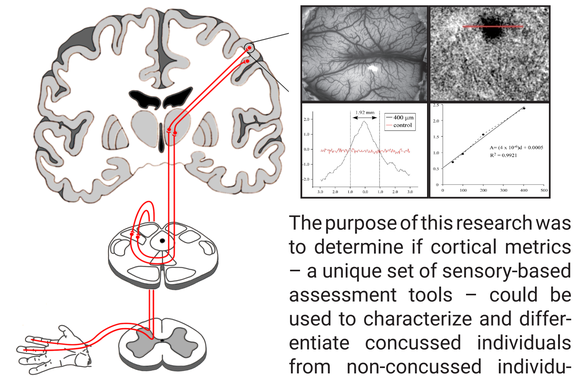
ASSESSING TRAUMATIC BRAIN INJURY VIA CORTICAL METRICS

Eric Francisco[1], Jameson Holden[1] & Mark Tommerdahl[1,2]

[1] Cortical Metrics, LLC. Carrboro, NC

[2] Department of Biomedical Engineering, University of North Carolina at Chapel Hill, Chapel Hill, NC

SUMMARY



The purpose of this research 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.

Cortical metrics takes advantage of the somatotopic relationship between skin and cortex. Biologically-based hypothesis-driven protocols can be designed to evoke interactions between adjacent cortical regions to investigate fundamental mechanistic changes that occur with cortical-cortical interactions. These interactions are altered with systemic alterations in cortical machinery (such as those that occur with neurological insult or trauma), and consequently, the cortical metrics are altered in a predictable manner. The measured changes in sensory percept can be easily and rapidly obtained (1-3 minutes per test) in a manner similar to reading an eye chart. A battery of tests is typically 10-20 minutes long.

METHODS

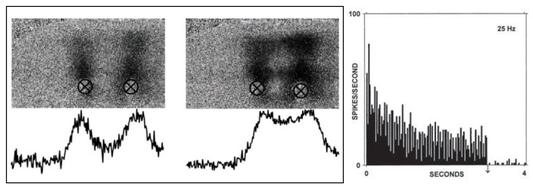
Forty-nine subjects (35 male, 14 female, mean age 20.1 years, standard deviation 4.7 years) were monitored post concussion to observe their performance and recovery. SCAT, ImPact and Balance testing were performed at every session in addition to our somatosensory testing. Subjects' results were compared to baseline tests they completed prior to the sports season and were also analyzed in comparison to population means collected from prior studies.

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.

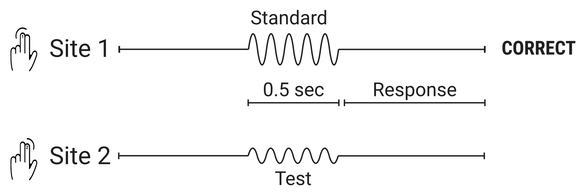
Since these protocols are designed to be sensitive to changes in systemic cortical alterations, we refer to them as cortical metrics. Identical stimuli are delivered to the skin and observations from human perceptual and animal neurophysiological studies are compared. Cortical correlates of perception 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.

PLASTICITY

In a previous study, we investigated the changes in perceptual metrics of amplitude discrimination that were observed in healthy human subjects with increasing intensity of stimulation (Francisco et al, 2008). The ability to perceive differences in vibrotactile stimulus amplitude increased systematically with stimulus magnitude in a linear fashion (i.e., followed Weber's Law, R2 = 0.9935). Further analysis revealed that the difference limens obtained in that study correlated well with the cortical activity in SI of squirrel monkeys evoked by different amplitudes of vibrotactile stimulation.

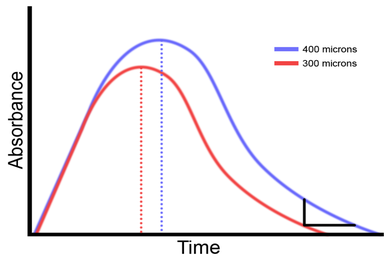


For the baseline **amplitude discrimination test**, a standard of 200 microns was used and the test stimulus initiated at 200 microns. These two stimuli were delivered simultaneously to D2 and D3, and the discrimination capacity was assessed using a 2AFC method published many times (Holden et. al 2013).

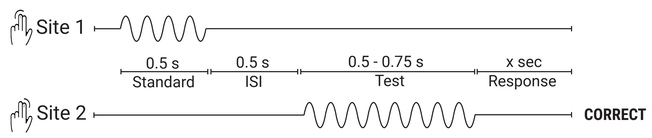


TIMING PERCEPTION

Difference limens (DLs) obtained for duration discrimination tasks for standard durations between 500 and 1500 ms are summarized below. The results demonstrate that subjects performed significantly better on the duration discrimination task for shorter standard durations than for longer standard durations. A linear least-squares fit was applied to the data, and an R^2 value of 0.989 was obtained for the linear regression. The high correlation coefficient demonstrates a strong relationship between DL and the duration of the standard stimulus, thereby verifying the application of Weber's Law for this particular discrimination task in the range of 500–1500 ms.

