Assessing Mild Cognitive Impairment Using Portable Electroencephalography: The P300 Component

Hannah H. Smith[1]

hannahs396@gmail.com

Abstract

Increased prevalence of mild cognitive impairments (MCIs) and dementias are a growing concern as the population ages, which produces a need for an objective, accessible, and cost-effective tool to facilitate early detection and intervention. This article investigates whether a portable electroencephalography (EEG) system can provide an effective measure of MCI using a visual oddball task to target the memory and attention event-related potential (ERP) component called the P300. In this study, 40 participants were separated into two groups: individuals with a diagnosed cognitive impairment and a healthy age-matched control group. Participants completed two typical pen-and-paper MCI assessments to gather behavioural data, which were followed by a perceptual EEG oddball task to gather brain data. Results show that the MCI group demonstrated decreased behavioural task performance in the pen-and-paper assessments and a modulated brain response during the oddball task when compared to healthy controls, which the portable EEG system revealed to be a decreased P300 peak amplitude. These results indicate the capability of portable EEGs to identify biomarkers for MCI and their potential use in the diagnostic process. This capability could provide major benefits to patients, their families, and physicians, and would also assist with Alzheimer's research. Future research could expand on these findings by applying a lifespan or disease-span approach to investigate P300 changes in the course of a healthy individual's life compared to P300 changes in individuals with MCI over the entire course of their disease. This research could also cultivate a greater understanding of how MCI progresses, which could improve diagnostic or treatment development.

***Keywords*:** mild cognitive impairment; electroencephalography; dementia; Alzheimer's disease

[1] This research was supported by the Jamie Cassels Undergraduate Research Award at the University of Victoria under the supervision of Robert Trska, Dr. Olave Krigolson, and Dr. Alexandre Henri-Bhargava.

Introduction

Mild cognitive impairment (MCI) is a growing concern in the twenty-first century since prevalence rates are increasing with an aging population without a concurrent increase in diagnostic and treatment capability (Patnode et al., 2020). MCI is included within the spectrum of cognitive decline and is characterized by a deterioration of cognition that does not notably impact an individual's ability to perform everyday activities independently (Langa & Levine, 2014). Additionally, individuals with MCI have a greater risk of developing dementia (Gauthier et al., 2006; Gillis et al., 2019; Langa & Levine, 2014; Owens et al., 2020). In this debilitating condition, one of six cognitive domains (learning and memory, executive function, complex attention, language, social cognition, and visuospatial processing) undergoes significant decline, which interferes with an individual's ability to perform daily activities (Patnode et al., 2020). Dementia can be caused by several factors including Alzheimer's disease (AD), vascular or traumatic brain injuries, and nutritional or metabolic disorders (Gale et al., 2018). Dementia most commonly affects the elderly and has a global prevalence of 7% in individuals over the age of 65 (Gale et al., 2018). Current estimates of dementia in Canadians alone are at over 700,000 people, and this number is predicted to increase steadily due to an aging population (Chambers et al., 2016). Unfortunately, the prevalence of MCI rates in Canada is more challenging to establish due to issues with current diagnostic testing, which is variable and can produce wide-ranging results (Owens et al., 2020). Current global prevalence estimates of MCI are between 16.8% and 19.2% for individuals over the age of 65, range from 22% to 27.6% for individuals over the age of 75, and are between 29% and 38% for individuals over the age of 85 (Qian et al., 2020).

With the increasing prevalence of dementia and expected increase in related diseases as the population ages (Correa-Jaraba et al., 2018; Patnode et al., 2020), early detection of MCI can significantly benefit patients, their families, and the Canadian healthcare system (Gale, 2018; Sabbagh et al., 2020). For example, patients can be instructed on lifestyle changes that can slow the progression of MCI and reduce symptoms (such as memory or attention deficits) to minimize the impact of the disease (Sabbagh et al., 2020). In short, early intervention can maximize treatment benefits and improve patient health outcomes (Sabbagh et al., 2020) by granting physicians and patients time to address and modify risk factors, such as improving dietary and exercise habits (Galvin, 2018). Additionally, early identification can allow patients and their families to prepare for the future, including planning for increased care needs as well as considering potential financial and legal situational changes (Sabbagh et al., 2020). With MCI contributing to between 40% to 60% of AD cases in adults over the age of 57 (Gillis et al., 2019), early detection is essential since advances in disease-modifying therapies may delay or halt AD while still in its prodromal MCI stage (Sabbagh et al., 2020). One major challenge to developing successful drug therapies has been the inability of researchers to accurately identify a substantial base of eligible patients in the early stages of AD to take part in research and clinical trials. Accordingly, widespread and accurate early detection of MCI could provide major benefits towards the research and development of successful AD therapies (Sabbagh et al., 2020).

Current Methods of Diagnoses

Several contemporary methods are used to screen for MCI; however, each method uses different diagnostic criteria and can produce results that may vary depending on whether the test was administered in a specialized clinic or primary care setting (Langa & Levine, 2014). Moreover,

current methods used to assess and diagnose dementia are intensive and may require a time-consuming, comprehensive workup that often includes a complete medical history, neurological testing for mental status, lab testing for physiologic or metabolic indicators, and a structural brain scan (Gale et al., 2018). Some common clinical interview tools include the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Memory Impairment Screen (MIS)/MIS by Telephone (MIS-T) (Owens et al., 2020). Despite this array of assessment tools, test performance can vary based on age, educational background, and culture, as well as anxiety and stress levels; hence, reliability may vary when using these methods (Gale et al., 2018; Galvin, 2018; Qian et al., 2020; Yokomizo et al., 2014). Additional limitations for interview-based assessments include the need for skilled administrators and repeated examination (Yokomizo et al., 2014), as well as potential inaccuracies in detecting milder cognitive impairment and changes in impairment in both abnormally high- and low-functioning individuals (Galvin, 2018). Informant-based assessments, such as the Aging and Dementia-8 Interview (AD8) and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), can mitigate biases implicit within clinical interview assessments; however, these assessments depend on the reliability of the informer to accurately diagnose MCI (Galvin, 2018). Furthermore, issues with limited appointment times in primary care settings, combined with untrained technicians and inconsistent diagnostic screenings, can lead to missed opportunities for the early diagnosis of MCI (Galvin, 2018). Self-assessment tools, such as the Self-Administered Gerocognitive Examination (SAGE), have successfully identified early stage MCI for some individuals. Yet, self-awareness of cognitive decline varies between individuals, and the test is limited by its inability to detect symptom denial (Galvin, 2018). Due to limitations with current diagnostic protocols, an objective, accessible, and reliable tool is needed to help accurately and efficiently diagnose MCI in both primary care and ambulatory settings. Utilizing a portable electroencephalography (EEG) device to identify event-related potentials (ERPs) as biomarkers for MCI could offer a potential solution.

What is EEG?

