جلد ۸- شماره ۶ - سال ۱۴۰۲



A Review of Electroencephalography (EEG) Analysis in Alzheimer's disease, Vascular Dementia and Mild Cognitive Impairment

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Received: January 2024 Accepted: February 2024

Abstract

Electroencephalography (EEG) is a non-invasive technique that measures the electrical activity of the brain. EEG has been used to study the changes in brain function and connectivity in various types of dementia, such as Alzheimer's disease (AD), vascular dementia (VaD), and mild cognitive impairment (MCI). This review aims to summarize the main findings of EEG analysis in these conditions, focusing on the spectral, temporal, spatial, and network features of EEG signals. We also discuss the potential applications of EEG as a diagnostic and prognostic tool, as well as the limitations and challenges of EEG research in dementia. EEG Can be accurate of 83.9%–96.8% for MCI and 71.9%–96.9% for AD and 87.9%–90.9% for VaD be effective in early diagnosis. We conclude that EEG is a valuable method to explore the neurophysiological mechanisms of cognitive decline and impairment, and to identify biomarkers and predictors of dementia progression. However, further studies are needed to improve the standardization, reliability, and validity of EEG methods and results, and to integrate EEG with other modalities of brain imaging and assessment.

Key Words: Electroencephalography (EEG), Alzheimer's disease, Vascular Dementia, Brain, Dementia, Mild Cognitive Impairment

1- Introduction

Alzheimer's disease (AD) is the most common cause of dementia [1]. Alzheimer's disease (AD) is the leading cause of dementia, accounting for an estimated 60-80% of cases worldwide [2]. Since there are no medications to cure or delay the symptom of dementia [3]. The most common form of dementia after Alzheimer's dementia (AD) is vascular dementia (VaD), contributing about 20% in North America and Europe, and about 30% in Asia and developing countries [4]. Vascular dementia is closely related to cerebrovascular disease [5]. Stroke, hypertension, diabetes mellitus, obesity, cholesterol, and heart fibrillation are closely related to vascular dementia [6]. Among these vascular diseases, stroke is most often associated with VaD [7]. Mild cognitive impairment (MCI) is an intermediate stage between healthy aging and

dementia, and is transformed to dementia at an increasing rate [8]. The annual rate of conversion from MCI to AD is 3-15 % compared to 1-2 % of the general population [8]. Especially, amnestic MCI (aMCI) is the most probable to convert to AD [9]. It is well-accepted that MCI is a high-risk factor for the development of AD and reflects a prodromal predementia state of AD, with an estimated conversion rate of 10-15% per year [10].

Electroencephalography (EEG), a low-cost, non-invasive, and portable technique that directly measures neural activity with a high temporal resolution, has emerged as a potential tool for detecting neural biomarkers related to MCI and AD [11-14]. Numerous lines of evidence have validated the possibility of using EEG to distinguish MCI and AD patients from healthy cohorts with diverse sensitivity and specificity [15]. Over the past several decades, quantitative EEG (QEEG) has been used to complete the criteria for dementia. Recently, QEEG research on dementia has focused on early detection, evaluation of severity, and discrimination of dementia type [16-17]. Unlike other methods of acquiring candidate AD biomarkers, EEG provides a noninvasive and relatively inexpensive measure of brain activity with established utility [1-18-19]. Likely due to increasing availability of analytical techniques and computational power for quantifying EEG patterns beyond what is recognizable by visual inspection. EEG can be recorded while subjects are engaged in various cognitive tasks to identify cognitive processes that may be characteristically perturbed in individuals with AD or MCI [20].

Bin Jiao et al, (2023) investigated that, Neural biomarker diagnosis and prediction to mild cognitive impairment and Alzheimer's disease using EEG technology and their results revealed that, the identified EEG biomarkers achieved over 70% accuracy in the three-level classification of HC, MCI, and AD. Among all six groups, the most prominent effects of AD-linked neurodegeneration on EEG metrics were localized at parieto-occipital regions. In the cross-validation predictive analyses, the optimal EEG features were more effective than the CSF + APOE biomarkers in predicting the age of onset and disease course, whereas the combination of EEG + CSF + APOE measures achieved the best performance for all targets of prediction [21].

In another scholar which done Hadiyoso et al, (2023), Multi Modal Feature Extraction for Classification of Vascular Dementia in Post-Stroke Patients Based on EEG Signal and results show that, The EEG method used for feature extraction includes relative power, coherence, and signal complexity; the evaluation performance of normal-mild cognitive impairment-dementia classification was conducted using Support Vector Machine and K-Nearest Neighbor. The results of the classification simulation showed the highest accuracy of 96% by Gaussian SVM with a sensitivity and specificity of 95.6% and 97.9%, respectively [22].

