International Journal of A J Institute of Medical Sciences 1 (2012) 98-103

Original Research Article

Correlation between neuropsychological test results and P300 latency in adults above 50 years

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Abstract

There is an increased incidence of cognitive impairment with age. P300 latency reflects speed of neural events underlying perception and discrimination of target stimulus. Delayed latency relates to slowed cognitive function in normal elderly. Mini mental state examination (MMSE) is a widely used screening test for cognitive impairment in older adults. This study was undertaken on 100 neurologically healthy male subjects of >50 years of age to determine cognitive status of subjects above 50yrs of age using mini mental state examination (MMSE), to record auditory P300 latency (ms) and to correlate MMSE scores with P300 latency. The mean age of the study group was 62.58±6.85 years. There were 57 subjects with MMSE score <25 out of which 15 were in the age group of 50-59yrs. Auditory P300 latency (ms) was significantly delayed in subjects with MMSE score <25 [(mean±SD) 321.08±10.31 ms] as compared to subjects with MMSE score ≥25 [309.54±7.16 ms, p=0.000]. There was significant negative correlation between P300 and MMSE (r=-0.3, p=0.05). This study emphasis its utility in detecting early cognitive impairment.

Keywords: Cognition; Event related potential; Healthy adults; Neuropsychological tests

Received 23rd July, 2012; Revised 1st October, 2012; Accepted 20th October, 2012.

1. Introduction

There is an increased incidence of cognitive impairment with age. Increasing age is the greatest risk factor for Alzheimer's disease. Event related potentials have been used as an electrophysiological index of cognitive impairment in recent years.[1] A long latency component of the event related potential (ERP), especially P300, occurs when a subject attends and discriminates stimulus events which differ from one another along some dimension (for example intensity, duration or modality).[2]

P300 is considered to be an endogenous potential as its occurrence links not to the physical attributes of a stimulus but to a person's reaction to the stimulus. P300 has been reported to be associated with cognitive processing, and the temporal lobes including amygdala have been proposed as its possible generator sites. Any factor which modifies the timing of neural mechanisms underlying perception and cognition may lead to changes in the morphology or latency of P300, i.e., delayed latency relates to slowed cognitive function in normal elderly. Cognitively impaired individuals have profound disabilities in performing social and daily life activities because there was a significant association between brain and physical performance. Thus, the P300 which reflects human cognitive processes has been used to examine higher brain function in neurological and neuropsychological disorders.[1] Mini mental state examination (MMSE) is a widely used screening test for cognitive impairment in older adults.[3]

The prevalence of disabling memory loss increases with each decade over the age of 50 years and <5% of all cases of Alzheimer's disease do occur in <60 years of age. The present study has been carried out to correlate neuro-psychological test result with P300 latency in adults more than 50 years of age so that MMSE can be used as a screening tool for early diagnosis of cognitive impairment.[4]

2. Materials and methods

The study group comprised of 100 neurologically normal, generally healthy male adults of age 50 years (mean age 62.58±6.85 years; range 50 to 78 years) from Sri RL Jalappa Hospital and Research and Sri Devaraj Urs Medical College, Kolar, Karnataka, India, December 2009 to August 2010 with no history of neurological or neuropsychological disorders. Informed consent was taken. Ethical clearance was obtained from Institutional Ethical Committee at the aforementioned medical college. First mental state examination (MMSE) score was administered and then P300 potentials were recorded in subjects who were selected.

Table 1: MMSE score in the study group

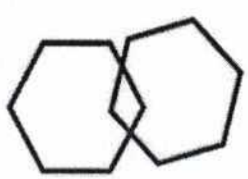
MMSE Score	Age			Total (no. of subjects)
	50-59 years	60-69 years	>70 years	
<25	15	22	20	57
>25	22	19	2	43
Total (no. of subjects)	37	41	22	100

