's detection threshold. The subject was instructed to respond as soon as the test stimulus on D3 was perceived, and the amplitude of the conditioning stimuli was randomized on a trial-by-trial basis. Four trials were tested for each of the four conditions, and each of the trials was completed once subjects responded to the perceived stimuli. The total duration of the protocol lasted no longer than five minutes, but may have varied according to subject performance.

Amplitude Discriminative Capacity in the Presence and Absence of Contralateral Conditioning Stimulus

Similar to the first experimental session, the subjects were seated comfortably in a chair with their left and right arms situated on two separate head units. Probe tips from the stimulator made contact with the glabrous skin of the second (index, D2) and third (middle, D3) digits of both the left and right hands. Visual cueing was similarly provided through the computer monitor during each of the experimental runs. Participants were instructed to maintain fingertip contact with the probe tips throughout the duration of the experiment.

Vibrotactile flutter stimulation (25 Hz) was simultaneously applied at half-second durations to the pairs of digits on each hand. The stimuli applied to digits D2 and D3 of the left, or attended, hand consisted of a test stimulus that was applied to one digit and a standard stimulus 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 were randomly selected among the paired digits on a trial-by-trial basis. The stimulus parameters delivered to D2 and D3 of the right hand were equivalent in amplitude, frequency, and duration to those applied to the left hand. Subjects were instructed to verbally indicate which digit on the left hand the larger stimulus was applied to. The test administrator then recorded the response by using the response device to choose the appropriate digit.

A modified von Békésy method (Cornsweet, 1962) was used to track subject performance throughout the amplitude discrimination protocol. With this adaptive tracking method, the difference between the amplitudes of the test and standard stimuli was adjusted on the basis of the previous response. Correct responses resulted in decreasing the test amplitude while incorrect responses resulted in increasing the test amplitude on subsequent trials. During the first ten trials, tracking was conducted with a bias of one in order to rapidly track down to a discriminative threshold. The remaining ten trials implemented a bias of two where subjects were required to deliver two consecutive correct responses for the test amplitude to decrease. This change in bias increases the accuracy of the results of the run by decreasing the probability of guessing the correct response (Tannan et al., 2006). While this psychophysical method introduces a bias to the metrics, this tracking paradigm has been demonstrated to have sufficient precision to differentiate between subtle differences in stimulus conditions in numerous studies (e.g., Francisco et al., 2008; Zhang et al., 2011). 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). Similar intensity discrimination tasks have been done with other senses, such as hearing (Pienkowski, 2009).

For each run, the initial test amplitude (400 µm) was twice the standard amplitude (200 µm) while the step size at which the test amplitude was increased or decreased was set at 10% of the standard stimulus amplitude. 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 twenty trials that were administered during the run. The data confirm that most subjects can reach their discrimination threshold within ten to fifteen trials. The total duration of the protocol lasted no longer than six minutes, but may have varied according to subject performance.

RESULTS

This study investigated the effects of lateral inhibition in the somatosensory cortex, and the ways in which these inhibitory mechanisms impact performance in two perceptual tasks. The threshold detection experiment assessed the effects of lateral inhibition locally – or the impact that stimulating one digit has on the percept of stimuli on neighboring digits. The amplitude discrimination task, in the absence and presence of conditioning stimuli on the opposite hand, demonstrates the effect that inter-hemispheric connectivity has on tactile sensory perception.

The results of the detection threshold tests (Figure 4) demonstrated that the amplitude of the conditioning stimuli on D2 and D4 has an impact on the threshold detected at D3. In particular, increasing the amplitude of the conditioning stimuli led to a detection threshold.

Figure 5 shows the results of the amplitude discrimination experiment obtained in the presence and absence of conditioning stimuli. Data were normalized to the value of "1" for each subject's DL for amplitude discrimination in the absence of conditioning and the bilateral conditioning value was determined by how much the DL changed in the presence of the conditioning stimulus on the opposite hand. The results show that a larger difference between the test and standard was necessary when the conditioning stimulus was active. This suggests that inhibition does cross the midline and affects the perceived amplitudes.