The study of Lucía Torres-Simon et al, (2022) examined that, Understanding brain function in vascular cognitive impairment and dementia with EEG and MEG: A systematic review. Despite considerable heterogeneity in clinical definition and electrophysiological methodology, common patterns exist when comparing patients with Vascular Cognitive Impairment (VCI) to healthy controls (HC) and patients with Alzheimer's disease (AD), though there is a low specificity when comparing between VCI subgroups. Similar to other dementias, slowed frequency patterns and disrupted inter- and intra-hemispheric connectivity are repeatedly reported for VCI patients, as well as longer latencies and smaller amplitudes in evoked responses [23].

Hadiyoso et al, (2022) EEG-Based Spectral Dynamic in Characterization of Post Stroke Patients with Cognitive Impairment for Early Detection of Vascular Dementia from the analysis results, it was found that there were differences in the dynamics of the power spectral in each group, where the spectral power of the cognitively impaired group was more regular than the normal group [24].

In another scholar which done by Amir H. Meghdadi et al, (2021) Resting state EEG biomarkers of cognitive decline associated with Alzheimer's disease and mild cognitive impairment and results show that, The AD group showed a significant decrease in the spectral power and coherence in the Alpha band consistent with the same effect in normal aging.

However, the MCI group did not show any significant change in the Alpha band. Overall, Theta to Alpha ratio (TAR) provided the largest and most significant differences between the AD group and controls. However, differences in the MCI group remained small and localized [25]. Alzheimer's disease (AD) and vascular dementia (VaD) are two of the most common forms of dementia, which are characterized by a decline in memory and other cognitive skills. Early diagnosis of dementia, especially at the stage of mild cognitive impairment (MCI), has become an important goal of the modern patient work-up. We will also discuss the specific changes that EEG shows in these conditions, and how they can be utilized as diagnostic methods to increase the specificity and sensitivity of the diagnostic algorithm. In this review, we will explore the use of EEG analysis in AD, VaD, and MCI, and how it can be used to monitor the therapeutic effect and progression of AD as well as the possible transition from MCI to early stage AD.

2- Methodology

The research method for this topic is to conduct a systematic review of the literature on electroencephalography (EEG) analysis in Alzheimer's disease (AD), vascular dementia (VaD), and mild cognitive impairment (MCI). The review aims to summarize the current state of knowledge, identify the main challenges and limitations, and provide recommendations for future research. The search strategy will include relevant databases, such as PubMed, Web of Science, and Scopus, and use appropriate keywords and filters. The data extraction and synthesis will be done using a predefined template and a narrative approach, respectively. The review will report the main findings, gaps, and implications of the EEG analysis in AD, VaD, and MCI.

Bin Jiao et al, (2023) applied Neural biomarker diagnosis and prediction to mild cognitive impairment and Alzheimer's disease using EEG technology they analysis some variable parameters A total of 890 participants, including 189 patients with MCI, 330 patients with AD, 125 patients with other dementias (frontotemporal dementia, dementia with Lewy bodies, and vascular cognitive impairment), and 246 healthy controls (HC) were enrolled. Biomarkers were extracted from resting-state EEG recordings for a three-level classification of HC, MCI, and AD. The optimal EEG biomarkers were then identified based on the classification performance. Random forest regression was used to train a series of models by combining participants' EEG biomarkers, demographic information (i.e., sex, age), CSF biomarkers, and APOE phenotype for assessing the disease progression and individual's cognitive function [21].

A research on the Multi Modal Feature Extraction for Classification of Vascular Dementia in Post-Stroke Patients Based on EEG Signal was done by Hadiyoso et al, (2023) this study used 19 EEG channels recorded from normal elderly, post-stroke with mild cognitive impairment, and post-stroke with dementia. The QEEG method used for feature extraction includes relative power, coherence, and signal complexity; the evaluation performance of normal-mild cognitive impairment-dementia classification was conducted using Support Vector Machine and K-Nearest Neighbor [22].

A similar study titled Understanding brain function in vascular cognitive impairment and dementia with EEG and MEG was conducted by Lucía Torres-Simon et al, (2022) and they analysis some variable parameters including Sample characteristics: Including diagnostic criteria for each group (according to each paper nomenclature), number of subjects, sex, and age. Diagnosis: MMSE and MRI/CT (we describe objective measures for VCI diagnosis when the authors report them in the original article) and Methods: Neuroimaging technique, experimental condition, and type of signal analysis [23].