EEG, or electroencephalography, is a device that continuously records brain activity that is then represented as a graph of the voltage difference between two brain regions over time (Olejniczak, 2006). EEG is generated via cortical pyramidal cells, which are the predominant neurons of the cerebral cortex (Biasiucci et al., 2019). When these postsynaptic cortical pyramidal cells receive excitatory or inhibitory neurotransmitters from surrounding neurons, their polarity changes. This change in polarity results in a dipole, which is a small separation of positive and negative charges. When many neurons work together in parallel to create many small dipoles, a local field potential is generated. This local field potential can be measured with EEG by capturing the summed change in the extracellular fluid charge created when many cortical pyramidal cells act in synchrony. EEG measurements typically show brain activity at four different bands of wavelengths: alpha, beta, delta, and theta, (On et al., 2013). These wavelengths are based on the frequency of oscillation and are determined by the firing rates of neurons: the faster the neurons fire, the higher the frequency rate. Thus, the increased synchrony of firing neurons results in waves with higher amplitudes (Musall et al., 2014). Delta waves are the slowest frequency (0.1-3 Hz) and occur during deep sleep whereas beta waves are high frequency (13-40 Hz) and dominate during wakeful states when individuals are alert and focused (On et al., 2013). All wavelengths can be detected at all times, but one usually dominates based on an individual's mental state (On et al., 2013).

What are ERPs?

In addition to its oscillatory characteristics, EEG may be indexed through time-locked brain responses. An ERP, or event-related potential, is a change in voltage that reflects the brain's response to an event (Coles & Rugg, 1996). ERPs can be identified by their amplitudes and latencies, and occur on a much smaller scale (microvolts) than EEG waveforms (tens of microvolts). Both EEG and ERPs are generated by summed post-synaptic potentials, which create electric fields through the synchronized activity of large groups of neurons. They differ in that EEG includes all brain activity, both related and unrelated to an event, whereas ERPs only include the brain's response to specific events (Coles & Rugg, 1996). As such, ERPs can capture the temporal aspect of EEG by illuminating the precise time in which the brain registers or responds to specific stimuli. Additionally, ERPs reveal processes impacted by experimental manipulation and can measure covert mental processes. Since ERPs reflect brain polarity changes produced by influxes of excitatory and inhibitory neurotransmitters, ERPs can provide biomarkers to measure the impaired brain functions and processes linked to neurotransmitters. Such measurements can provide specific insight into diseases caused by neurotransmitter abnormalities when compared to other, more indirect, biomarking methods (Luck, 2014). Importantly, ERP studies using portable EEG could help further our understanding of the neurochemical changes associated with MCI.

EEG Portability Can Improve Diagnostic Power and Effectiveness

Traditionally, EEG has been confined to a lab setting due to long setup times, low equipment portability, and the availability of highly trained technicians to administer EEG tests (Gottlibe et al., 2020). However, recent advancements have created EEG systems that are cost- and time-effective, as well as highly mobile, accessible, and user-friendly (Gottlibe et al., 2020). These systems are useful for conducting ERP research, and their portability has increased the potential to apply ERP methods to new settings (Krigolson et al., 2017; 2021). These devices have also demonstrated success in clinical contexts and, so far, have provided practitioners with quick, non-invasive techniques with which to assess the brain changes associated with stroke and chronic pain in patients with dementia (Gottlibe et al., 2020; Pu et al., 2021). This tool is especially useful for non-verbal populations or patients who have lost the cognitive capacity to articulate their experiences, as seen in patients with dementia (Pu et al., 2021).

Using EEG to identify biomarkers for MCI/AD has several advantages over current methods. Cerebrospinal fluid analysis for biomarkers (such as tau, phosphorylated tau, and beta amyloid)[2] can provide diagnostic information and useful insights on the prognosis of MCI (Vemuri et al., 2009); however, the technique (lumbar puncture) from which cerebrospinal fluid is obtained is invasive and can cause anxiety and discomfort in patients (Duits et al., 2016). Other methods, such as structural magnetic resonance imaging (MRI) or computer tomography (CT) scans, can provide accurate information about structural abnormalities indicative of MCI and can have predictive power for future clinical decline in individuals (Vemuri et al., 2009). Nevertheless, the equipment required to apply these techniques is expensive and often inaccessible to populations in rural areas (Burdorf, 2021). In contrast, a portable EEG system is non-invasive, widely available,

[2] Beta amyloid is a peptide whereas tao and phosphorylated tao are proteins that show differences in both structure and number in individuals with MCI and AD.

cost-effective, and capable of revealing a direct connection between brain health, neuronal activity, and cognitive impairments, including MCI (Smailovic & Jelic, 2019).

EEG Markers for MCI and Dementia

Several neurophysiological characteristics of MCI and AD have been identified through the use of full EEG systems, which demonstrates the capability of EEG to diagnose and track the course and progression of neurodegenerative diseases. For example, resting state alpha rhythms exhibit changes over time in patients with MCI (Babiloni et al., 2014). Furthermore, resting state eyes-open and eyes-closed tasks have successfully identified individuals with MCI from healthy individuals (Kavcic et al., 2021). Additionally, theta/gamma and alpha3/alpha2 ratios have been used to distinguish individuals with MCI who will progress to AD from individuals with MCI who will remain stable or regain their health (Moretti et al., 2011). However, undertaking a comparison of the resting state values of healthy individuals versus individuals with MCI often produces overlapping results that do not present clinically significant differences sufficient for the diagnostic process (Deiber et al., 2009). As a solution, the sensitivity and utility of early stage diagnostic tests can be increased by looking at the functional activation of brain regions during distinct cognitive tasks that engage areas experiencing cognitive decline due to MCI (Deiber et al., 2009). This narrowing of focus is often accomplished through ERP research, since the latter employs tasks designed to elicit specific components associated with different brain areas and aspects of cognition. Using ERPs to assess for MCI can provide specific information regarding each patient's disease that could, in turn, be used to help create individualized care plans.

EEG and P300 for MCI

ERP researchers have identified several components that show electrophysiological differences in individuals with MCI, of which the P300 stands apart (Gu et al., 2019). The P300 ERP component, henceforth referred to as P3, has been associated with several neural processes, such as context updating, attention, and memory encoding (Donchin & Coles, 1988; Polich, 2012). For instance, Polich (2007) has associated the amplitude of P3 with stimulus, attention, and cognitive load, whereas the latency of P3 reflects stimulus evaluation and task difficulty. Another theory proposed by Nieuwenhuis et al. (2005) has contended that P3 is involved in decision-making and reflects the activity of the locus coeruleus-norepinephrine system. This system has been implicated in reward expectancy and information processing, both of which register decline in individuals with dementia (Perry et al., 2017). Furthermore, Krigolson and Holroyd (2007) have suggested that P3 may reflect locus coeruleus activity on the posterior cortex during error-processing tasks, specifically for stimulus-response optimization. Importantly, this versatile component encompasses several domains of cognition impacted by MCI, which renders P3 a promising candidate for comparison in this study.

Comparing ERP components in individuals with MCI versus their healthy counterparts can be useful for identifying and diagnosing MCI (Gu et al., 2019; Jiang et al., 2015), tracking disease progression (Jiang et al., 2015), distinguishing between subtypes of MCI (Correa-Jaraba et al., 2018; Gu et al., 2019), and predicting the potential progression of MCI to AD (Chapman et al., 2011). In particular, the association of P3 with memory consolidation and attention (Chapman et al., 2011) has shown high sensitivity for detecting MCI as well as high specificity in identifying and distinguishing different subtypes of MCI (Correa-Jaraba et al., 2018). As previously

mentioned, P3 demonstrates decreased amplitude and increased latency in individuals with MCI, and these differences are heightened as the disease progresses (Jiang et al., 2015). Accordingly, tasks that elicit P3, such as this study's visual oddball task, can be useful for MCI assessment and diagnosis. Previously, pupil responses to oddball tasks have been studied and associated with MCI (Jiménez et al., 2021). Moreover, the Fast Fourier Transform[3] delta and theta wave differences during oddball tasks show promise for early MCI detection and the identification of MCI subtypes that may progress to AD (Tülay et al., 2020). Recently, oddball tasks that elicit P3 have been used to identify MCI associated with early stages of Parkinson's disease (Hünerli et al., 2019). However, these changes associated with MCI have only been revealed using full EEG systems and have yet to be observed with portable EEG systems. Since portable EEG systems are better suited for the widespread clinical assessment of MCI, it is important to demonstrate that portable EEG systems can accurately detect the ERP changes associated with MCI previously identified by their full-system counterparts.

