Assessing and Treating Memory Loss with Electrophysiology:

EEG and ERP Biomarkers for Early Memory Loss

Early Detection Conundrum. Physicians are uniquely charged to effectively determine the cause of patient complaints and to do so early in the course of a potential disease in order to maximize convalescence. This is especially salient for the growing number of patients presenting with memory loss[1]. When patients present with concerns of needing greater mental effort to perform daily activities, the physician needs a very fast, easy-to-use, low-cost, objective, and sensitive test. Yet, neuropsychological tests historically available to physicians are often time consuming, subjective, lack sensitivity, and fail to directly measure actual human physiology. Only Electroencephalography (EEG), which has been employed extensively in clinical research, provides a non-invasive and office based option for objectively measuring brain function. But, due to expensive and sensitive equipment along with difficult and time consuming data interpretation, EEG has historically been out of reach from practicing doctors.

eVox: Office Based Solution. Evoke Neuroscience, Inc. is the leading medical device company providing low cost nervous system physiology measurement and biofeedback treatment equipment designed specifically to suit the needs of medical doctors and their patients. The eVox system incorporates a portable and automated 24-channel amplifier, providing 19-channel EEG and event related potentials (ERP), and 3-channel electrocardiography (ECG) to offer physician-determined care to patients presenting early symptoms of cognitive dysfunction. The physician utilizes brain physiology to help recognize early dementia conditions and offer non-invasive neurotherapy treatments predicated on the Evoke assessment.

Brain Mapping Biomarkers. A hallmark symptom of dementia and other memory and cognitive disorders is memory loss. Up until recently, most providers have relied on self-report questionnaires and effort-based computerized testing for determining a diagnosis. Even when applied optimally, these assessments often fall short in the detection of early or less severe disease presentations. Further, they do not rely on objective biomarkers that allow doctors to target specific brain regions and functional neurobiological networks from which the memory dysfunctions supervene.

The brain's capacity for normal productive function relies heavily on a complex array of interconnected networks that facilitate communication within and across brain structures. Thus, to understand and influence brain function, and more specifically memory, there is a need to isolate key functional biomarkers. Three electrophysiology measurement categories relevant to memory function are 1) thalamic generated alpha frequency (posterior alpha peak frequency), 2) the P300 component of event related potentials, and 3) brain structure (Brodmann Areas) scoring against a normal reference group. With the eVox system, these biomarkers are fast and easy to obtain with low cost equipment, and assessment can occur within any office setting with limited staff training or time.

Peak Alpha Frequency. The alpha frequency band (8 – 12 Hz), the most dominant EEG frequency found in the brain, is known to be a good measure of information processing capacity[2]. One might even describe this function as the most salient feature of memory. Peak alpha frequency for the parietal and occipital scalp locations reflects functioning of the thalamus. Low posterior peak alpha frequencies (<8Hz) have been correlated with cognitive disturbances and dementia[3,4], while elevated frequencies (>12Hz) have been correlated with central nervous system over-arousal conditions[5].

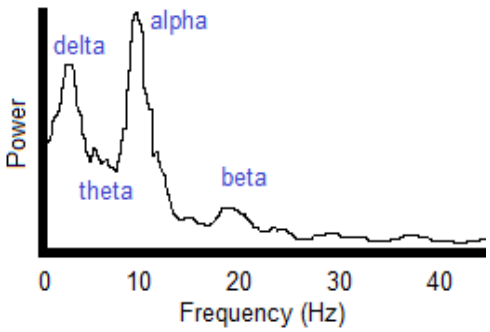

Figure 2*. Graphical display of EEG power and alpha frequency range.*

P300 Memory functions and cognitive processes within the brain can be measured using event related potentials (ERPs)[6]. With the use of ERPs, one can quantify time locked neuronal responses following presented stimuli. The time delay, or latency, between stimulus onset and a patient's physical response reflects brain processing speed, while the component's amplitude reflects neuronal recruitment and subsequent activation. Longer latency measures and low amplitudes are associated with aging and dementia conditions and indicate cortical and subcortical dysfunctions.

Fundamental elements of memory involve the degree of attention to a stimulus and the subsequent encoding of information for storage and retrieval. Two ERP components that are useful to measure these cognitive processes are known as P300a and P300b, respectively[7]. The P300a component is mediated by dopamine and reflects frontal working memory functions or dysfunctions. The P300b component, however, is mediated by norepinephrine and is generated in the medial temporal lobe. So, these two components can be useful in differential diagnosis, neurofeedback and neuromodulation therapy, and to track treatment effects or disease course (Figure 3).

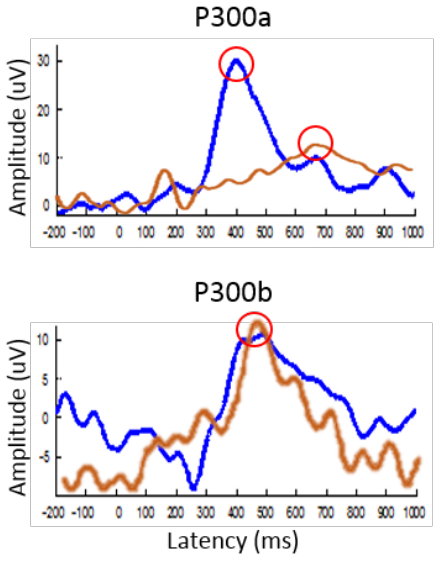

Figure 3*. P300a and P300b morphology of a healthy control patient (blue) and a 45 year old male (orange) with early frontotemporal dementia, reflecting low P300a amplitude and elongated P300a latency*

Brodmann Areas and LORETA Imaging. Brodmann Areas (BA) represent regions of the cortex cytoarchitecturally organized into functional locations and are a well-respected and widely referenced system for brain mapping. The physician's ability to derive statistical scores on the BAs throughout the patient's brain allows not just determination of deviation from normalcy, but a system by which treatment benefits and disease course can be objectively monitored. When used in parallel with imaging libraries, scalp surface EEG low-resolution brain electromagnetic tomography (LORETA, sLORETA) allows added insight to differential diagnosis and treatment effects[8,9]. For example, Alzheimer's disease presents with EEG power abnormalities more globally than frontotemporal dementia; the ability to source localize to specific brain structures, using BAs, aids the clinician in cross-correlating known structures found to be hallmarks of particular diseases. The sensitivity of EEG and source localization with sLORETA allows for a useful assessment measure when considering memory impairment etiology, personalized treatment interventions, and treatment response patterns.

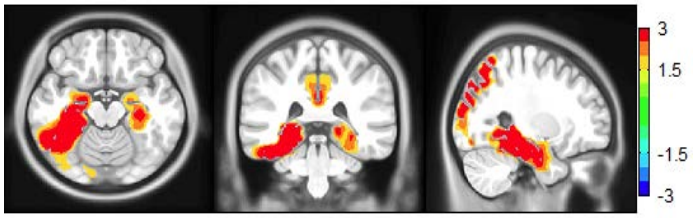

Figure 4. *sLORETA images showing (left to right) axial, coronal, and sagittal views of brain areas found to be outside normal reference group ranges.*

Conclusions. There has been a clear need for objective memory-related measures that guide and inform physicians in their provision of more targeted medication and non-medication therapies. In addition to electrophysiology biomarkers, the eVox system also offers a method by which non-invasive therapy can be delivered. Physicians appreciate the eVox system as an office-based, low cost tool yielding sensitive measures to help patients see the value of treatment compliance, additional biomarker information to support differential diagnosis, and a more individualized neurofeedback intervention option.

References

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