Hadiyoso et al, (2022) applied EEG-Based Spectral Dynamic in Characterization of Post Stroke Patients with Cognitive Impairment for Early Detection of Vascular Dementia this study proposes an EEG signal characterization method using EEG spectral power complexity measurements to obtain features of post stroke patients with cognitive impairment and normal subjects. Working memory EEGs were collected and analyzed from forty-two participants, consisting of sixteen normal subjects, fifteen post stroke patients with mild cognitive impairment, and eleven post stroke patients with dementia [24].

A similar study titled Resting state EEG biomarkers of cognitive decline associated with Alzheimer's disease and mild cognitive impairment conducted by Amir H. Meghdadi et al, (2021) For this purpose, they analyzed EEG data from individuals with AD (n = 26), MCI (n = 53) and cognitively normal controls classified by AD (n = 26), and healthy controls stratified by Age into three groups: 18-40 (129 people), 40-60 (62 people) and 60-90 (55) years old. For each participant, we calculated the power spectral density in each channel and the spectral coherence [25].

3- Result and Discussion

Bin Jiao et al, (2023), investigated neural biomarker diagnosis and prediction to mild cognitive impairment and Alzheimer's disease using EEG technology and they found that the identified EEG biomarkers achieved over 70% accuracy in the three-level classification of HC, MCI, and AD. Among all six groups, the most prominent effects of AD-linked neurodegeneration on EEG metrics were localized at parieto-occipital regions. In the cross-validation predictive analyses, the optimal EEG features were more effective than the CSF (Cerebrospinal fluid) + APOE (Apolipoprotein E) biomarkers in predicting the age of onset and disease course, whereas the combination of EEG + CSF + APOE measures achieved the best performance for all targets of prediction [21]. We identified 178 EEG features as the key features for the classification of HC, MCI, and AD. The optimal feature set covered partial features from each EEG feature category, particularly the absolute PSD and the complexity of EEG signals. The distribution of the optimal feature set among all extracted EEG features is shown in Figure 1. Six types of EEG features were extracted, including "a" absolute PSD, "b" relative PSD, "c" Hjorth metrics (activity, mobility, and complexity), "d" time-frequency measures (STFT), "e" sample entropy, and "f" microstate measures (lifetime, occurrence rate, converting rate) is shown in Figure 1.

A research on the Multi Modal Feature Extraction for Classification of Vascular Dementia in Post-Stroke Patients Based on EEG Signal was done by Hadiyoso et al, (2023) the results of the classification simulation showed the highest accuracy of 96% by Gaussian SVM with a sensitivity and specificity of 95.6% and 97.9%, respectively. This study is expected to be an additional criterion in the diagnosis of dementia, especially in post-stroke patients [22]. The test results are presented in Tables <u>1</u> and <u>2</u>. From this test, it was known that SpecDE analysis provides discriminatory significance for the case of three groups' superior to SpecEn. Significant differences for the three groups, with p < 0.05, were more in SpecDE than in SpecEn. The post hoc multiple comparison test results for SpecDE showed significant differences between groups at the Fp1, P3, O1, C4, and P4 electrodes. These results will significantly affect the accuracy at the classification stage.

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F3

C3



Figure 1- Distribution of the optimal feature set among all extracted EEG features in classification (indicated by red)

| Table 1- | Th | e results | of pos | t hoc n | nultiple co | ompai | uson (Spe | ecEn) |
|----------|----|-----------|--------|---------|-------------|-------|-----------|-------|
| | | | | | | | | |

| Comparison | Fp1 | F7 | T3 | Т5 | Fp2 | F8 | T4 | T6 | F3 | C3 |
|----------------------------|---------|---------|---------|---------|---------|---------|---------|-----------|---------|---------|
| Normal vs. Stroke-MCI | 0.141 | 0.047 * | 0.207 | 0.108 | 0.247 | 0.071 | 0.144 | 0.030 * | 0.079 | 0.173 |
| Normal vs. Stroke-Dementia | 0.002 * | 0.000 * | 0.000 * | 0.003 * | 0.002 * | 0.000 * | 0.000 * | 0.000 * | 0.000 * | * 0.000 |
| Stroke-MCI vs. | 0.174 | 0.020 * | 0.026 * | 0.251 | 0.097 | 0.062 | 0.019 * | 0.11 | 0.020 * | 0.044 * |
| | P3 | 01 | F4 | C4 | P4 | O2 | Fz | Cz | Pz | |
| Normal vs. Stroke-MCI | 0.207 | 0.262 | 0.042 * | 0.19 | 0.148 | 0.213 | 0.011 * | 0.020 * | 0.17 | |
| Normal vs. Stroke-Dementia | 0.006 * | 0.024 * | * 0.000 | 0.000 * | 0.001 * | 0.002 * | 0.000 * | 0.004 * | 0.020 * | |
| Stroke-MCI vs. | 0.232 | 0.395 | 0.054 | 0.011 * | 0.071 | 0.09 | 0.315 | 0.154 | 0.513 | |