Statement of Purpose

To facilitate the early detection and diagnosis of MCI, a widely available, objective, and easy-to-use diagnostic tool is needed for clinical and non-clinical settings. Advances in EEG technology potentiate the creation of an accessible, cost-effective, and portable EEG tool capable of screening for early stage MCI in both primary and outpatient settings. The current study aims to discern if a portable EEG system can be used as an effective measure for MCI, specifically through using a visual oddball task to target memory and attention components, such as P3. We predict that individuals with MCI will demonstrate both decreased task performance and ERP changes in components associated with the oddball task when compared to healthy, age-matched individuals. Furthermore, we predict a correlation between individual behavioural assessment scores and P3 peak amplitudes. In other words, we anticipate that, as behavioral scores increase, P3 amplitudes will also increase.

Methodology

Participants

This study took place at the University of Victoria, British Columbia. Participants were assigned to one of two distinct groups: individuals with a clinically diagnosed cognitive impairment referred to this study by the Royal Jubilee Hospital in Victoria (MCI group: n = 20, 6 females, 14 males, *M* age = 76.0 ± 7.8), and apparently healthy age- and sex-matched individuals gathered from Victoria and the Greater Vancouver Island region (Control group n = 20, 8 females, 12 males, *M* age = 71.3 ± 3.9). The recruitment of the MCI group was accomplished either through the Permission to Contact (PTC) program at the Royal Jubilee Hospital Specialist Memory Clinic or through direct-contact patient referrals from clinical research assistants, research nurses, general practitioners, and specialist physicians. MCI group participant identification was accomplished through approved Island Health Standard Operating Procedures (SOP) via the PTC program, or through the Specialist Memory Clinic after a confirmed MCI or early stage dementia diagnosis. Control group participants were recruited through word-of-mouth promotions, media streams, and

[3] A Fast Fourier Transform, or FFT, can be applied to raw EEG data to convert time domains to frequency domains to reveal their sinusoidal waveforms.

local newspapers. Participants did not disclose any known psychiatric, drug, or addiction disorders; nor did participants disclose any cognitive disorders in addition to the disorder under study. Moreover, all participants had functional or corrected-to-functional vision. Participants provided informed consent and were compensated $10.00 CAD for parking upon completion of each session. Ethical standards outlined in the revised Declaration of Helsinki (1964) were followed, and ethics for this study were approved by the Human Research Ethics Board at the University of Victoria (HREB: H19-02910).

Apparatus and Procedure

Informed consent, including a briefing on all aspects of this study, was provided to all subjects prior to participation. Trained researchers then provided an outline of the project to the control and MCI groups, which was followed by a set of surveys and assessments that included questions on demographics (i.e., age, sex, handedness, etc.), medical history, current medications, and a confirmation of diagnosis.

Surveys and Assessments

To aid in participant screening and assessment, the Montreal Cognitive Assessment (MoCA v. 8.2; 8.3) was administered to both control and MCI groups (Nasreddine et al., 2005). Research by Costa et al. (2014) has indicated that the MoCA can sensitively assess cognitive capacity in individuals with mild dementia as well as MCI. As described by Costa et al. (2014), individuals who score lower than 14/30 may not have the capacity to provide informed consent and may struggle to complete assigned study tasks. For this reason, the present study set a minimum MoCA criterion score of 14 for participation, and all individuals who scored below 14 were informed of their ineligibility to continue their participation in this study (n = 0, MoCA score MCI M = 23.0 [21.4, 24.5], MoCA score control M = 26.9 [25.8, 28.0]). After administering the MoCA to ensure eligibility to provide informed consent, participants completed two short-form questionnaires. In cases in which a participant was accompanied by a study partner (i.e., a spouse, friend, family member, or caretaker), the Functional Activity Questionnaire (FAQ) was completed by the study partner (Pfeffer et al., 1982). If the participant arrived alone, or their study partner was unavailable during the session, researchers asked for permission to contact a spouse or family member to administer the FAQ by phone. If neither the in-person nor remote administration of the FAQ to a study partner were viable options, then participants were asked to complete the survey themselves. Next, participants completed the Geriatric Depression Scale short form (GDS-15) to provide insights concerning participant mood, affect, and outlook (Sheik & Yesavage, 1986). Finally, participants completed the Repeatable Battery for the Assessment Neuropsychological State (RBANS A & B)—a pen-and-paper test used to assess cognitive decline by measuring memory, visuospatial/constructional ability, language, and attention (Randolph et al., 2012). The approximate run time for this section was 60 minutes, which included breaks offered to participants prior to and following the administration of the RBANS to ensure participant comfort.

Electroencephalography and Cognitive Tasks

After a short break following completion of the RBANS, brain data was recorded using a portable EEG system. To begin, participants' baseline brain measurements were recorded, first in

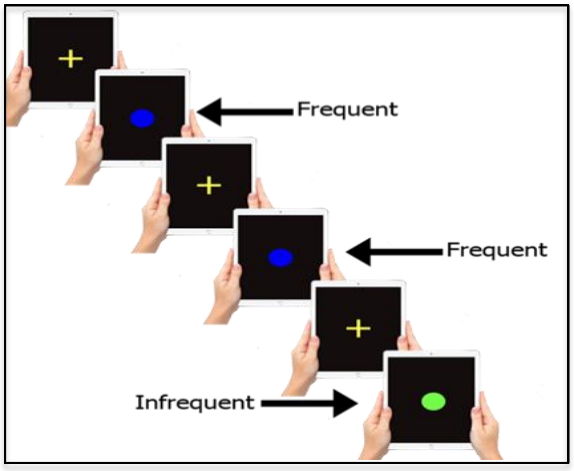
an eyes-open condition followed by an eyes-closed condition. In the eyes-open condition, participants were instructed to remain still and focus on any position in front of them while continuous EEGs were recorded for 2 minutes. Data markers were placed at the beginning and end of the 2-minute eyes-open recording. After 2 minutes, participants were asked to close their eyes and continuous EEGs were recorded for another 2 minutes to establish their eyes-closed baseline. Again, data markers were placed at the beginning and end of the eyes-closed recording. After obtaining baseline measurements, EEGs were recorded while participants completed an ordered series of perceptual tasks: (1) a Go-No-Go response task, (2) a n-Back memory task, (3) an oddball response task, and (4) a reward processing task. The present study reports exclusively on the oddball response task. The approximate run time for the completion of all EEG tasks in this session was 60 minutes.

