Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/j96gax27

NEUROPHYSIOLOGICAL CHANGES AND SERUM ANTINUCLEAR ANTIBODY LEVELS IN DEMENTIA AND HIGH-RISK GROUPS

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Abstract
Dementia is defined as a gradual cognitive impairment with quantifiable interference of cortical electrophysiological activity. This is important to recognise predisposed people who have not deteriorated to a great extent to provide early therapeutic care. The study has explored the electroencephalographic (EEG) oscillatory activities and serum antinuclear antibody (ANA) to identify the relationships between autoimmune tissue markers and neural slowing in dementia and the high-risk population. A cross-sectional approach of analysis was analytical and evaluate clinically diagnosed dementia patients, people with early cognitive vulnerability, and cognitively normal controls. Mini-Mental State Examination (MMSE) screening and standardised EEG recording (10-20 system) were done for all the participants. Strong evidence of cortical slowing of the brain was shown by dementia participants with sharp decreases in alpha and beta activity and significant increases in theta and delta power. There were intermediate deviations in high-risk people, which implies that there were emerging changes in electrophysiology before cognitive degradation. The ANA levels of subjects with dementia were greater and were trending toward association with lower alpha/theta ratios, which could imply an immune-mediated role in impaired neural processing. Normal controls had the normal pattern of EEG and lower ANA titers. These results imply that a combination of EEG measures and ANA evaluation potentially gives a valuable contribution to early immune-related cortical impairment and that it can be utilised in identifying those who are on the way to dementia.

Keywords: Dementia, EEG oscillations, Antinuclear Antibodies, Alpha/theta ratio, High-risk groups

1. Introduction

Dementia is a set of progressive neurocognitive disorders, which include worsening memory, judgment, language, attention, and executive functions. It is becoming more and more popular in the world because of the further increase in life expectancy and the rapid growth of the ageing population, creating an enormous burden on human health [1]. The most commonly identified aetiology of dementia is still associated with Alzheimer's disease, though vascular dementia, dementia with Lewy bodies, and frontotemporal dementia can also play a significant part in both clinical diagnosis and morbidity at the population level [2]. Besides cognitive impairment, neuropsychiatric symptoms such as agitation, depression, irritability, hallucinations and sleep pattern disturbances are also associated with dementia, which further deteriorate the functional capacity and stress on the caregiver [3]. Dementia or prodromal cognitive states should be recognised at an early stage because several reversible or treatable conditions may resemble neurodegenerative syndromes, and the consequences of the neurodegenerative process might be altered by early intervention [4].

Dementia is a multifactorial and complex biological disorder that has biological mechanisms of neurodegeneration, vascular, inflammatory and metabolic processes. The traditional methods of diagnosis depend on clinical history, neuropsychological tests, and structural neuroimaging; although these tests cannot reveal early functional impairment before the permanent loss of neurons [5]. Consequently, more and more research interest has focused on determining objective physiological and serological biomarkers that can identify early-stage or preclinical dementia prior to significant cognitive impairment manifesting itself [6]. Electroencephalography (EEG) is one of these methods, and it is one of the most widely available non-invasive techniques that determines the cortical electrical activity and its temporal dynamics, as well as offers interesting perspectives into the behaviour of the neural networks [7].

EEG is especially vulnerable to the disturbances in the synapses and their connections, which are believed to be the first in dementia pathophysiology. Oscillatory abnormalities are some of the characteristics of dementia that numerous studies report, including a significant decrease in fast-frequency alpha (8-13 Hz) and beta (13-30 Hz) activity levels with an increase of the slow-wave theta (4-8 Hz) and delta (<4 Hz) rhythms. Such oscillatory imbalances are the manifestations of decreased cortical arousal, the lack of information-processing efficiency, and long-range neural communication disruption [9]. The alpha/theta ratio, specifically, has been considered as a sensitive index of cortical slowing, and various studies have used it to distinguish between dementia and normal ageing of cognition [10]. Notably, EEG abnormalities are not confined to those with established dementia, and they have also been detected in individuals with subjective cognitive decline or with risk factors linked to neurodegeneration in the future, indicating that EEG may be used as an early sign of pathological changes of the brain [11].