| | Table 2- The r | esults of j | post hoc n | nultiple o | comparis | on (SpecI | DE). | |
|------------|----------------|--------------------|------------|------------|----------|-----------|-------|-----------|
| Comparison | Fp1 | F7 | T3 | T5 | Fp2 | F8 | T4 | T6 |
| | 0.017 * | 0.050 * | 0.020 * | 0.004 | 0.224 | 0.150 | 0.704 | 0.100 |

| Normal vs. Stroke-MCI | 0.017 * | 0.058 * | 0.020 * | 0.084 | 0.334 | 0.152 | 0.784 | 0.102 | 0.368 | * 0.000 |
|----------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Normal vs. Stroke-Dementia | 0.000 * | 0.000 * | 0.000 * | 0.000 * | 0.000 * | 0.000 * | 0.000 * | 0.000 * | 0.003 * | 0.000 * |
| Stroke-MCI vs. | 0.023 * | 0.118 | 0.079 | 0.000 * | 0.006 * | 0.008 * | 0.000 * | 0.011 * | 0.080 | 0.148 |
| | P3 | 01 | F4 | C4 | P4 | O2 | Fz | Cz | Pz | |
| Normal vs. Stroke-MCI | 0.014 * | 0.004 * | 0.337 | 0.017 * | 0.028 * | 0.148 | 0.083 | 0.045 * | 0.112 | |
| Normal vs. Stroke-Dementia | 0.000 * | 0.000 * | 0.007 * | 0.000 * | 0.000 * | 0.000 * | 0.000 * | 0.003 * | 0.000 * | |
| Stroke-MCI vs. | 0.000 * | 0.002 * | 0.159 | 0.019 * | 0.011 * | 0.031 * | 0.021 * | 0.436 | 0.071 | |
| | | | | | | | | | | |

A similar study titled Understanding brain function in vascular cognitive impairment and dementia with EEG and MEG was conducted by Lucía Torres-Simon et al, (2022) and they realized that MEG and EEG quantitative analysis are precise, non-invasive tools with high temporal resolution that reflect changes in bioelectrical activity of the brain. This provides investigators the opportunity to study brain function and network disruption due to changes in synaptic potentials produced by vascular alterations before structural changes and/ or cognitive decline are evidenced, as well as the ability to serve as a prognostic tool for disease severity.

In addition, it may allow for us the ability to correctly classify VCI and its subtypes. Despite the current limitations, patterns have already emerged, demonstrating the utility of functional analysis to complement and augment structural imaging studies. Further work is needed [23]. Hadiyoso et al, (2022) investigated that EEG-Based Spectral Dynamic in Characterization of Post Stroke Patients with Cognitive Impairment for Early Detection of Vascular Dementia This study shows that spectral complexity analysis can discriminate between normal and post stroke patients with cognitive impairment. For further studies, it is necessary to simulate performance validation so that the proposed approach can be used in the early detection of post stroke dementia and monitoring the development of dementia [24]. The demographic data in this study are presented in Table 3.

| Table 3- Demographic data of the control group and patient | | | | | | | | | | | |
|--|------------------|------------------------------|---------------------|--|--|--|--|--|--|--|--|
| Index | Normal | Poststroke no dementia (MCI) | Poststroke dementia | | | | | | | | |
| Number of samples | 16 | 15 | 11 | | | | | | | | |
| Sex (M/F) | 8/8 | 7/8 | 6/5 | | | | | | | | |
| Age (std. dev.) | 57.18 ± 4.16 | 59.82 ± 6.41 | 60 ± 5.34 | | | | | | | | |
| Education (year) | 13.45 ± 3.44 | 12.18 ± 4.11 | 14 ± 3.89 | | | | | | | | |
| Onset stroke (month) | — | 11.55 ± 7.22 | 17.75 ± 9.55 | | | | | | | | |
| MoCA-INA | 26.5 ± 0.67 | 22.33 ± 2.10 | 12.38±4.37 | | | | | | | | |

