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Neurosensory Assessments of Concussion

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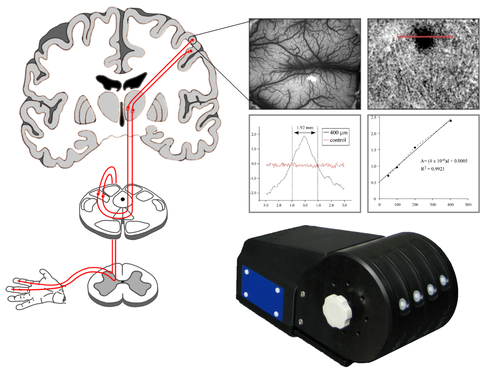
Abstract

The purpose of this pilot study was to determine if cortical metrics - a unique set of sensory-based assessment tools - could be used to characterize and differentiate concussed individuals from non-concussed individuals. A second aim was to determine if the CNS status of concussed subjects could be tracked to recovery. In order to pursue these aims, a portable, noninvasive tactile stimulator was designed and fabricated to deliver stimuli to adjacent finger tips. Taking advantage of the somatotopic relationship between skin and cortex, biologically-based hypothesis-driven protocols were designed to evoke interactions between adjacent cortical regions and investigate fundamental mechanistic changes that occur with cortical-cortical interactions. We predicted that these interactions would be altered with systemic alterations in cortical machinery, such as those that occur with neurological insult or trauma, and consequently, the sensory percept of these paired tactile stimuli would be altered in a predictable manner.
Student-athletes, aged 18-22, were recruited into the study from a varsity athletic training center that made determinations of post-concussion return-to-play status. Multiple metrics of sensory percept were obtained with a battery of individual protocols, each lasting 1-3 minutes, and each with a modified von Bekesy tracking algorithm, from participants post-concussion. The protocols used were designed to assess metrics related to an individual's capacity for information processing speed, lateral inhibition, adaptation, feed-forward inhibition and synchronization. Performance of each subject on the battery of 6 sensory tests was treated as localizing this subject in a multi-dimensional "cortical metrics" space (i.e., an abstract space in which each coordinate axis corresponds to each of the battery's sensory tests). Principal Component Analysis (PCA) was used to generate individual CNS profiles of data collected from concussed vs. non-concussed populations. Hotelling's t-square statistic indicates with 99% confidence that these 2 populations are statistically distinct, and CNS profiles could be tracked to recovery.

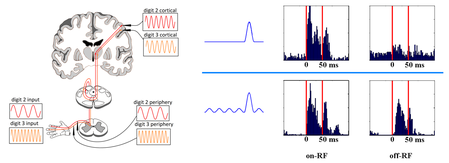
Methods



CM5 vibrotactile stimulator and general experimental model
Sensory perceptual tests were designed in order to rapidly and effectively measure a subject's capacity to differentiate two vibrotactile stimuli delivered to the fingertips (digits 2 and 3). Protocols were designed in order to specifically assess specific parameters that could be assessed in vivo or in vitro animal experimentation. Since these protocols are designed to be sensitive to changes in systemic cortical alterations, we refer to them as cortical metrics. Identical stimuli are delivered to the skin and observations from human perceptual and animal neurophysiological studies are compared. Cortical correlates of perception are used to determine how features of functional connectivity of cortex are related to sensory percepts. Resulting cortical metrics are used to assess changes that occur with a number of neurological disorders. Current clinical subject populations include autism, concussion, alcoholism, fibromyalgia, TMJD, IBS, migraine, vulvodynia, focal dystonia, Parkinson's, and carpal tunnel syndrome. Specific metrics are demonstrated in subsequent results section.

