# From Lab to Clinic: The Practicality of Using Event Related Potentials in the Diagnosis of Alzheimer's Disease

Minny Suh[1,3], Prayerna Uppal[3], Katherine Turk, M.D. [2,3], Andrew Budson, M.D. [2,3]

[1]Department of Anatomy & Neurobiology, Boston University School of Medicine [2]Department of Neurology, Boston University School of Medicine
[3]Center for Translational and Cognitive Neuroscience, VA Boston Healthcare System

## Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder that begins insidiously, typically first involving memory and then progressing to affect all cognitive domains. Clinicians generally agree upon four broad stages of AD: **mild cognitive impairment (MCI) due to AD, mild, moderate, and severe AD dementia**. Each stage is characterized by structural changes of the brain which result in deterioration of behavioral and cognitive functions.

## Objectives

To investigate whether event related potentials (ERPs)

1. are a biomarker of disease severity staging in AD.
2. differentiate AD from non-AD related cognitive impairment in a heterogeneous group of patients.

### *Event-Related Potentials (ERPs)*

ERPs are time-locked, quantitative electroencephalographic (EEG) recordings that measure cognitive responses to stimuli. ERP components are thought to be produced by specific regions of the brain.

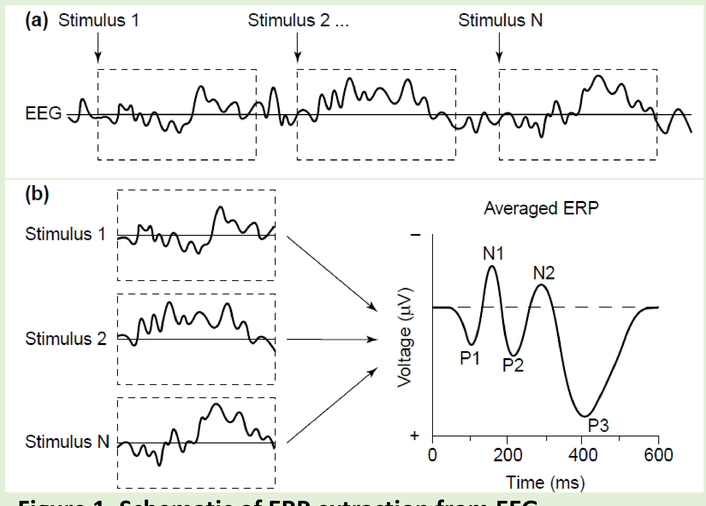


**Figure 1. Schematic of ERP extraction from EEG**

P50, N100, and P200 are thought to represent **sensory gating**, a protective mechanism that filters irrelevant sensory information.
N200, P3a, and P3b are thought to represent mechanisms of higher cognitive functioning, such as attention and memory.

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

## Hypothesis

AD patients will have ERP amplitudes and latencies in abnormal ranges for specific components according to the regions of brain affected by AD pathology and commensurate with the severity of AD (see figure 3).

## Study Design

### *Participants*

Data from 22 veterans seen in the Memory Disorders Clinic aged between 55 and 92 years old and who scored 10 or above on the Montreal Cognitive Assessment (MoCA) were used for this analysis. Veterans were not excluded based on comorbid conditions or pharmacological intake.

**Chart 1. Demographic data of participants**

| Characteristics | Non-AD (n = 13) | AD (n = 9) |
|---|---|---|
| Age | 72.1 ± 2.09 | 78.1 ± 1.77* (*P* = .027) |
| Education (years) | 15 ± 1.01 | 13.7 ± 0.62 |
| MoCA | 22.5 ± 1.16 | 19.4 ± 1.03 |
| MMSE | 27.2 ± 0.60 | 24.2 ± 1.46 |

Note: Data are represented as mean ± SEM. *$P$ < .05 compared with non-AD.