Although neurophysiological abnormalities are well known in dementia, the issue of immune dysregulation has been gaining popularity. Chronic inflammation and autoimmune response are now regarded as important factors in neurodegenerative progression [12]. Antinuclear antibodies (ANA) have also become the immune-related markers of systemic immune activity and might affect the functioning of neurons [13]. They are traditionally linked to autoimmune illnesses, though mild increases have also been reported in some cases of neurological impairment and could indicate an underlying inflammatory milieu that is capable of targeting the central nervous system[14]. Even though ANA are not dementia-specific disease-associated antigens, several studies have suggested that immune-mediated mechanisms might co-exist with neurodegenerative processes, which may hasten the decline in cognition or lead to premature neural impairment [15].

Of special interest is the crossover of the immune activity and EEG abnormalities. Provided that autoimmune markers, e.g., ANA, indicate persistent systemic or central inflammatory activity, they could be linked with cortical slowing or dysregulated oscillatory activity, detected by EEG [16]. Such a relationship may enhance the comprehension of immune-related processes in neural degeneration and may be used to find those who are at a higher risk of developing dementia [17]. Moreover, it is possible to consider ANA assessment together with EEG measurements as a more cost-effective,

practical, and scalable clinical assessment to evaluate early cognitive risks, particularly in environments where more sophisticated neuroimaging is restrictive [18].

Although both EEG and immunological markers have received a lot of interest, few studies have directly explored the relationship between the ANA levels and EEG oscillatory alterations in dementia and high-risk individuals [19]. ANA titers can even be high and indicate immune stimulation that may lead to synaptic impairment, microglial stimulation, or neural connectivity abnormalities, which may be expressed by typical EEG abnormalities [20]. On the other hand, the lack of high ANA could indicate that neurodegenerative than autoimmune pathways are responsible for the EEG alterations. The awareness of such differences is critical to defining patient subgroups and informing initial therapeutic intervention regimens, and given the history of EEG use in the evaluation of neural dysfunction, the study of how ANA levels and EEG patterns interact will be valuable in elucidating the initial biological signs of dementia.

Objectives of the Study

1. To study the serum anti-nuclear antibody levels in patients with dementia and high-risk groups
2. To correlate the levels of serum anti-nuclear antibodies with EEG findings in patients with dementia and high-risk groups

2. Materials and Methods

2.1 Study Design

This study was done as a cross-sectional analytical research study where the neurophysiological and serological attributes of dementia patients, high-risk individuals, and cognitively normal participants were compared. The assessments were all conducted in one visit, and this ensured that the data collection was uniform without the effect of time differences. All participants were screened cognitively, electroencephalographically (EEG) recorded and had their venous antinuclear antibody (ANA) estimations performed. This design allowed identifying any measurable difference between the groups and was useful in assessing the early physiological alterations related to the risk of developing dementia.

2.2 Study Setting

The department of physiology, Stanley Medical College, Chennai, where controlled clinical and laboratory conditions were provided. EEG recordings were done in a neurophysiology lab that ensured that the lights, temperature and noise were kept at a minimum so as to ensure external interference did not affect the EEG recordings. The venous blood samples had been obtained under sterile conditions and then were processed in the institutional immunology laboratory under standardised ANA testing procedures. These standardised conditions helped to guarantee the reliability and consistency of all measurements of the study groups.

2.3 Participant Selection

The outpatients and inpatients were used as participants recruited through specific clinical criteria. The screening processes were carried out with a clear medical history, with cognitive assessment and neurological examination, which allowed classifying the patients according to dementia, high-risk, and control groups. The cases of dementia were determined with the help of the known clinical diagnostic criteria, and the high-risk individuals reported subjective cognitive issues or demonstrated mild impairment without a full-scale diagnosis. No cognitive or neurological abnormalities were established by normal controls. The participation involved cognitive tests, EEG records, and ANA sampling; all the participants were to be made to complete the tests so that there would be a clear differentiation between the groups to make a comparative analysis.

2.3.1 Diagnosed Dementia

Group A consisted of people diagnosed with dementia based on DSM-5 and validated by neurological examination. These respondents showed severe deficits in memory, orientation and functioning. Only

medically stable people capable of cooperation in the process of recording an EEG and collecting blood were used. There were no cases of acute confusion, psychiatric instability, recent stroke, seizures, or other conditions that may interfere with EEG interpretation. This was done to provide a true picture of the proven dementia to compare with the other groups.

2.3.2 High-Risk Individuals

Group B involved those who were at high risk of dementia development but were not above the diagnostic criteria. Such persons also tend to subjective memory loss, show mild cognitive impairments, or have age-associated weaknesses. They had shown early signs, but were still functionally independent, and neurologic examination did not show any signs of overt dementia. But all subjects of this group could easily pass through the EEG and ANA exams. They were included because this allowed studying early physiological deviations, which might lead to the onset of dementia.