The Oddball Task

Basic onscreen instructions were provided to participants prior to the oddball task. Next, participants were instructed to respond to infrequent stimuli presented intermittently amid more frequent stimuli. In this study, green circles (40 mm in diameter; green: 117/251/67; #75fb4c) served as the infrequent stimuli to which participants were instructed to respond by tapping their screen. Blue circles (40 mm in diameter; blue: 0/0/244; #0000f4) served as the frequent stimuli to which participants were told not to respond. All circles were presented for 1000 ms in the centre of the screen. If participants failed to respond to the presentation of an infrequent (green) stimulus within 1000 ms, the trial would automatically end. Each block of time consisting of 30 trials began with the appearance of a 10 mm fixation cross "+" (yellow: 254/254/84; #fefe54) in the centre of the screen for 400 ms with a 200 ms jitter, which caused the duration of the fixation cross to vary by +/- 200 ms and was included to ensure that participants could not unconsciously predict the timing of the fixation cross and to remove the possibility of unwanted or unintentional background cognitive processing. The fixation cross was also used as an interstimulus interval to reduce testing times (see Figure 1), as opposed to using a blank screen between trials. Finally, a black background (black: 0/0/0/; #000000) was featured throughout the task.

Participants completed six blocks of the oddball task, of which each contained 30 trials. For each trial, there was a 70% probability of a frequent (blue) stimulus being presented, and a 30% probability of an infrequent (green) stimulus being presented (70.14% frequent; 29.86% infrequent); however, participants were not aware of these stimuli probabilities. The order of stimulus presentation was random; however, presentation software assured that no more than two infrequent (green) stimuli would appear in a row to ensure the green circle would always be perceived as the infrequent stimulus. Participants were told the number of missed responses from the current block upon completion of that block.

Figure 1: Depiction of the Oddball Task



Note. Image shows all stimuli within the oddball task including the fixation cross, frequent (blue) stimuli, and infrequent (green) stimuli.

Electroencephalography and Data Acquisition

Prior to donning the portable EEG system, participants were asked to wipe their skin at the electrode sites with a 70% isopropyl swab to remove makeup and reduce natural skin oils to improve the signal quality. Participants were then equipped with a Cognionics Developer Kit (CGX) portable EEG system capable of sampling at a 500 Hz rate to record EEG data. A standard 10-10 EEG layout was applied (Seeck et al., 2017), which designated the placement of 3M Red Dot Electrodes in the following locations: Fp1, Fp2, TP9, TP10, FPz, and AFz. During the recording process, FPz served as the ground electrode and AFz served as the reference electrode. EEG data collected from the CGX were sent via Bluetooth to proprietary iOS software, which also displayed the tasks and experimental stimuli (recording device: iPad Pro, 11-inch 2nd Gen). A known Bluetooth lag and jitter (Krigolson et al., 2017) was used during data collection in lieu of temporally synchronizing experimental stimuli and event markers, as is typically done in ERP studies (Luck, 2014). Due to the wireless design of the Bluetooth, there was a small (~50 ms) lag once the signal was sent from the black box to the iPad for recording. This delay caused some minor variability, or jitter, in the initial timing of the CGX's signal lock, which was accounted for in this study's data analysis. EEG-Bluetooth jitter was solely influenced by the initial locking of the CGX's signal to the custom software since, once locked, the signal stayed connected and, thus, did not vary over time. Throughout the recording, when any task-relevant information was drawn (such as the presentation of a stimulus or the start/end of blocks), EEG data were "marked" for subsequent analysis at those specific times. Furthermore, the signals, which differed between participants but not between trials, and a visual inspection of the variance per second on the raw EEG data (or unprocessed stream of data coming from each channel) were used to assess signal quality.

Data Processing and Analysis

Data were processed offline using the Brain Vision Analyzer 2 software (Version 2.1.2, Brain Products, GmbH, Munich, Germany), as well as the MATLAB software with an EEGLAB toolbox (Delorme & Makeig, 2004) and a custom code. Continuous EEG data were not re-referenced offline, since the two posterior electrodes (TP9 and TP10) were the focus of ERP analysis and were appropriately referenced to electrode AFz at the time of recording. Next, a dual-pass Butterworth filter (passband 0.1 to 30 Hz), which is a filter that is applied twice to flatten the EEG signal, was applied to the continuous EEG data to remove signals unassociated with brain activity. The aforementioned filter was then followed by a 60 Hz notch filter to remove the ambient signal associated with outlet voltages. No lateralized effects (hemispheric-specific responses) were present upon preliminary data analysis, which meant that both the left and right sides of the brain were producing similar responses. To improve the signal-to-noise ratio of ERP measures (Oken & Chiappa, 1986), pooled frontal (Fp1 and Fp2) and posterior (TP9 and TP10) virtual electrodes were created by averaging across each pair of frontal and posterior electrodes. Accordingly, ERP analysis evaluated only the new average posterior virtual electrode instead of each individual electrode, which provided cleaner data due to the lack of hemispheric-specific responses (Krigolson et al., 2017); however, both the averaged frontal and posterior electrodes were examined during EEG analysis using a Fast Fourier transform (FFT) to assess EEG frequencies.

ERP Analysis

To evaluate ERPs, epochs (or segments of data) surrounding frequent and infrequent stimuli were generated from the filtered continuous EEG data, which started 200 ms prior to stimulus onset and extended to 800 ms post-stimulus onset. An absolute difference of 100 uV was used as the criterion measure in an artifact rejection algorithm, and segments with differences greater than 100 uV were discarded (on average: 24.80% [19.97%, 29.63%]). The artifact rejection algorithm was an algorithm employed to remove any areas of unusable data due to participant movement, blinking, etc. The remaining segments in both conditions (frequent, infrequent) were averaged for each participant, then the average frequent ERP waveform was subtracted from the average infrequent ERP waveform to generate a difference wave. The averages of all conditional (frequent, infrequent) and difference waveforms were produced for each participant to generate a grand average ERP. Next, P3 peak amplitudes were found for each participant by determining the voltage of the local maximal amplitude within a +25/-25 ms window surrounding the grand average component peaks. To simplify, 50 ms windows at the typical locations of ERP components were inspected on the grand average waveform to look for component peaks, and the highest part, or local maximal amplitude, of the P3 component was noted. Due to the small number of electrodes used, and the placement of reference electrodes relative to active channels in many portable EEG tools, the ERPs generated via these systems presented as inverted or upside down (Krigolson et al., 2017). That is to say, P3 is typically a positive-going component, which means that the component peaks upwards towards a positive voltage; however, in using this method, the peak deflected negatively in the opposite direction, as is typical, and presented as inverted. To clarify the correlations between peak values and behavioural scores, and to facilitate a clearer understanding of the data drawn, ERP data were multiplied by -1 to show positive P3 waveforms and peak values. In conducting these analyses, clean and easy to interpret data was produced that can be utilized in later statistical comparisons.