MMSE involves standardized questions that tap a range of cognitive abilities, including orientation for place and time, memory and attention, language skills and visuospatial abilities. It is a practical test to track the change in a patient's cognitive state of a possible 30 points, a score less than 25 suggest possible cognitive impairment and a score less than 20 indicate definite impairment.[5] MMSE is a short questionnaire consisting of six domains of mental function as illustrated in Table 2.[6] These include orientation, registration, attention and calculation, recall, language, and copy. Orientation assesses the patient's orientation to time and place. Testing the patient's ability to record new information is called registration. Attention and calculation tests the patient's ability to perform a series of subtraction tests. Recall tests the patient's ability to remember the three words used in the test of registration. The patient's language abilities are tested by asking the patient to name, follow a verbal order, read, and write a sentence. Lastly, the patient is required to copy two overlapping pentagons. Each correct answer is credited with one score. People with scores of less than 25 are considered to be suffering from various degrees of intellectual impairment according to the cut off points. There is no time limit to complete the questionnaire but normally, the assessment lasts for 10 to 15 minutes. MMSE can be used to assess the mental state of the same patient at regular intervals for comparison or it can be used to compare cognitive capacity between different patients groups.[7]

MMSE is a simple assessment tool that can be used to detect cognitive impairment. It is easy to administer and it provides an objective method to evaluate the cognitive state of a person by observing rather than self-reported functioning.[7]

Table 2: Mini Mental State Examination (MMSE)[6]

Maximum score	Score	
		Orientation
5	--	What is the (year) (season) (date) (day) (month)?
5	--	Where are we: (state) (country) (town or city) (hospital) (floor)?
		Registration
3	--	Name three common objects (e.g., "apple, table, penny"): Take one second to say each. Then ask the patient to repeat all three after you have said them. Give one point for each correct answer. Then repeat them until he or she learns all three. Count trials and record. Trials: ____
5		**Attention and calculation**
	--	Spell "world" backwards. The score is the number of letters in correct order. (D__L__R__O__W__)
3		**Recall**
	--	Ask for the three objects repeated above. Give one point for each correct answer. (Note: recall cannot be tested if all three objects were not remembered during registration)
		Language
2		Name a "pencil" and "watch".
	--	Repeat the following: "No ifs ands or buts"
1	--	Follow a three-stage command
3	--	"Take a paper in your right hand, fold it in half and put it on the floor"
1	--	Close your eyes
1	--	Write a sentence
1	--	Copy the following design



Total --
Score --

Each subject participated in an 'oddball paradigm' using auditory stimulation. The stimulus was a pure tone delivered by aurally through headphones at intensity of 75 dB SPL (sound pressure level) and with the inter-stimulus interval of 1.4 s. Subjects were asked to silently count target tones (75dB SPL, low frequency [20%], high pitch [2000Hz]) presented binaurally, ignoring the standard tones (75dB SPL, high frequency [80%], low pitch [750Hz] non-target tones). The subject had to tell the examiner upon the number of target tones heard upon completion of the task. Tone duration was 100ms with a rise/fall of 10ms. Amplifiers had a band pass of 0.1-50 Hz. The stimulus rate was 0.5Hz. Electroencelographic (EEG) activity was recorded from scalp sites (Cz, Fz and Pz) with Ag/AgCl electrodes placed on the sites using International 10-20 system and were referred to linked earlobes. Linked earlobes were used as a reference and the forehead was used as the ground. Activity was sampled for a period of 500ms. All electrode impedances were below 5 kΩ, and the subjects were reminded to fix their gaze in front on a circled point to minimize ocular movement as much as possible to avoid EEG contamination from eye movements.

MMSE score thus obtained was correlated with P300 wave latency. The data were suitably arranged into tables for discussion under different headings. Descriptive statistical analysis was carried out on this data. Results on continuous measurements are presented as mean $\pm$ standard deviation. Significance was assessed at 5% level of significance. Pearson correlation between MMSE and P300 latency was done. Conclusions were drawn based on the outcome of this statistical analysis.

3. Results

Table 1 depicts MMSE score in different age groups of study population. There were 15 subjects with MMSE score <25 in age group of 50-59 years and; 22 and 20 in the age group of 60-69 years and >70years respectively. Significant negative correlation was found between MMSE score and age in years (r=-0.405, p=0.01) as illustrated in Table 3. Negative correlation (r = -0.42) was found between MMSE score and P300 latency with p value 0.01 (Fig.1).

Table 4 shows prolongation of P300 latency and decrease in MMSE score as age advances. There is more prolongation of P300 latency in subjects with MMSE score <25 as compared to subjects with MMSE score >25.