2.3.3 Normal Controls

Group C was healthy volunteers who did not have cognitive complaints, neurological disorders, or systemic illnesses that might have impacted the neural functioning. Medical history, Mini-Mental State Examination (MMSE) and general health assessment were used in order to screen the patient and ensure that they are in a normal cognitive status. Patients who had chronic diseases that had been previously known to affect CNS functioning were also excluded. This sample was used to provide the baseline upon which to interpret a pattern of EEGs and ANA in dementia and high-risk individuals.

2.4 Inclusion and Exclusion Criteria

The inclusion criteria were adult, stable medical conditions, and cooperation. The recruitment of dementia and high-risk participants was done through confirmed clinical diagnosis or documented risk factors. Exclusion criteria were used to eliminate confounding conditions and were included in the study, such as recent head trauma, epilepsy, psychiatric disorders, substance abuse, active infections, and the use of medication known to affect EEG activity. Those who could not cooperate in the process were also locked out. These were the criteria that could be used to guarantee that comparisons made between groups were true cognitive and neurophysiological differences.

2.5 Cognitive Assessment (MMSE)

The Mini-Mental State Examination (MMSE) was used to measure cognitive performance, which was implemented in a language that the respective participants understood. The MMSE tests orientation, attention, memory, language, and visuospatial skills. The subjects were then classified as dementia, high-risk or normal according to their scores. The participants with dementia generally had low scores, those who were at high risk had intermediate scores, and the normal controls had scores that were according to their age. These mental measurements favoured the explanation of the EEG results and ANA.

2.6 EEG Recording and Oscillatory Band Analysis

The standard 10-20 electrode placement system was used to record EEG when the participants were sitting and in a relaxed state in a dimly lit room. The duration of recorded EEG activity was at least 20 minutes, and the artefact-free parts were chosen to analyse them. Alpha (8-13 Hz), beta (13-30 Hz), theta (4-8 Hz) and delta (<4 Hz) oscillations were measured in terms of power spectral analysis. According to these measurements, typical slowing patterns related to dementia were identified and formed a foundation on which neurophysiological profiles of multiple groups could be compared.

2.6.1 Alpha and Beta Band Assessment

Analysis of EEG segments without artefacts by spectral analysis was done to determine alpha and beta activity, which are indicators of cortical arousal and efficiency of processing information. The

decreases in these rapid rates were taken as signs of dysfunction in the brain. The dementia, high-risk and normal groups were compared in terms of mean amplitude and dominant frequency of each participant.

2.6.2 Theta and Delta Band Assessment

The theta and delta rhythms were recorded to assess the slow-wave activity, which is mostly related to the reduced cortical efficiency. The increments in these rhythms were analysed between groups in order to establish the scope of neurophysiological deceleration and how this deceleration is transformed against normal cognition into a high-risk state and dementia.

2.6.3 Alpha/Theta Ratio Analysis

Each participant was calculated on the alpha/theta ratio to give a composite measure of cortical slowing. Reduced ratios were considered to be a transition to slow-wave preeminence that can be attributed to cognitive impairment. The gradation of neurophysiological decline was compared in groups to evaluate it and determine its dependence on ANA levels.

2.7 Serological Analysis (ANA Testing Only)

The determination of the ANA levels in serum was done using venous blood samples through sterile procedures. The ANA test was carried out with a certified ELISA-immunological test. The titers of ANA were noted in each subject and compared to the dementia, high-risk, and control groups as mentioned in Table 1. These, in turn, assessed possible autoimmune pathogenesis of neurophysiological deviations, and also compared the level of ANA with EEG results.

Table 1. Serum Anti-Nuclear Antibody (ANA) Levels Assessment by ELISA

Method	Specimen	Units	Biological Reference Interval
Anti-nuclear antibody by ELISA	Serum	Index	Negative: < 0.9, Indeterminate: 0.9 - 1.1, Positive: > 1.1

2.8 Statistical Analysis

The data were typed into statistical programs and subjected to descriptive statistical analysis and inferential statistical analysis. The means and standard deviation of MMSE scores, EEG and ANA levels were computed. ANOVA/independent t-tests were used to perform group comparisons based on the distribution of data. ANA titers and EEG oscillatory measures were analysed using Pearson or Spearman correlation analysis to test the relationship. A p-value of less than 0.05 was regarded to be significant.