Statistical Analysis

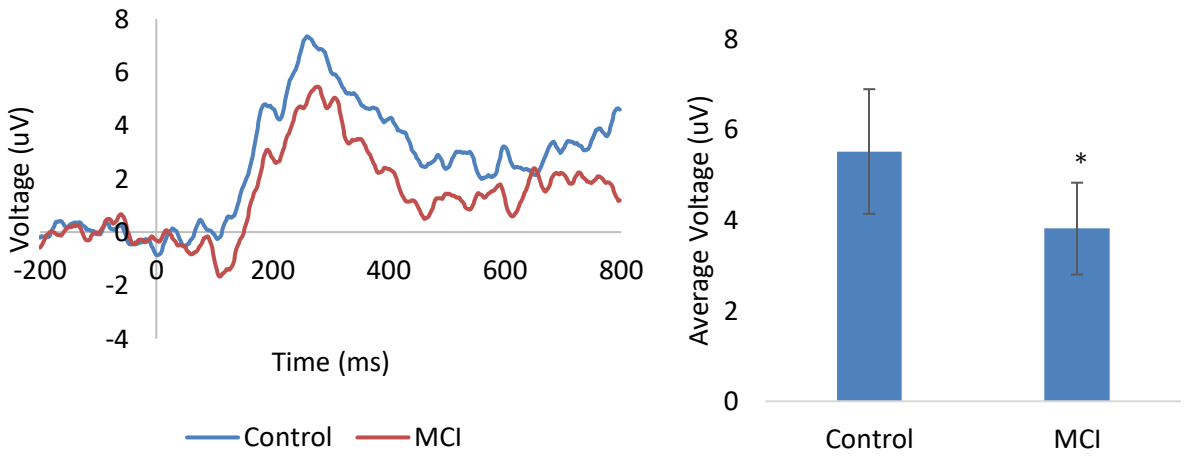
Behavioural and brain data were compared in two ways: (1) inferential statistics were conducted using independent sample t-tests (alpha value = 0.05); (2) correlational statistics were conducted using Pearson's r correlation equations. Initially, t-tests were run to compare the MCI and control groups' behavioural task scores. Total RBANS and MoCA scores were compared between groups, along with selected subcategory scores within the RBANS and MoCA tests to assess aspects of cognition associated with P3. These subcategories consisted of the RBANS attention, immediate memory, and delayed memory subcategories, as well as the Memory Index Score (MIS) subcategory from the MoCA. T-tests were also used to compare performance on the oddball task by identifying the number of correct responses, false positives, premature responses, and missed infrequent responses. Additionally, t-tests were used to compare the peak values of the P3 component during the oddball task for the MCI and control groups. Following t-tests, Pearson's r correlations were run to analyze the relationship between peak values and behavioural scores for both groups. Peak values were then compared to the total RBANS, MoCA, and individual subcategory scores listed above. Finally, mean values and 95% confidence intervals were included with all of the descriptive statistics, and statistical analyses were carried out using Microsoft Excel.

Results

An examination of behavioural data confirmed that the MCI group scored significantly lower than the control group on all pen-and-paper behavioural MCI assessments. Independent t-tests revealed significantly lower total RBANS scores [$t(38) = 17.05$, $p < .001$, Cohen's D = 1.26] and lower total MoCA scores [$t(38) = 3.95$, $p < .001$, Cohen's D = 1.39] in the MCI group. Further analysis comparing the subcategories related to attention and memory indicated that the MCI group scored significantly lower than the control group in all comparisons made—namely, RBANS attention [$t(38) = 15.95$, $p < .001$, Cohen's D = 1.19], RBANS immediate memory [$t(38) = 17.15$, $p < .01$, Cohen's D = 0.98], RBANS delayed memory [$t(38) = 20.40$, $p < .001$, Cohen's D = 1.13], and the MoCA Memory Index Score (MIS) [$t(38) = 5.00$, $p < .001$, Cohen's D = 1.70].

Inspection of oddball behavioural data demonstrated that the control and MCI groups performed similarly on most measures with the exception of missed infrequent responses. More specifically, the paired t-tests revealed no significant differences in correct responses, false positives, or premature responses ($p > .05$). While both groups scored well on missed infrequent responses, with averages of less than one, the MCI group performed with decreased accuracy [$t(38) = 0.40$, $p < .05$, Cohen's D = -0.71] when compared to the control group (see Table 1 for all t-test data). Furthermore, an analysis of EEG data revealed a decreased P3 response in the MCI group during the oddball task when compared to the healthy control group. Specifically, when peak values of the P3 ERP component were compared (see Figure 2), the MCI group showed significantly reduced peak amplitudes [$t(38) = 1.70$, $p < .05$, Cohen's D = 0.66] of P3 during the oddball task, which meant that these participants had a smaller or less synchronized brain response that was reflected in a smaller change in voltage.

Figure 2:
Comparison of Difference Waves and Peak P3 Amplitude for Control and MCI Groups



Note. Left graph illustrates the P3 difference wave (Frequent–Infrequent) for the control and MCI groups. Right graph visualizes the peak amplitude of the P3 ERP component for the control and MCI groups; error bars represent a 95% confidence interval.*$p < .05$.

Table 1: *Comparison of Control and MCI Behavioural and Brain Responses Using Paired t-Tests*

	Control			MCI			
	M	*SD*	95% CI	*M*	*SD*	95% CI	*P*
Age	71.3	3.9	1.8	76.0	7.8	3.7	.0311*
Peak Value	5.5	2.9	1.4	3.8	2.2	1.0	.0438*
RBANS	99.9	13.0	6.1	82.9	14.1	6.6	.0003***
MoCA	26.9	2.3	1.1	23.0	3.3	1.5	.0001***
RBANS Attn	108.6	14.8	6.9	92.6	11.9	5.6	.0006***
RBANS IM	101.5	13.9	6.5	84.4	20.5	9.6	.0036**
RBANS DM	96.3	14.5	6.8	75.9	20.9	9.8	.0009***
MoCA MIS	12.9	2.8	1.3	7.9	3.1	1.4	.0000***
Oddball CR	53.3	3.3	1.4	53.1	3.0	1.3	.8423
Oddball FA	0.4	0.6	0.3	0.8	1.1	0.5	.2094
Oddball PR	0.4	0.7	0.3	0.6	0.9	0.4	.2246
Oddball MI	0.2	0.4	0.2	0.6	0.7	0.3	.0303*

Note. RBANS = Repeatable Battery for the Assessment of Neuropsychological State; MoCA = Montreal Cognitive Assessment; Attn = attention subcategory; IM = immediate memory subcategory; DM = delayed memory subcategory; MIS = Memory Index Score; CR = correct response; FA = false positive; PR = premature response; MI = missed infrequent response. *$p < .05$, **$p < .01$, ***$p < .001$

Correlational statistics comparing peak values with pen-and-paper behavioural scores revealed mixed results. Specifically, stronger correlations between peak values and behavioural scores were seen in the control group for all conditions besides immediate memory, which indicated a stronger correlation in the MCI group. These findings are summarized in Table 2, which presents all Pearson's r comparisons made in this study and their coefficients. The strongest correlations for the control group were between peak values and delayed memory subcategory scores as well as between peak values and total MoCA scores, both of which showed moderately strong relationships with the r values of -0.62 and -0.50, respectively. To have a strong correlation with a high coefficient meant that, as one measure increases (i.e., peak value), the other measure either increases or decreases concurrently (i.e., delayed memory or MoCA scores). In contrast, these trends disappeared completely in the MCI group, in which peak values and delayed memory subcategory scores demonstrated no correlation (r = -0.01), and peak values and total MoCA scores showed a weak correlation (r = 0.12). The strongest correlation in the MCI group was between peak values and immediate memory subcategory scores, with a weak relationship (r = -0.30). This weak relationship meant that, as peak values increased for MCI participants, there was no strong concurrent increase or decrease in immediate memory scores.