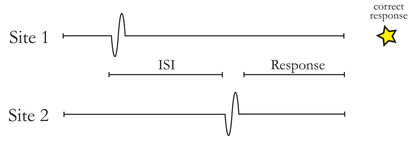
Synchronization

Extracellular recordings were obtained from SI cortical regions corresponding to D2 and D3 in the squirrel monkey. When a vibrotactile pulse was delivered, a significant above background response was evoked at D2 (top left quadrant) but not at D3 representation (top right quadrant). When weak but synchronized sinusoidal stimuli were delivered to both digits prior to the pulse (bottom half of figure), the pulse at D2 evokes a response at both the D2 and D3 representation (note absence of evoked activity before zero msec during subthreshold stimulation). From this type of data, we hypothesized that this
response was the result of functional connectivity between neighboring cortical ensembles, and that delivery of synchronized conditioning stimuli would impact the topography of temporal perception, unless there was a systemic neurological deficit.

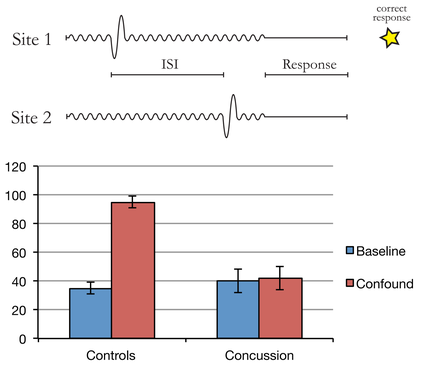


Temporal Order Judgement

Baseline test: In order to determine temporal order judgment (TOJ), two sequentialtaps were delivered, one to each digit tip, with an initial interstimulus interval (ISI) of 150 ms. The ISI was subsequently reduced as a result of subject response as defined by a 2AFC Protocol. The Stimulus location that recieved the first of the two pulses was randomized on a trial by trial basis. Subjects were quiered as to which stimulus came first.

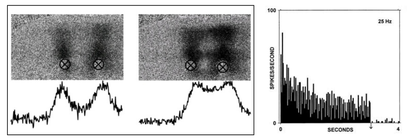


Illusory conditioning: TOJ was assessed in the presence of simultaneously delivered synchronized 25Hz conditioning stimulation prior to the TOJ task. In healthy controls, this synchronized conditioning typically significantly impacts TOJ, although it does not impact TOJ in some neurologically compromised individuals



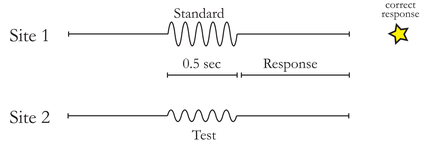
Lateral Inhibition & Adaptation

Simultaneously delivered vibrotactile stimuli to two adjacent digit tips activate near-adjacent cortical regions in the primary somatosensory cortex. Parametric comparisions (e.g., differences in amplitude) of the stimuli delivered to the two sites yields insight into the subject's GABAergically mediated lateral inhibitory interactions between such cortical regions. One of our working hypotheses is that subjects with hyperexcitability or compromised GABA systems (such as occurs with many brain injuries) will perform more poorly on amplitude discrimination tasks.
Continuing skin stimulation normally results in an overall decrease in cortical response. Whenever there is a systemic cortical alteration, such as might occur with a neurological deficit, it usually results in an imbalance in excitation and inhibition, and the individual will not adapt normally.

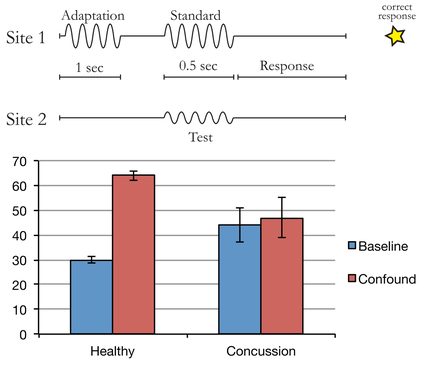


Amplitude Discrimination

Baseline metric: Amplitude discriminative capacity is defined as the minimal difference in amplitudes of two mechanical sinusoidal vibratory stimuli in which an individual can successfully identify the stimulus of larger magnitude. Two stimuli are delivered simul- taneously to D2 and D3, and discrimination capacity was assessed using a previously described 2AFC tracking protocol.