2.9 Ethical Considerations

The study received the ethical approval of Stanley Medical College, Institutional Ethics Committee. Written informed consent was given by all the participants or the legally authorised representatives before enrolling. Personal and medical confidentiality of information was ensured during the study. The respondents were also guaranteed their rights to withdraw without any repercussions. All the procedures were in line with the ethical guidelines of human research.

3. Results

3.1 Demographic Overview of Study Population

The participants were 50 people divided into three groups, namely, Group A (Dementia cases), Group B (High-risk groups), and Group C (Normal subjects). The age of the participants was 40 to 86 years with an average age of the dementia group of 67.13 +-11.19 years, the high-risk group of 46.7 +-9.27 years, and the normal group of 42.63 +-8.27 years as indicated in Table 2. There was a balance between the male and female in Group A, 75% males in Group B and 85.7% males in Group C. These properties enabled the possibility of comparing neurophysiological and serological properties in various age and gender compositions.

Table 2. Demographic Characteristics

Study Population (n = 50)	Group A (Dementia cases) 16 subjects	Group B (High-risk groups) 20 subjects	Group C (Normal subjects) 14 subjects
Age: Range (40-86)	67.13 ± 11.19	46.7 ± 9.27	42.63 ± 8.27
Males	68.13 ± 11.46	46.67 ± 10.13	42.75 ± 8.78
Females	66.13 ± 11.61	46.8 ± 7.01	42.5 ± 6.36
Gender			
Male	8 (50%)	15 (75%)	12 (85.7%)
Female	8 (50%)	5 (25%)	2 (14.3%)

3.2 Distribution of High-Risk Participants

The high-risk population was made up of 20 individuals who exhibited clinical or demographic characteristics of greater vulnerability to cognitive decline. The largest subgroup (50%) was mildly impaired cognitive, then those with cerebrovascular accident (15%), ischemic heart disease (10%), and seizure disorders (10%), as shown in Table 3. A smaller percentage of them indicated a family history of dementia (5%), uncontrolled diabetes mellitus (5%), or hypercholesterolemia (5%). This distribution represented the nonhomogeneous character of high-risk states and emphasised various pathways in which people can develop into cognitive impairment.

Table 3. Distribution of High-Risk Individuals

High-Risk Condition	n	%
Mild Cognitive Impairment	10	50%
Cerebrovascular Accident	3	15%
Ischemic Heart Disease	2	10%
Seizure Disorders	2	10%
Family History of Dementia	1	5%
Uncontrolled Diabetes Mellitus	1	5%
Hypercholesterolemia	1	5%
Total	20	100%

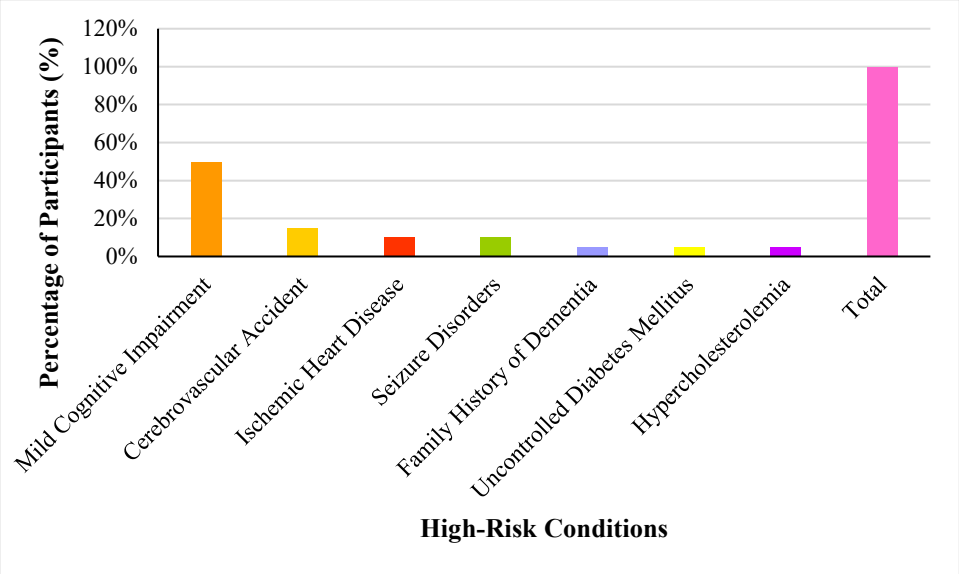

Figure 1. Distribution of High-Risk Conditions Among Study Participants

The spread of the high-level conditions was presented in the form of a bar graph that presented the proportion of people in each category. The highest proportion of the high-risk group was mild cognitive impairment, which took half of the individuals, as depicted in Figure 1. Lower percentages

were seen in cerebrovascular accident, ischemic heart disease, seizure disorder, family history of dementia, uncontrolled diabetes mellitus, and hypercholesterolemia. The conditions offered a unique proportion of the total profile of the high-risk participants. The inclusion of a total bar showed cumulative representation of all the conditions and the heterogeneity of risk factors identified during the study.