Abbreviations: AD, Alzheimer's disease, any stage; MoCA, Montreal cognitive assessment; MMSE, mini-mental state examination

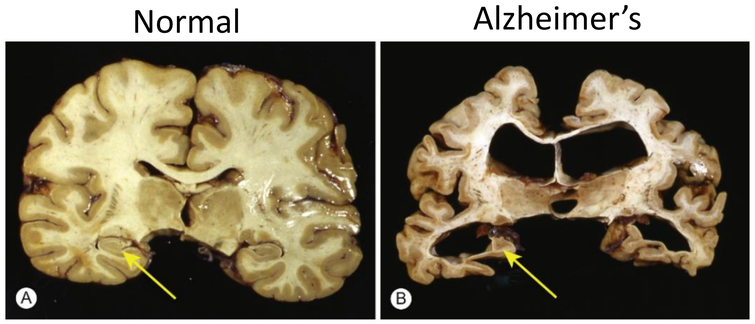


**Figure 2. Comparison of a healthy brain and a brain at severe stage of AD**

Image credit: Budson, A. E., & Solomon, P. R. (2011). Memory loss: A practical guide for clinicians. *Memory Loss: A Practical Guide for Clinicians.*

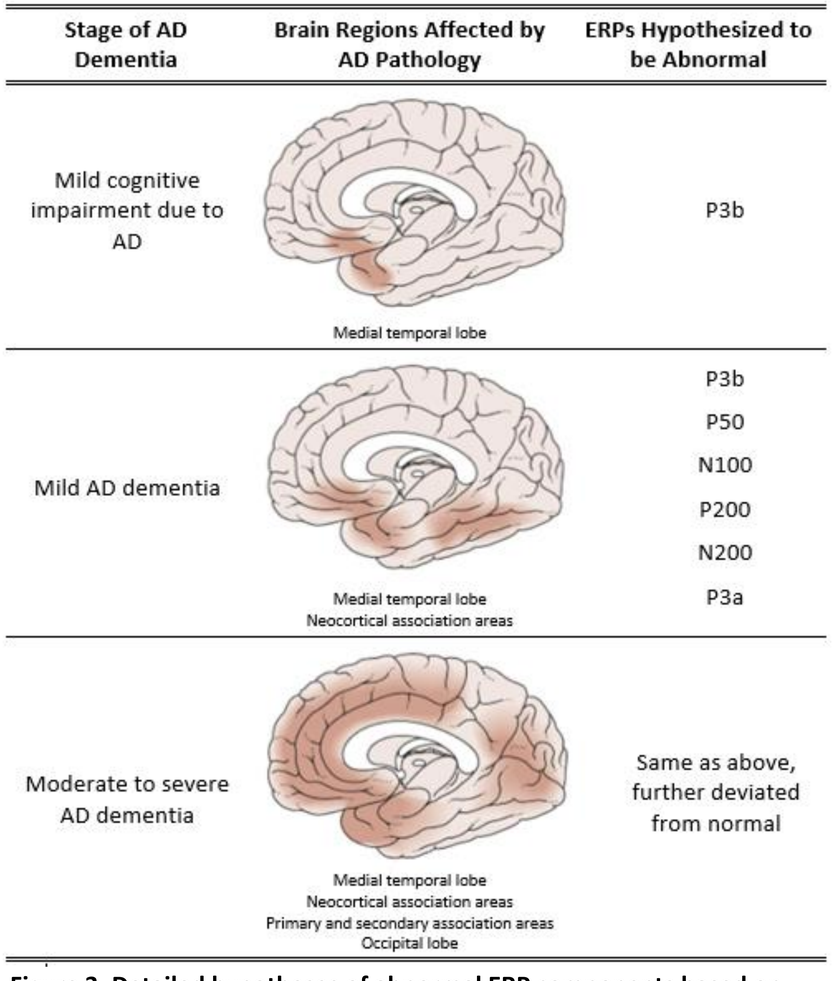


**Figure 3. Detailed hypotheses of abnormal ERP components based on regions of brain affected by AD pathology at each stage of AD dementia**

Image credit: Budson, A. E., & Solomon, P. R. (2011). Memory loss: A practical guide for clinicians. *Memory Loss: A Practical Guide for Clinicians.*

### *Methods*

All veterans were administered a neuropsychological test battery and an EEG with an auditory oddball task. Veterans were given a diagnosis of MCI due to AD, mild, or moderate to severe AD based on blinded ERP data, and based on clinical data which included results from neuroimaging, clinical history, neurological examination and neuropsychological tests. For group comparisons, veterans were divided into non-AD and AD groups based on clinical diagnosis.