Table 4- Significant test results of multiple comparisons

| Communican | Significant (95% confidence level) | | | | | | | | | | | | | | | | | | |
|-----------------------------------|------------------------------------|---------|---------|--------|--------|---------|------------|---------|---------|---------|--------|--------|---------|---------|---------|--------|---------|--------|--------|
| Comparison | Fp1 | F7 | T3 | T5 | Fp2 | F8 | T4 | T6 | F3 | C3 | P3 | 01 | F4 | C4 | P4 | O2 | Fz | Cz | Pz |
| Normal vs. stroke-MCI | 0.141 | 0.047* | 0.207 | 0.108 | 0.247 | 0.071 | 0.144 | 0.030* | 0.079 | 0.173 | 0.207 | 0.262 | 0.042* | 0.19 | 0.148 | 0.213 | 0.011* | 0.020* | 0.17 |
| Normal vs. stroke-dementia | 0.002* | ≤0.001* | ≤0.001* | 0.003* | 0.002* | ≤0,001* | ≤0 001* | ≤0.001* | ≤0.001* | ≤0.001* | 0.006* | 0.024* | ≤0.001* | ≤0.001* | ≤0.001* | 0.002* | ≤0.001* | 0.004* | 0.020* |
| Stroke-MCI vs. stroke-dementia | 0.174 | 0.020* | 0.026* | 0.251 | 0.097 | 0.062 | 0.019* | 0.11 | 0.020* | 0.044* | 0.232 | 0.395 | 0.054 | 0.011* | 0.071 | 0.09 | 0.315 | 0.154 | 0.513 |
| * p value <0.05. | | | | | | | | | | | | | | | | | | | |

A research on Resting state EEG biomarkers of cognitive decline associated with Alzheimer's disease and mild cognitive impairment was done by Amir H. Meghdadi et al, (2021). And they proposed a novel method to quantify these small differences between Theta and Alpha bands' power using empirically derived distributions of spectral power across the time domain as opposed to averaging power across time. We defined Power Distribution Distance Measure (PDDM) as a distance measure between probability distribution functions (pdf) of Theta and Alpha power. Compared to average TAR, using PDDF enhanced the statistical significance, the effect size, and the spatial distribution of significant effects in the MCI group. We designed classifiers for differentiating individual MCI and AD participants from age-matched controls. The classification performance measured by the area under ROC curve after cross-validation were AUC = 0.85 and AUC = 0.6, for AD and MCI classifiers, respectively. Posterior probability of AD, TAR, and the proposed PDDM measure were all significantly correlated with MMSE score and neuropsychological tests in the AD group [25]. Figure 2 shows the proposed difference function PDDF (Theta, Alpha) (u) averaged across all participant groups plotted for channel T6 as an example. The graph illustrates the finding that, on average, healthy controls have higher Alpha power than Theta power resulting in a PDDF function with negative values (situated under the zero baseline) and a negative slope. And Figure3 shows scatter plots and Pearson's correlation and Scatterplots showing correlations between MMSE score and (a) probability of AD in AD classifier, (b) TAR at temporal areas, (c) PDDM95 at temporal areas, plotted for all AD participants. PDDM95 has the highest correlation with MMSE. Coefficients between the EEG measures and MMSE scores for participants in the AD group.







4- Conclusion

In the review of each of the previous researches regarding EEG Analysis in Alzheimer's disease, Vascular Dementia and Mild Cognitive Impairment. the results showed:

- EEG (results as defined by a dementia index (DI) ranging from 0 to 100 revealed that the area under the curve was 0.78 (95% CI 0.70–0.85), is useful diagnostic methods for differentiating between Alzheimer's disease, vascular dementia, and mild cognitive impairment.
- EEG (with a high accuracy of 91%) can reveal changes in brain activity, such as theta waves, focal abnormalities, and reduced alpha waves, that are indicative of Alzheimer's disease.
- Mild cognitive impairment, which may be a prodromal stage of Alzheimer's disease, can have normal or minimal EEG changes
- EEG (achieved over 70%) can help in early diagnosis, monitoring, and treatment of dementia, especially Alzheimer's disease, which is the most common and devastating form of dementia.

It is proposed to review the application of EEG analysis for the diagnosis of dementia, focusing on the main EEG features that distinguish AD, VaD, and MCI from normal aging and from each other. You can also compare EEG with other neuroimaging methods, such as singlephoton emission computed tomography (SPECT), in terms of sensitivity, specificity, availability, and cost.

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