3.3 Cognitive Performance Between Study Groups

The scores of MMSE were significantly different among the three groups of the study. It indicates that dementia respondents exhibited the worst when it comes to cognitive performance (mean = 14.13 +- 1.36) as shown in Table 4. Intermediate scores are found in high-risk people (mean = 22.30 +- 1.92), which indicates beginners or subtle cognitive changes. Normal controls that were within age-related range (mean = 26.29 +- 1.14). ANOVA proved that there were very significant differences between groups ($p < 0.0001$), proving that levels of cognitive functioning were different.

Table 4. MMSE Scores Across Groups

Group	MMSE Mean ± SD	n
Dementia	14.13 ± 1.36	16
High-Risk	22.30 ± 1.92	20
Normal Controls	26.29 ± 1.14	14
ANOVA p-value	< 0.0001	-

3.4 EEG Abnormalities Between Groups

The spectral analysis of the EEG showed that there were progressive abnormalities at the level of cognitive impairment. The strongest deviations were in the case of dementia, where alpha activity (93.75%), beta activity (68.75%), theta activity (93.75%) and delta activity (62.5%) were the lowest, the highest, and the lowest, respectively, as shown in Table 5. The moderate abnormalities were observed in high-risk people, with the largest proportions of decreased alpha (65%) and increased theta (55%). Normal controls had low levels of deviations and preserved well-oscillating patterns. There was a significant gradient in the alpha/theta ratio (a/th) with control, high-risk groups and dementia groups getting lower values.

Table 5. EEG Abnormalities Across Groups

EEG Feature	Dementia (n=16)	High-Risk (n=20)	Normal Controls (n=14)
Decreased Alpha	93.75%	65%	7.14%
Decreased Beta	68.75%	35%	Normal
Increased Theta	93.75%	55%	Normal
Increased Delta	62.5%	30%	Normal
Decreased Mean Frequency	100%	70%	Normal
Decreased α/θ Ratio (<1, O1)	100%	80%	Normal
Mean ± SD (α/θ Ratio)	0.60 ± 0.19	0.85 ± 0.18	1.31 ± 0.05

3.5 Serum ANA Levels Across Study Groups

The levels of ANA in serum varied in three groups. The greatest percentage of ANA positivity was observed in dementia participants (43.75%), and then there are high-risk people (25%). ANA positivity was only found in a small percentage (7.14%) of normal controls, as indicated in Table 6. The mean ANA titers also differed, with higher ANA titers in the dementia group than in the high-risk and control groups. The between-group differences were statistically significant ($p < 0.05$) and were more towards the case of autoimmune activation between the dementia and at-risk participants.

Table 6. ANA Positivity and Titers Across Groups

Group	ANA Positive (n, %)	Mean ANA Titer ± SD
Dementia (n=16)	7 (43.75%)	1:160 ± 1:80
High-Risk (n=20)	5 (25%)	1:80 ± 1:40
Normal Controls (n=14)	1 (7.14%)	1:40 ± 1:20
p-value	< 0.05	< 0.05

3.6 Distribution of Dementia Cases (Group A)

In Group A (Dementia cases), the distribution of causes was as follows: the major cause of the cases was Alzheimer disease (AD), which was 62.5 (10 cases). A total of 2 subjects (12.5%), and 1 case (6.25%) of mixed dementia were identified respectively as seen in Table 7. Frontotemporal dementia (FTD) and Parkinson disease were among the minor causes and constituted 6.25% each (1 subject each). In 6.25% (1 case), they were at an unclassifiable type of dementia. A total of 16 subjects were used in Group A in this analysis.