Group comparisons were conducted using the Mann-Whitney U and Krusker-Wallace tests for non-parametric data in age, education, MoCA and MMSE scores. A multivariate ANCOVA with bias-corrected and accelerated bootstrapping was used to determine group differences in the *z*-scores of ERP measures between clinically diagnosed AD and non-AD groups.

## Results

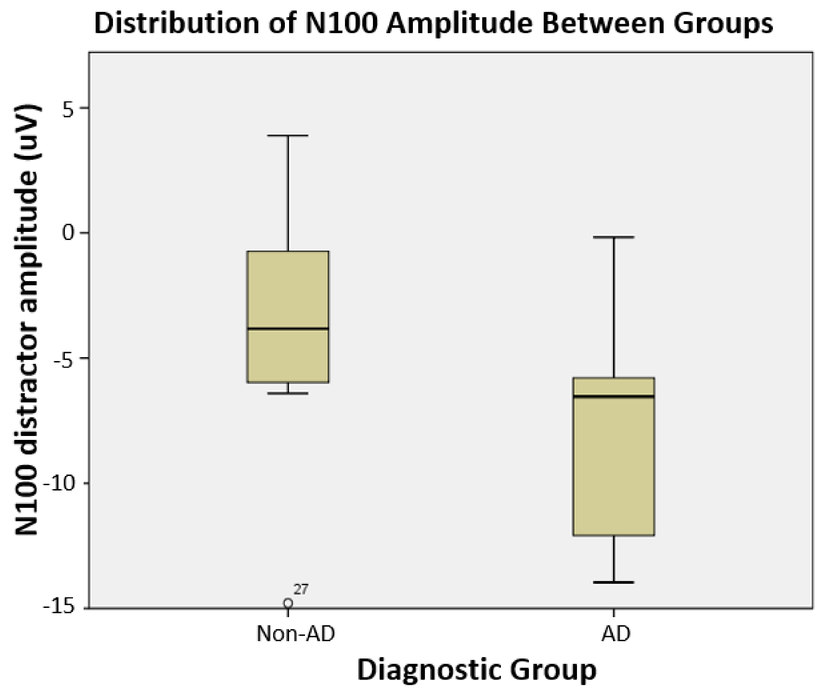


**Figure 4. Boxplot of significant group differences in N100 distractor amplitude.**

Mean and standard error of the mean differed significantly between groups for N100 distractor amplitude (*P* = 0.015). Specific measures were non-AD at 3.40 ± 1.4 μV and AD at -7.80 ± 1.6 μV.

**Chart 2. Individual diagnoses within the Non-AD group**

| Diagnoses within the Non-AD group | |
|---|---|
| Normal aging (1) | Chronic traumatic encephalography (1) |
| Possible Lewy body dementia (1) | Multiple sclerosis (1) |
| Non-AD; normal aging with other psychiatric disease (1) | Depression due to medication and alcohol (1) |
| Possible frontotemporal dementia, depression (1) | MCI not due to AD (1) |
| Non-neurodegenerative processes; multifactorial including bipolar disease and prior history of heavy alcohol use. Family history of AD (1) | Etiology yet unknown (4) |

## Summary

- N100 amplitude is a promising biomarker for the differentiation of AD from non-AD related cognitive impairment
- The group difference in N100 amplitude suggests that sensory gating is significantly impaired in mild AD than in non-AD related cognitive impairment.
- More data is needed to determine whether ERPs are a biomarker of disease severity staging in AD.