Table 2*: Pearson's Correlations Comparing P3 Peak Values to Behavioural Scores*

	Pearson's coefficient, r	
	Control	MCI
Peak vs RBANS	-0.30	-0.02
Peak vs MoCA	-0.50	0.12
Peak vs Attention	-0.04	-0.09
Peak vs IM	-0.18	-0.30
Peak vs DM	-0.62	-0.01
Peak vs MIS	-0.32	-0.06

Note. Peak = P3 peak value; RBANS = Repeatable Battery for the Assessment of Neuropsychological State; MoCA = Montreal Cognitive Assessment; Attention = RBANS attention subcategory; IM = RBANS immediate memory subcategory; DM = RBANS delayed memory subcategory; MIS = MoCA Memory Index Score.

Discussion

This study confirms that MCI patients demonstrate modulated behavioural and brain responses compared to healthy, age-matched controls. Furthermore, this study affirms that these brain changes can be measured via a portable EEG system. As expected, the MCI group scored significantly lower on the traditional pen-and-paper MCI assessments used to measure behaviour in this study (the RBANS and MoCA). In addition to scoring lower overall on assessed tasks, the MCI group also scored lower in all of the subcategories that pertained to attention and memory within the MoCA and RBANS tests. In contrast, few differences were seen between groups when measuring oddball task performance; however, an analysis of brain data revealed that the MCI group exhibited a reduced P3 response during the visual oddball task. Additionally, it was noted during the oddball task that the control group exhibited moderately strong relationships between peak P3 values and pen-and-paper behavioural scores, whereas the MCI group had weak to non-existent relationships within these same categories.

As such, the pen-and-paper behavioural results of this study support the first hypothesis that the MCI group would demonstrate decreased task performance compared to the control group. This study found that the control group outperformed the MCI group on all pen-and-paper measures. This finding aligns with previous MCI and dementia literature (see Nasreddine et al., 2005; Randolph et al., 2010) that found the MoCA and RBANS assessments designed to aid in MCI diagnostic processes distinguished individuals with MCI from those without. The present study chose to compare cognitive processes associated with the P3 component (attention and memory) with subcategories that assessed only those processes. Previously, MCI had been shown to affect attention and memory (Klekociuk & Summers, 2014; Saunders & Summers, 2011), and the present study arrived at similar findings since the MCI group scored lower than the control group on each of the attention and memory subcategory assessments.

Conversely, the results from the oddball task revealed little difference in behavioural task performance between groups, while simultaneously illustrating brain differences in their P3 responses. Our ERP results support this study's second hypothesis since the MCI group displayed a reduced peak amplitude for the P3 ERP component during the oddball task. Previous studies have arrived at similar findings, in which patients with MCI or AD demonstrate reduced P3 amplitudes across varying experimental tasks and conditions (see Cecchi et al., 2015; Jiang et al., 2015; Parra et al., 2012); however, few extant studies have demonstrated this finding using a portable EEG system. The reduced peak amplitude of P3 in the MCI group suggests alternative brain activations, which could indicate the development of MCI. Accordingly, a reduced P3 amplitude may serve as a biomarker for MCI, and the fact that this difference can be detected using a portable EEG tool enhances its potential for widespread use.

As previously stated, P3 is correlated with attention and memory, both of which are implicated in MCI (Klekociuk & Summers, 2014; Saunders & Summers, 2011). With this connection in mind, we had expected to discern a relationship between the peak values of the P3 component and behavioural scores assessing attention and memory cognitive processes; however, this hypothesis was only partially supported. The total RBANS and MoCA scores, along with several subcategory scores, demonstrated weak-to-moderate correlations with peak values in the

control group; however, in the MCI group, these relationships were not present. Moreover, the relationships between behavioural scores and peak values for both control and MCI groups were negative, which meant that as peak value amplitudes increased behavioural scores decreased. One possible explanation for this finding could be that, as brain health declines (due to natural aging processes or pathologically via MCI), tasks that require attention and memory become harder to complete. This added challenge could increase the workload for areas of the brain associated with attention and memory, which may prompt these systems to work harder to achieve the same (or worse) scores for tasks when compared to healthy counterparts. This increased workload could be reflected in the larger P3 amplitude and lower task scores seen in the present study. Additionally, the negative relationship between P3 amplitudes and task scores was seen in both groups, which meant that cognitive decline, due to natural aging processes or MCI, resulted in similar neurological outcomes and behavioural responses.

Conclusions

This study demonstrated that a portable EEG system could serve as a viable tool for MCI diagnosis and assessment. Specifically, the reduced amplitude of the P3 component exhibited in MCI patients could serve as a biomarker for MCI. Future research could expand this study to include a lifespan scope that tracks changes in P3 amplitudes as healthy populations age naturally, or by applying a disease-span approach that tracks P3 amplitude changes as MCI populations experience disease progression.

References

Babiloni, C., del Percio, C., Lizio, R., Marzano, N., Infarinato, F., Soricelli, A., Salvatore, E., Ferri, R., Bonforte, C., Tedeschi, G., Montella, P., Baglieri, A., Rodriguez, G., Famà, F., Nobili, F., Vernieri, F., Ursini, F., Mundi, C., Frisoni, G. B., & Rossini, P. M. (2014). Cortical sources of resting state electroencephalographic alpha rhythms deteriorate across time in subjects with amnesic mild cognitive impairment. *Neurobiology of Aging*, *35*(1), 130–142. https://doi.org/10.1016/J.NEUROBIOLAGING.2013.06.019

Biasiucci, A., Franceschiello, B., & Murray, M. M. (2019). Electroencephalography. *Current Biology*, *29*(3), R80–R85. https://doi.org/10.1016/J.CUB.2018.11.052

Burdorf, B. T. (2021). Comparing MRI and CT machine accessibility among urban and rural county hospitals. *Journal of Public Health Research*, *11*(1), 2527. https://doi.org/10.4081/JPHR.2021.2527

Cecchi, M., Moore, D. K., Sadowsky, C. H., Solomon, P. R., Doraiswamy, P. M., Smith, C. D., Jicha, G. A., Budson, A. E., Arnold, S. E., & Fadem, K. C. (2015). A clinical trial to validate event-related potential markers of Alzheimer's disease in outpatient settings. *Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring*, *1*(4), 387–394. https://doi.org/10.1016/J.DADM.2015.08.004

Chambers, L. W., Bancej, C., & Mcdowell, I. (2016). *Prevalence and monetary costs of dementia in Canada.* www.alzheimer.ca

Chapman, R. M., McCrary, J. W., Gardner, M. N., Sandoval, T. C., Guillily, M. D., Reilly, L. A., & DeGrush, E. (2011). Brain ERP components predict which individuals progress to Alzheimer's disease and which do not. *Neurobiology of Aging*, *32*(10), 1742–1755. https://doi.org/10.1016/J.NEUROBIOLAGING.2009.11.010

Correa-Jaraba, K. S., Lindín, M., & Díaz, F. (2018). Increased amplitude of the P3a ERP component as a neurocognitive marker for differentiating amnestic subtypes of mild cognitive impairment. *Frontiers in Aging Neuroscience*, *10*(19), 1–13. https://doi.org/10.3389/FNAGI.2018.00019

Coles, M. G. H., & Rugg, M. D. (1996). Event-related brain potentials: An introduction. In M. D. Rugg & M. G. H. Coles (Eds.), *Electrophysiology of mind: Event-related brain potentials and cognition* (pp. 1–26). Oxford University Press.