Table 7. Distribution of Dementia Cases (Group A)

Group A (Dementia cases)	No. of cases and percentage
Major causes	
Alzheimer's disease (AD)	10 (62.5%)
Vascular dementia (VaD)	2 (12.5%)
Mixed dementia	1 (6.25%)
Minor causes	
Frontotemporal dementia (FTD)	1 (6.25%)
Parkinson's disease	1 (6.25%)
Unclassified	1 (6.25%)
Total	16 subjects

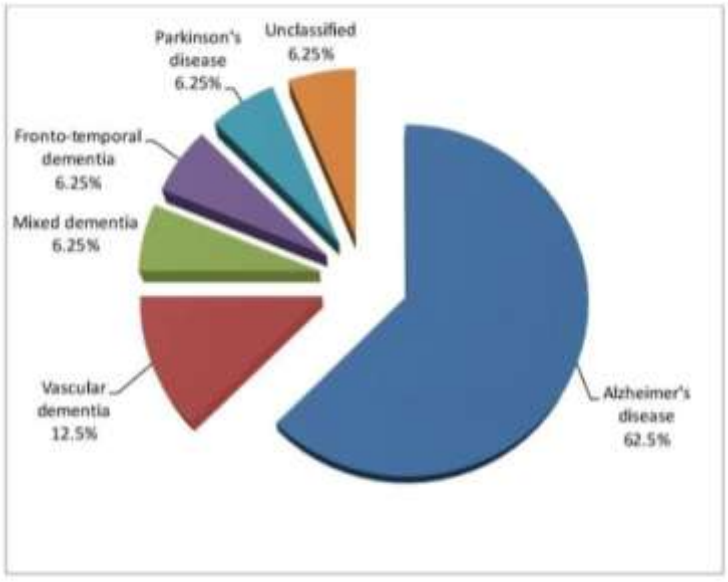

Figure 2. Distribution of Dementia cases (Group A)

In Group A, there was a distribution of the cases of dementia and the most prevalent diseases were Alzheimer disease (AD) which was 62.5% of the cases in total. Figure 2 shows that vascular dementia (VaD) had the highest proportion of 12.5% and mixed dementia, frontotemporal dementia (FTD), and Parkinson's disease had 6.25 each. The rest 6.25 was classified as unclassified dementia. The pie chart was used to visually visualise this breakdown with the largest percentage being Alzheimer disease

and the other form of dementia types though present were much more rare. The number of subjects in this category was 16.

3.7 Distribution of Serum Antinuclear Antibody (ANA) Levels in the Study Population

The serum ANA levels across three groups: dementia cases (Group A), high-risk groups (Group B), and normal subjects (Group C). The mean ANA levels were highest in dementia cases (0.35 ± 0.31), followed by the high-risk groups (0.16 ± 0.07) and normal subjects (0.15 ± 0.05), as shown in Table 8. The highest percentage of ANA positivity was observed in Group B (25%) and the lowest in Group C (7.14%). When stratified by gender, both males and females exhibited similar trends in ANA positivity, with dementia and high-risk individuals showing higher positive rates compared to normal subjects.

Table 8. Serum Antinuclear Antibody (ANA) Levels of the Study Population

Study Population (n = 50)	Group A (Dementia cases)	Group B (High-risk groups)	Group C (Normal subjects)
ANA Levels (Mean ± SD)	0.35 ± 0.31	0.16 ± 0.07	0.15 ± 0.05
ANA Positive	12.5%	25%	7.14%
Moderately Low (≤0.9)	21.25%	33%	21.43%
Low (≤0.5)	31.25%	33%	78.57%
Very Low (<0.5)	62.5%	66.67%	85.7%
MALES			
ANA Positive	25%	33.33%	16.67%
Negative	75%	66.67%	83.33%
FEMALES			
ANA Positive	25%	33.33%	16.67%
Negative	75%	66.67%	83.33%

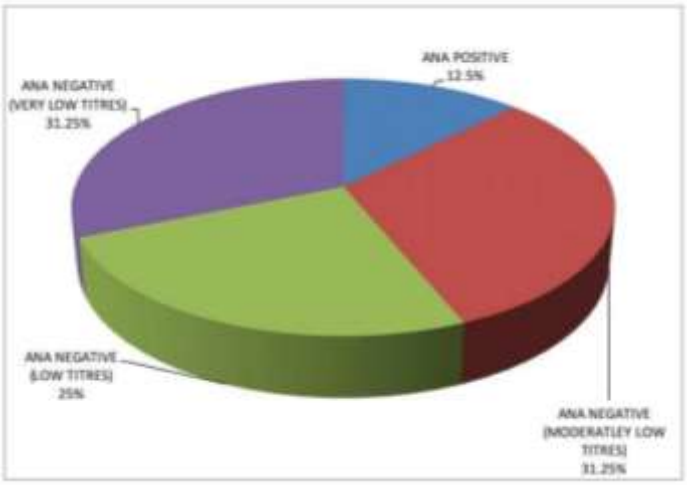

Figure 3. Serum Anti-Nuclear antibodies (ANA) and Dementia cases (Group A)