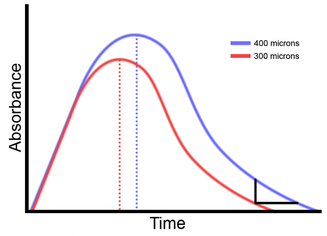


Illusory conditioning: The amplitude discrimination procedure described above was repeated in the presence of a vibrotactile conditioning stimulus delivered 1 second prior stimula to the presentation of the pair of test and standard stimuli (see Figure 2). The result of deliver such a protocol modification is that the difference limen (DL) is typically significantly elevated due to a healthy subject's ability to adapt to the stimulus



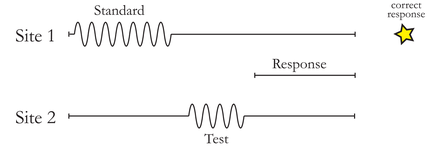
Timing Perception

Several series of experiments in non-human primates using high resolution optical imaging methods (Simons et al, 2005, 2007) were conducted. Observations from those experiments demonstrated that increasing stimulus amplitude results in an increasing duration of the optical response (see figure below; note the different durations of response for different magnitudes of stimulation). Additional experiments examining the source of the optical signal (Lee et al, 2005) led us to hypothesize that if neuron-glial interactions were significantly impacted, such as they would be with neuro-inflammation, the response duration of the optical signal would not be different with an increase in amplitude.

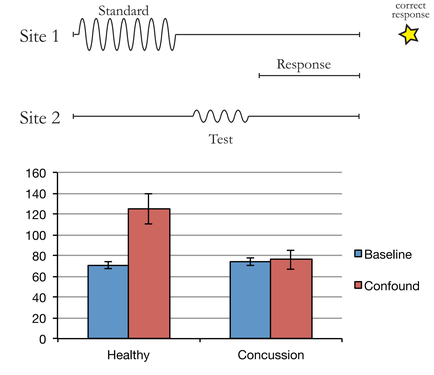


Duration Discrimination

Baseline metric: Duration discriminative capacity is the minimal difference in durations of two stimuli for which an individual can successfully identify the stimulus of larger duration.Sequential stimuli were delivere to D2 and D3. Discrimination capacity was assessed using a 2AFC tracking protocol and subjects were queried as to which of the two digits received the longer stimulus duration.

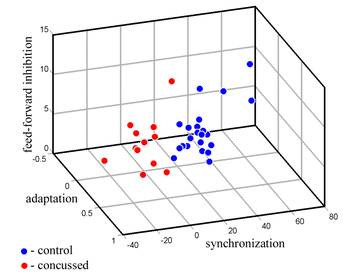


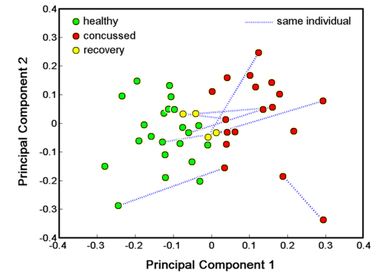
Illusory confound: Duration discriminatiion capacity was accessed in the presence of an increased standard amplitude. Increasing the amplitude results in a neurophysiological response that is longer in duration and would predictably make it more difficult for healthy controls to discriminate duration.



Analysis

To fully appreciate the differences between subject populations, we will utilize modern mathematical approaches of multi-variable analysis. Quantitative performance of each subject on the battery of N sensory tests will be treated as localizing this subject in an N-dimensional "cortical metrics" space (i.e., an abstract space in which each coordinate axis corresponds to one of the battery's sensory tests). Principal Component Analysis (PCA) and Linear Discriminant Analysis (LDA; PLS-DA in particular) is used to graphically display the test-performance data collected in the different subject populations.





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