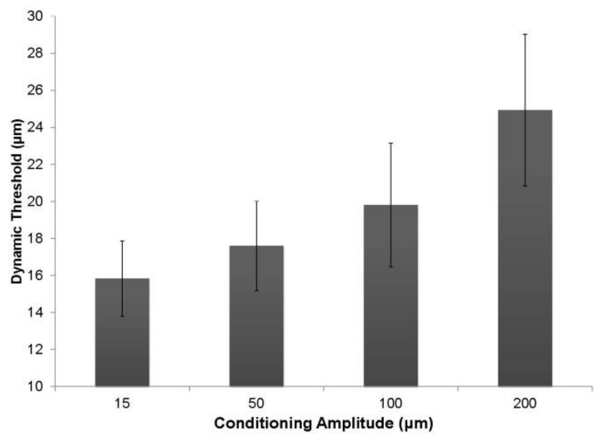

Figure 4. Detection Threshold versus Amplitude of Conditioning Stimuli. Different values of conditioning stimuli were simultaneously applied to D2 and D4 while average detection thresholds for D3 were determined and plotted with standard error of the mean.

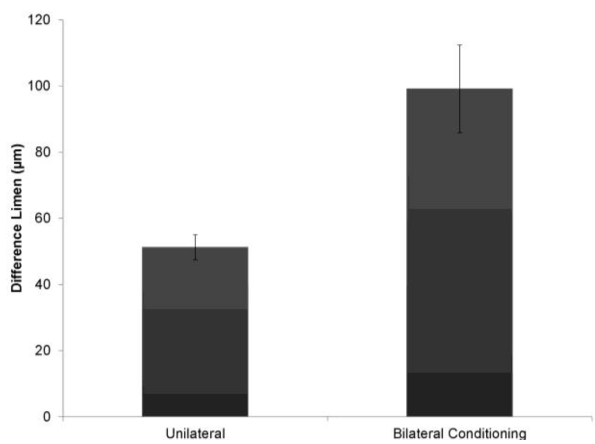

Figure 5. Unilateral versus Bilateral Amplitude Discrimination. Average difference limens for each condition are plotted with standard error of the mean.

DISCUSSION

In the somatosensory cortex, digit representations are considered to be somatotopic where receptive fields are spatially localized in accordance to the ways in which digits are anatomically organized. In particular, the cortical columns representing the receptive field of D2 are adjacent to those of D3, which are, in turn, adjacent to those of D4. The unilateral and bilateral exercises explored the lateral inhibitory mechanisms among these adjacent and near-adjacent cortical regions.

Detection threshold is measured in the unilateral exercise and is defined as the minimal stimulus that can be perceived. In this exercise, detection thresholds were measured in the presence of different amplitudes of conditioning stimulation on the adjacent digit tips. The conditioning stimuli excite the cortical columns of D2 and D4 as well as activate inhibitory surrounds around these regions thus inhibiting the adjacent cortical regions, which includes the cortical representation of D3. Increasing the amplitude of the stimuli on these pairs of digits results in increased excitation of their respective columns, resulting in an increased inhibitory effect. These inhibitory mechanisms suggest that the detection threshold of D3 is altered by changes in the amplitudes of the conditioning stimuli. The amplitude of the test stimulus must be large enough to generate the necessary activation in columns surrounding D3 to overcome the inhibitory effect they are experiencing from the adjacent columns of D2 and D4.

Tactile information is integrated across callosal connections, and prior observations in non-human primates demonstrated that stimulating two hands can result in a decrease in stimulus evoked activity relative to stimulating one hand (Tommerdahl et al., 2006). The unilateral vs. bilateral exercise demonstrated how inter-callosal connections can serve to integrate information across the body midline. The unilateral stimulus condition served as a baseline of amplitude discriminative capacity that was altered when stimuli were delivered to both hands in the bilateral condition. When the conditioning stimulus was applied to the right hand, the ability of the subject to discriminate between amplitudes was impacted significantly. This demonstrates that activity occurring on one side of the body crosses the midline and influences the perception of stimuli on the opposite hand.

The two exercises in this laboratory were designed to demonstrate the effects of sensory inhibition on sensory perception, as well as to introduce the concepts of fundamental experimental design. By the end of this laboratory, students were familiar with the concept of sensory inhibition, as well as with the concept of detection thresholds and amplitude discrimination capacity. The data gathered in the experiments is simple enough for each of the students to analyze themselves, and this reinforces the concepts presented throughout the experiments. The methods used provide a basis for the students to design new experiments on their own in subsequent laboratory exercises. This is the second laboratory exercise reported using these methods (first exercise reported in Holden et al., 2011b), and we anticipate that student based designs will lead to additional laboratory exercises that demonstrate concepts of centrally mediated information processing.

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Received July 17, 2012; revised November 06, 2012; accepted November 08, 2012.

This work was supported, in part, by NIH 1-R21-NS072811-01A1.

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