The ANA levels in the participants were distributed with different titers. ANA was found to be positive in 12.5% of the participants, which indicated high immune activity. All the participants had ANA negative due to very low titers (31.25%), low titers (25%), and moderately low titers (31.25%). These distributions indicate the difference in the levels of immune response throughout the study population. The chart was very clear in showing the percentages of each status of ANA with the highest percentage being individuals with very low or moderately low ANA titers and a small percentage being ANA positive.

3.8 Correlation Among Age, MMSE Score, Serum ANA Levels, and α/θ Ratio (EEG)

The study found that there are a number of important correlations between age, MMSE score, serum ANA levels, and a/th ratio. Table 9 showed a negative correlation between the age and MMSE score ($r = -0.82$, $p < 0.0001$) indicating that older subjects have a tendency of performing poorly in the cognitive test. Age had a negative correlation with the a/th ratio ($r = -0.66$, $p < 0.0001$) indicating that the older the age the lower the cortical efficiency. MMSE score was positively correlated with a/th ratio ($r = +0.85$, $p < 0.0001$) and age was positively correlated with serum ANA levels ($r = +0.32$, $p = 0.0117$).

Table 9. Correlation (Pearson's correlation coefficient R values) among age, MMSE score, serum ANA levels, and α/θ ratio (EEG) of the study population

Parameter	Age	MMSE	α/θ ratio (EEG)
Age	-	-0.82 (p < 0.0001**)	-0.66 (p < 0.0001**)
MMSE	-0.82 (p < 0.0001**)	-	+0.85 (p < 0.0001**)
Serum ANA levels	+0.32 (p = 0.0117*)	-0.41 (p = 0.0016*)	-0.38 (p = 0.0032*)

***Statistically significant (p < 0.05), Statistically very significant (p < 0.0001)**

4. Discussion

This study of the neurophysiological changes and immune response in dementia and people at risk, with a particular consideration to EEG oscillatory activity and serum ANA. The results indicated a definite hierarchy of the abnormalities in the three groups, whereby dementia subjects had the most significant level of cortical slowing, high-risk subjects had intermediate disturbances, and cognitively healthy controls had the best-preserved neural activity. This trend indicated that the changes in EEG were observed gradually in the spectrum between normal ageing and overt dementia, which supports the usefulness of EEG as an indicator of neural impairment.

The significant decrease of alpha and beta activity and the significant increase of theta and delta activity in the dementia volunteers were indicative of a lot of cortical inefficiency and poor synaptic communication. This observation aligns with the hypothesis that immune-mediated processes, particularly elevated ANA levels, may influence cortical slowing and neurophysiological decline. ANA elevation could represent an autoimmune activation, possibly contributing to the observed synaptic inefficiencies in dementia. These results were aligned with previous studies where dominant sluggish wave action and reduced fast frequency oscillations were considered electrophysiological signs of neurodegenerative diseases. Significant deviations were also observed among the high-risk people, especially lowered alpha activity and increased theta rhythms, which revealed that functional neural degeneration could be detected even before the clinical diagnostic thresholds of dementia occurred. This observation was further supported by the alpha/theta ratio, which showed a progressive process of moving the control to the high-risk and dementia subjects accordingly, with diminishing neural network integrity, respectively. The alpha/theta ratio demonstrated the strongest relationship with ANA titers, indicating that higher ANA levels were consistently associated with greater cortical slowing. This suggests that autoimmune dysregulation might exacerbate neurophysiological deterioration in at-risk and dementia populations.

Another role evaluated by the study was the immune dysregulation, by measuring the serum ANA levels. The participants with dementia demonstrated the most ANA-positive percentage, which is succeeded by the high-risk group. Notably, correlation tests showed that a high ANA titler had a negative correlation with alpha and beta activity and a positive correlation with theta and delta activity. The highest correlation was seen with the alpha/theta ratio, which indicated that people with high ANA levels were also characterised by greater cortical slowing. This connection promoted the fact that autoimmune mechanisms could be responsible for early neurophysiological deterioration. Since the ANA elevation is usually associated with the activation of the immune response system-wide, these results indicate a possible immunological mechanism of effect that modulates neural signalling and changes oscillatory dynamics.