Costa, A. S., Reich, A., Fimm, B., Ketteler, S. T., Schulz, J. B., & Reetz, K. (2014). Evidence of the sensitivity of the MoCA alternate forms in monitoring cognitive change in early Alzheimer's disease. *Dementia and geriatric cognitive disorders*, *37*(1-2), 95–103. https://doi.org/10.1159/000351864

Deiber, M. P., Ibañez, V., Missonnier, P., Herrmann, F., Fazio-Costa, L., Gold, G., & Giannakopoulos, P. (2009). Abnormal-induced theta activity supports early directed-attention network deficits in progressive MCI. *Neurobiology of Aging*, *30*(9), 1444–1452. https://doi.org/10.1016/J.NEUROBIOLAGING.2007.11.021

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21. https://doi.org/10.1016/J.JNEUMETH.2003.10.009

Donchin, E., & Coles, M. G. H. (1988). Is the P300 component a manifestation of context updating? *Behavioral and Brain Sciences*, *11*(3), 357–374. https://doi.org/10.1017/S0140525X00058027

Duits, F. H., Martinez-Lage, P., Paquet, C., Engelborghs, S., Lleó, A., Hausner, L., Molinuevo, J. L., Stomrud, E., Farotti, L., Ramakers, I. H. G. B., Tsolaki, M., Skarsgård, C., Åstrand, R., Wallin, A., Vyhnalek, M., Holmber-Clausen, M., Forlenza, O. v., Ghezzi, L., Ingelsson, M., … Blennow, K. (2016). Performance and complications of lumbar puncture in memory clinics: Results of the multicenter lumbar puncture feasibility study. *Alzheimer's & Dementia*, *12*(2), 154–163. https://doi.org/10.1016/J.JALZ.2015.08.003

Gale, S. A., Acar, D., & Daffner, K. R. (2018). Dementia. *The American Journal of Medicine*, *131*(10), 1161–1169. https://doi.org/10.1016/J.AMJMED.2018.01.022

Galvin, J. E. (2018). Using informant and performance screening methods to detect mild cognitive impairment and dementia. *Neurology of Aging, 7*, 19-25. https://doi.org/10.1007/s13670-018-0236-2

Gauthier, S., Reisberg, B., Zaudig, M., Petersen, R. C., Ritchie, K., Broich, K., Belleville, S., Brodaty, H., Bennett, D., Chertkow, H., Cummings, J. L., de Leon, M., Feldman, H., Ganguli, M., Hampel, H., Scheltens, P., Tierney, M. C., Whitehouse, P., & Winblad, B. (2006). Mild cognitive impairment. *The Lancet*, *367*(9518), 1262–1270. https://doi.org/10.1016/S0140-6736(06)68542-5

Gillis, C., Mirzaei, F., Potashman, M., Ikram, M. A., & Maserejian, N. (2019). The incidence of mild cognitive impairment: A systematic review and data synthesis. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *11(1)*, 248. https://doi.org/10.1016/J.DADM.2019.01.004

Gottlibe, M., Rosen, O., Weller, B., Mahagney, A., Omar, N., Khuri, A., Srugo, I., & Genizi, J. (2020). Stroke identification using a portable EEG device—A pilot study. *Neurophysiologie Clinique*, *50*(1), 21–25. https://doi.org/10.1016/J.NEUCLI.2019.12.004

Gu, L., Chen, J., Gao, L., Shu, H., Wang, Z., Liu, D., Yan, Y., Li, S., & Zhang, Z. (2019). Deficits of visuospatial working memory and executive function in single- versus multiple-domain amnestic mild cognitive impairment: A combined ERP and sLORETA study. *Clinical Neurophysiology*, *130*(5), 739–751. https://doi.org/10.1016/J.CLINPH.2019.01.025

Hünerli, D., Emek-Savaş, D. D., Çavuşoğlu, B., Dönmez Çolakoğlu, B., Ada, E., & Yener, G. G. (2019). Mild cognitive impairment in Parkinson's disease is associated with decreased P300 amplitude and reduced putamen volume. *Clinical Neurophysiology*, *130*(8), 1208–1217. https://doi.org/10.1016/J.CLINPH.2019.04.314

Jiang, S., Qu, C., Wang, F., Liu, Y., Qiao, Z., Qiu, X., Yang, X., & Yang, Y. (2015). Using event-related potential P300 as an electrophysiological marker for differential diagnosis and to predict the progression of mild cognitive impairment: a meta-analysis. *Neurological Sciences*, *36*(7), 1105–1112. https://doi.org/10.1007/S10072-015-2099-Z

Jiménez, E. C., Sierra-Marcos, A., Romeo, A., Hashemi, A., Leonovych, O., Valenzuela, P. B., Puig, M. S., Supèr, H. (2021). Altered vergence eye movements and pupil response of patients with Alzheimer's disease and mild cognitive impairment during an oddball task. *Journal of Alzheimer's Disease, 82*(1), 421-433. https://doi.org/10.3233/JAD-201301

Kavcic, V., Daugherty, A. M., & Giordani, B. (2021). Post-task modulation of resting state EEG differentiates MCI patients from controls. *Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring*, *13*(1), 1-6. https://doi.org/10.1002/DAD2.12153

Klekociuk, S. Z., & Summers, M. J. (2014). Lowered performance in working memory and attentional sub-processes are most prominent in multi-domain amnestic mild cognitive impairment subtypes. *Psychogeriatrics*, *14*(1), 63–71. https://doi.org/10.1111/PSYG.12042

Krigolson, O. E., Hammerstrom, M. R., Abimbola, W., Trska, R., Wright, B. W., Hecker, K. G., & Binsted, G. (2021). Using Muse: Rapid mobile assessment of brain performance. *Frontiers in Neuroscience*, *15*(634147), 1-11. https://doi.org/10.3389/FNINS.2021.634147

Krigolson, O. E., & Holroyd, C. B. (2007). Hierarchical error processing: different errors, different systems. *Brain research, 1155*, 70-80. https://doi.org/10.1016/j.brainres.2007.04.024

Krigolson, O. E., Williams, C. C., Norton, A., Hassall, C. D., & Colino, F. L. (2017). Choosing MUSE: Validation of a low-cost, portable EEG system for ERP research. *Frontiers in Neuroscience*, *11*(109), 1-10. https://doi.org/10.3389/fnins.2017.00109

Langa, K. M., & Levine, D. A. (2014). The diagnosis and management of mild cognitive impairment: A clinical review. *Journal of the American Medical Association, 312*(23), 2551-2561. https://doi.org/10.1001/jama.2014.13806

Luck, S. J. (2014). *An introduction to the event-related potential technique.* MIT Press.