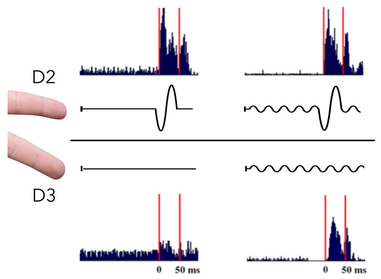


For the **duration discrimination test**, a standard of 500 ms was used and the test stimulus initiated at a duration of 750 ms. These two stimuli were delivered sequentially to D2 and D3, and the discrimination capacity was assessed using the same 2AFC tracking method as in the amplitude discrimination tasks.

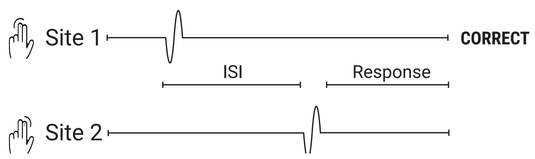


CONNECTIVITY

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 evoked 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.

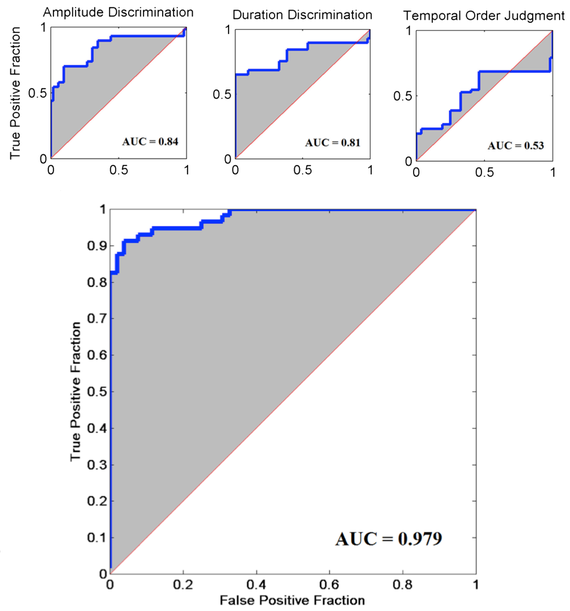


In order to determine **temporal order judgment (TOJ)**, two sequential taps were delivered, one to each digit tip, with an initial inter-stimulus interval (ISI) of 150 ms. The ISI was subsequently reduced as a result of subject response as defined by a 2AFC Protocol. The stimulus location that received the first of the two pulses was randomized on a trial by trial basis. Subjects were queried as to which stimulus came first.



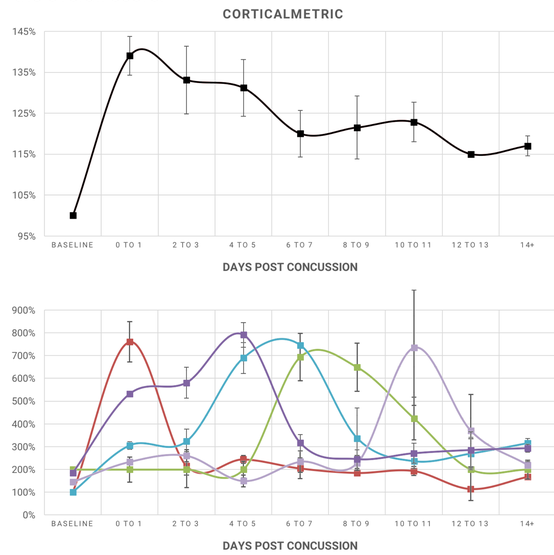
ROC ANALYSIS

A multiparametric approach (PCA based) is utilized to combine multiple measures into one cortical metric.



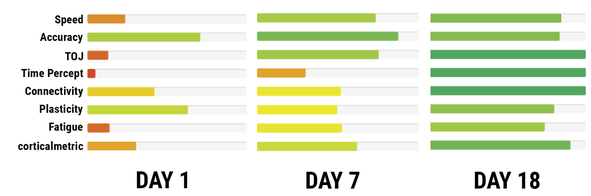
TIME COURSE

The time course for our 49 post concussion subjects shows how each cortical metric changed across recovery and contributed to the overall score.



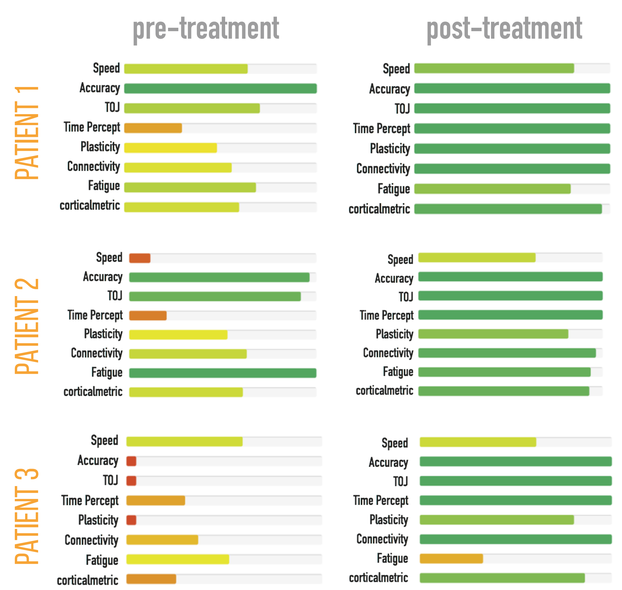
TRACKING RECOVERY

By comparing values to population averages, recovery from concussion can be monitored easily by looking at global performance.



TREATMENT EFFICACY

The same data view makes it easy to observe the effects of treatments as well.



Acknowledgements

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cortical metrics