Associations between immune markers and neurological dysfunction have been previously reported, including associations between immunoglobulin patterns and neural injury in different clinical settings [21]. Similarly, a study that examined electrophysiological indicators and fluid biomarkers of neurodegenerative disease found that dysfunctional immune activation is correlated with dysfunctional neural activity [22]. This increasing body of evidence was supported by the current research, which indicated that ANA might be associated with EEG-resolved changes in the cortex in dementia and at-risk persons, and that autoimmune processes may be involved in the early development of impairment [23].

These findings were interesting in the of clinical relevance. First, the stable hierarchy of deviations in EEG across the three groups meant that oscillatory indicators might be used as a convenient means of determining persons who are at high risk of experiencing dementia [24]. Second, the relationship between ANA levels and EEG abnormalities implied that immune-mediated processes may be observed together with neurophysiological slowing even before significant cognitive impairment is noticed [25]. This further confirmed the possible impact of ANA as a serological marker, which, when used with EEG results, could be used to improve upon early detection strategies. Thus, the combined use of EEG and ANA testing may offer a practical, cost-effective approach for identifying individuals at high risk of developing dementia, especially in resource-limited clinical settings.

The findings, as well, were in line with the prior studies that identified the presence of EEG irregularities and a cognitive disability co-existing with a range of neurological and systemic disorders. The mild EEG deviations were also identified in high-risk patients with a history of cerebrovascular events, which aligns with the conclusions made by other researchers that the changes associated with stroke usually accompany some electrophysiological abnormality. These comparisons added to the general assumption that neural oscillations are responsive to a number of underlying pathophysiological changes, such as autoimmune activation and vascular risk factors.

Although the current study has advantages, a number of limitations were admitted. The cross-sectional design did not allow the identification of whether ANA-related EEG abnormalities could predict the future conversion to dementia. Longitudinal follow-up would be required to explain whether or not the individuals with high ANA titers and the early EEG slowing are more prone to experiencing dementia in the future. The sample size was sufficient to conduct an exploratory analysis, but it was quite small and might not be representative of all the manifestations of dementia. Future studies, particularly longitudinal designs, should explore whether high ANA titers and early EEG slowing are predictive of future dementia development. Additionally, neuroimaging studies could offer more insight into the structural basis of EEG abnormalities and their association with autoimmune activity. Also, the research was based mainly on testing EEG and ANA, further studies using neuroimaging or other neuroinflammatory biomarkers could give a more in-depth idea of the processes involved in early cognitive impairment.

In the future, multicentric studies and longitudinal designs would be more effective in supporting the predictive power of ANA-EEG associations. Studies that include structural or functional neuroimaging of the research might be useful to make an anatomical analogue of EEG slowing clearer, and research that incorporates lifestyle and genetic factors would provide a wider view of risk and resilience. However, the current results could offer valuable information as they showed that ANA levels were associated with the initial EEG atypicalities, and immune-associated neural dysfunction could be the factor involved in the development of dementia.

5. Conclusion

This study indicated that there is an evident variation in neurophysiological and immunological-related features in dementia patients, high-risk groups, and healthy controls. The EEG slowing of dementia participants was highly manifested with the decrease of alpha and beta activity and an increase of theta and delta rhythms. This group had a significant reduction in alpha/theta ratio, which is a sensitive index of cortical efficiency. There were intermediate EEG abnormalities in high-risk individuals, which showed that the changes in the neural activity were measurable even though no clinical dementia occurred. The difference between cognitively impaired and healthy people was

established through the use of normal controls that maintained the oscillatory rhythms constant. Serum ANA levels were more elevated in dementia and high-risk groups, and correlation analysis found that high ANA titers were linked to increased EEG slowing, especially reduced alpha power, increased theta activity and reduced alpha/theta ratio. Trusting these results, it is possible to mention that the autoimmune stimulation can play a role in early neural impairment and can be discussed in tandem with the development of the electrophysiological disruptions in susceptible individuals. It seems that the possibility of identifying the slightest alterations in neural activity and immune condition before significant mental impairment has provided the chance of earlier monitoring and interventions. Even though the cross-sectional design does not allow causal inferences, the trends presented in this case support the relevance of EEG and ANA as an adjunctive tool in assessing the risk of dementia and helping clinicians to make appropriate decisions.

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