Moretti, D. v., Frisoni, G. B., Fracassi, C., Pievani, M., Geroldi, C., Binetti, G., Rossini, P. M., & Zanetti, O. (2011). MCI patients' EEGs show group differences between those who progress and those who do not progress to AD. *Neurobiology of Aging*, *32*(4), 563–571. https://doi.org/10.1016/J.NEUROBIOLAGING.2009.04.003

Musall, S., von Pföstl, V., Rauch, A., Logothetis, N. K., & Whittingstall, K. (2014). Effects of neural synchrony on surface EEG. *Cerebral Cortex*, *24*(4), 1045–1053. https://doi.org/10.1093/CERCOR/BHS389

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J. L., & Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, *53*(4), 695–699. https://doi.org/10.1111/J.1532-5415.2005.53221.X

Nieuwenhuis, S., Aston-Jones, G., & Cohen, J. D. (2005). Decision making, the P3, and the locus coeruleus-norepinephrine system. *Psychological Bulletin*, *131*(4), 510–532. https://doi.org/10.1037/0033-2909.131.4.510

Oken, B. S., & Chiappa, K. H. (1986). Statistical issues concerning computerized analysis of brainwave topography. *Annals of Neurology*, *19*(5), 493-494. https://doi.org/10.1002/ana.410190511

Olejniczak, P. (2006). Neurophysiologic basis of EEG. *Journal of Clinical Neurophysiology*, *23*(3), 186–189. https://doi.org/10.1097/01.wnp.0000220079.61973.6c

On, F. R., Jailani, R., Norhazman, H., & Zaini, N. M. (2013). Binaural beat effect on brainwaves based on EEG. *IEEE 9th International Colloquium on Signal Processing and Its Applications*, 339–343. https://doi.org/10.1109/CSPA.2013.6530068

Owens, D. K., Davidson, K. W., Krist, A. H., Barry, M. J., Cabana, M., Caughey, A. B., Doubeni, C. A., Epling, J. W., Kubik, M., Landefeld, C. S., Mangione, C. M., Pbert, L., Silverstein, M., Simon, M. A., Tseng, C.-W., & Wong, J. B. (2020). Screening for cognitive impairment in older adults: US preventive services task force recommendation statement. *Journal of the American Medical Association*, *323*(8), 757–763. https://doi.org/10.1001/JAMA.2020.0435

Parra, M. A., Ascencio, L. L., Urquina, H. F., Manes, F., & Ibáñez, A. M. (2012). P300 and neuropsychological assessment in mild cognitive impairment and Alzheimer dementia. *Frontiers in Neurology*, *3*(172), 1-10. https://doi.org/10.3389/fneur.2012.00172

Patnode, C. D., Perdue, L. A., Rossom, R. C., Rushkin, M. C., Redmond, N., Thomas, R. G., & Lin, J. S. (2020). *Evidence Synthesis Number 189 Screening for Cognitive Impairment in Older Adults: An Evidence Update for the U.S. Preventive Services Task Force*. https://www.ncbi.nlm.nih.gov/books/NBK554654/

Perry, D. C., Datta, S., Sturm, V. E., Wood, K. A., Zakrzewski, J., Seeley, W. W., Miller, B. L., Kramer, J. H., Rosen, H. J. (2017). Reward deficits in behavioural variant frontotemporal dementia include insensitivity to negative stimuli, *Brain*, *140*(12), 3346–3356. https://doi.org/10.1093/brain/awx259

Pfeffer, R. I., Kurosaki, T. T., Harrah, C. H., Chance, J. M., & Filos, S. (1982). Measurement of functional activities in older adults in the community. *Journal of Gerontology*, *37*(3), 323–329. https://doi.org/10.1093/GERONJ/37.3.323

Polich, J. (2012). Neuropsychology of P300. *The Oxford handbook of Event-Related Potential components*. https://doi.org/10.1093/OXFORDHB/9780195374148.013.0089

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*, *118*(10), 2128–2148. https://doi.org/10.1016/J.CLINPH.2007.04.019

Pu, L., Lion, K. M., Todorovic, M., & Moyle, W. (2021). Portable EEG monitoring for older adults with dementia and chronic pain - A feasibility study. *Geriatric Nursing*, *42*(1), 124–128. https://doi.org/10.1016/J.GERINURSE.2020.12.008

Qian, X., Dai, W., Xu, R., & Ling, H. (2020). One intelligent framework for screening and intervention of Mild Cognitive Impairment (MCI). *The Journal of Engineering*, *2020*(13), 422–425. https://doi.org/10.1049/JOE.2019.1209

Randolph, C., (2012). *The Repeatable Battery for the Assessment of Neuropsychological Status update.* Pearson. https://www.pearsonassessments.com/store/usassessments/en/Store/Professional-Assessments/Cognition-%26-Neuro/Repeatable-Battery-for-the-Assessment-of-Neuropsychological-Status-Update/p/100000726.html

Randolph, C., Tierney, M. C., Mohr, E., & Chase, T. N. (2010). The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): Preliminary clinical validity. *Journal of Clinical and Experimental Neuropsychology, 20*(3), 310–319. https://doi.org/10.1076/JCEN.20.3.310.823

Sabbagh, M. N., Boada, M., Borson, S., Chilukuri, M., Doraiswamy, P. M., Dubois, B., Ingram, J., Iwata, A., Porsteinsson, A. P., Possin, K. L., Rabinovici, G. D., Vellas, B., Chao, S., Vergallo, A., & Hampel, H. (2020). Rationale for early diagnosis of mild cognitive impairment (MCI) supported by emerging digital technologies. *The Journal of Prevention of Alzheimer's Disease, 7*(3), 158–164. https://doi.org/10.14283/JPAD.2020.19

Saunders, N. L. J., & Summers, M. J. (2011). Longitudinal deficits to attention, executive, and working memory in subtypes of mild cognitive impairment. *Neuropsychology*, *25*(2), 237–248. https://doi.org/10.1037/A0021134

Seeck, M., Koessler, L., Bast, T., Leijten, F., Michel, C., Baumgartner, C., He, B., & Beniczky, S. (2017). The standardized EEG electrode array of the IFCN. *Clinical Neurophysiology*, *128*(10), 2070–2077. https://doi.org/10.1016/j.clinph.2017.06.254

Sheik, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale: Recent evidence and development of a shorter version. *Clinical Gerontology: A Guide to Assessment and Intervention*, *5*(1–2), 165–173. https://doi.org/10.1300/J018v05n01_09

Smailovic, U., & Jelic, V. (2019). Neurophysiological markers of Alzheimer's disease: Quantitative EEG approach. *Neurology and Therapy*, *8*(2), 37–55. https://doi.org/10.1007/S40120-019-00169-0

Tülay, E. E., Güntekin, B., Yener, G., Bayram, A., Başar-Eroğlu, C., & Demiralp, T. (2020). Evoked and induced EEG oscillations to visual targets reveal a differential pattern of change along the spectrum of cognitive decline in Alzheimer's Disease. *International Journal of Psychophysiology*, *155*, 41–48. https://doi.org/10.1016/J.IJPSYCHO.2020.06.001

Vemuri, P., Wiste, H. J., Weigand, S. D., Shaw, L. M., Trojanowski, J. Q., Weiner, M. W., Knopman, D. S., Petersen, R. C., & Jack, C. R. (2009). MRI and CSF biomarkers in normal, MCI, and AD subjects: Predicting future clinical change. *Neurology*, *73*(4), 294–301. https://doi.org/10.1212/WNL.0B013E3181AF79FB

Yokomizo, J. E., Simon, S. S., & Bottino, C. M. de C. (2014). Cognitive screening for dementia in primary care: A systematic review. *International Psychogeriatrics*, *26*(11), 1783–1804. https://doi.org/10.1017/S1041610214001082