Utility of Event Related Potentials in a Memory Disorders Clinic

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Background

Early and accurate diagnosis of Alzheimer's disease (AD) remains central to studying the pathophysiology of AD and to clinical trials aimed at altering disease course. Event related potentials are a potential diagnostic biomarker for earlier, more accurate diagnosis of AD.

Characteristics of an Effective Diagnostic Biomarker

- Acts as a fundamental feature of the pathophysiologic process of AD
- Validated in neuropathologically confirmed AD cases
- Is precise
- Is reliable, minimally invasive, simple to perform, and inexpensive

(Mueller, Weiner, Thal et al., 2005)

What are Event-Related Potentials (ERPs)?

ERPs are derived from electroencephalographic (EEG) waveforms that are time-locked to tasks. An EEG is recorded while a participant is exposed to repeated stimuli. The responses to each stimulus are averaged together to increase the signal to noise ratio. The result is a graph of positive/negative peaks that correspond to the cognitive processing of the brain in response to that stimulus.

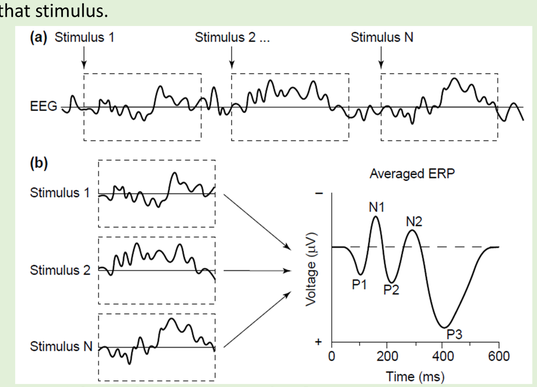
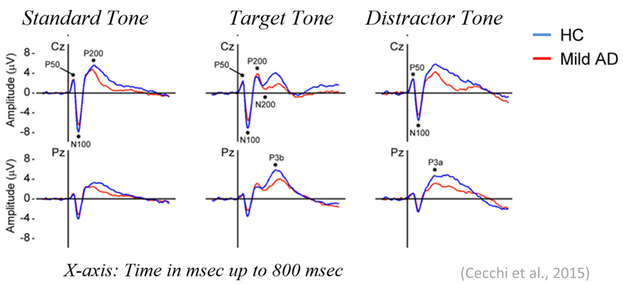


Figure 1. Schematic of ERP extraction from EEG

Image credit: Luck, S. J., Woodman, G. F., & Vogel, E. K. (2000). Event-related potential studies of attention. *Trends in Cognitive Sciences.*

ERP features are found to be altered in early AD and preclinical stages of the disease.



(Cecchi et al., 2015)

Figure 2. Comparison of ERP peaks between mild AD patients and healthy elderly controls. Generally, mild AD patients show reduced amplitudes and increased latencies compared to healthy elderly controls.

Image credit: Neuronetrix™

Figure 3. Seven-electrode COGNISION system used to record ERPs.

- FDA-approved
- Non-invasive
- Highly standardized
- Procedure takes <1hr
- Well-tolerated by patients

Objectives

Based on the early findings of ERP research, we hypothesized that ERP features will be clinically useful in the diagnosis of AD in an outpatient memory disorders clinic. **As the first step, we investigated the correlation of the number of ERP features in the abnormal range to the clinical screening measure, the Montreal Cognitive Assessment.**

Methods

Participants consisted of 80 veterans aged between 55 and 100 years who were seen in the Memory Disorders Clinic between July 2016 to June 2017. Participants were excluded if unable to comprehend consent. All underwent standard clinical workup (history and physical, neuroimaging, and neurobehavioral status exam) and an EEG with a three-tone auditory oddball task. ERP results were reviewed by two behavioral neurologists blinded to the clinical details of each subject. ERP amplitude and latency were rated in the abnormal or healthy older adult range based on literature. Statistical analysis was conducted using Pearson's correlation.

Table 1. Summary of demographic information for all participants

Characteristics	All participants [range] (n=80)
Age	72.7 ± 8.6 [50, 92]
Years of Education	14.1 ± 3.0 [8, 26]
MOCA	19.6 ± 5.4 [7, 30]

Table 2. List of individual ERP features recorded. Amplitude, latency, and average amplitude were recorded for all ERP waves.

ERP Features Examined			
	By Stimulus		
Behavioral Measures	Standard	Target	Distractor
Button press accuracy (%)	P50	N100	P50
False alarms (%)	N100	P200	N100
Mean reaction time (msec)	P200	P3b	P3a
		Slow wave	

Results

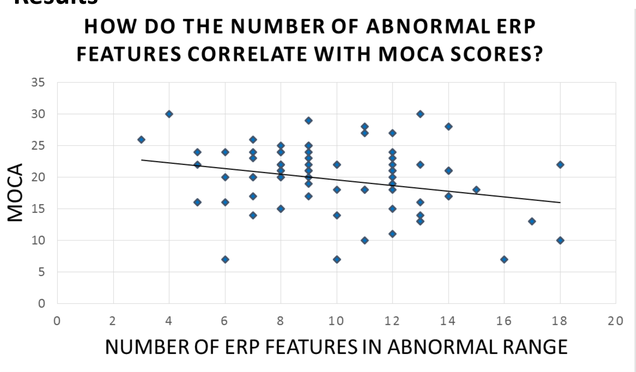


Figure 4. Scatterplot of MOCA scores and ERP features in the mild AD range. Pearson's coefficient =-.279 p=.012 (n=80)

Table 3. Significant correlations between MOCA and individual ERP features in all participants (n=80)

MOCA and ERP features across all individuals		
	r =	*P* =
Button press accuracy (%)	.382	<.001
False alarms (%)	-.308	.006
N100 standard amplitude (μV)	-.220	.050
N100 target average amplitude (μV)	-.272	.015
P3b target average amplitude (μV)	-.224	.046
Slow wave target latency (msec)	-.351	.002

Total of 23 correlations performed.

Conclusion

- Results show that greater number of abnormal ERP features correlates with poorer performance on the MOCA, suggesting that ERPs correlate well with the screening measures of cognitive decline.
- Results provide support for the clinical utility of ERPs.
- Future work will examine the relationships of ERPs to clinical diagnosis and other AD biomarkers.