Table 3: Pearson correlation between MMSE and age

Variables		Age (in years)	MMSE score
MMSE score	Pearson correlation	1.000	-.405*
	Significance (2 tailed)	-	.01
	Number of subjects	100	100
Age (in years)	Pearson correlation	-.405*	1.000
	Significance (2 tailed)	.01	-
	Number of subjects	100	100

* Correlation is significant at the 0.01 level (2-tailed).

Table 4: Mean ±SD of MMSE score and P300 (ms) in study group

MMSE Score	Age					
	50-59 Years		60-69 Years		>70 Years	
	MMSE	P300(ms)	MMSE	P300(ms)	MMSE	P300(ms)
<25	19.93+1.38	314.73+10.4	18.22+1.72	322.23+9.50	17.12+1.17	335.78+9.75
>25	25.45+1.26	308.44+8.75	24.05+2.27	310.13+5.06	23.00+0.11	311.25+2.65

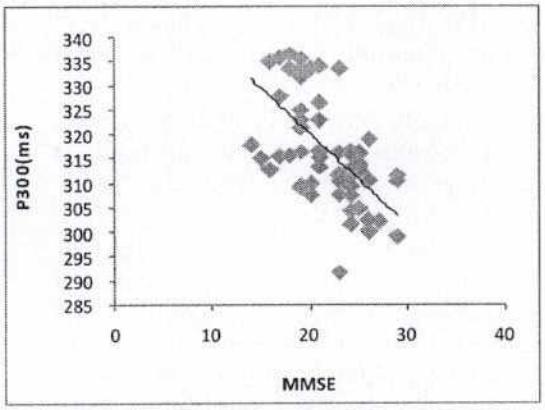


Fig 1: Pearson correlation between P300 latency and MMSE

4. Discussion

Event-related potentials are thought to be neurophysiologic signs of cognitive processes.[1] P300 wave is a positive deflection in the human event-related potential. It is most commonly elicited in an "oddball" paradigm when a subject detects an occasional "target" stimulus.[8] P300 (latency) event related potential is an accurate predictor of memory impairment.[9] Patients with cognitive deficits need more time to process information.[10] Decline in cognitive function is associated with aging.[7] MMSE is a widely used, validated and reliable method of screening for Alzheimer's disease.[11] Our study showed that there was a significant negative correlation between age and MMSE. An extensive four year study on 18,056 participants concluded that age was significantly correlated with MMSE performance (P<0.001). Inverse relationship existed between MMSE and age.[7]

In the present study, from Fig I, it was shown that neuropsychological test result-MMSE was significantly correlated with P300 (negative correlation). Study done on 118 neurologically healthy subjects has shown that there was a significant negative correlation between MMSE and P300 latency (r=-0.3, p=<0.05) patients.[1] In the present study, we also observed decrease in efficiency of human cognitive processes with aging (prolonged P300 latency, reduced MMSE score) as a sensitive index of cerebral function (Table 3). Regardless of patient's depression status, increased P300 latency predicts proper performance on executive function tasks requiring speeded performance.[12] P300 latency is a useful index of cognitive function that reflects reduction in cerebral function due to aging.[1] Study done on healthy adults showed that P300 latency was prolonged with MMSE scores lower.[7] Study done on elderly subjects showed prolongation of P300 latency.[13] P300 latency is considered to reflect the speed of neural events underlying perception and discrimination of the target or rare stimulus; matching that particular information against memory; and making an appropriate decision whether to respond or not. Thus, slowed neural processing involved in stimulus evaluation or decision-making functions is postulated to underlie the associated impairment of P300 latency. In other words, P300 latency appears to be strongly correlated with attention and short term memory.[2]

The prevalence of disabling memory loss increases with each decade over the age of 50 years and <5% of all cases of Alzheimer's disease do occur in <60 years of age.[4] With the above background, the present study was carried out to correlate neuropsychological test result (MMSE) with P300 latency in adults more than 50 years of age so that MMSE can be used as a screening tool for early diagnosis of cognitive impairment.

5. Limitations

1. Only male subjects were included in study sample.
2. Effect of hypertension and diabetes on P300 latency was not studied.
3. Cross sectional study. There was no follow up of the cases.

Acknowledements

The authors would like to acknowledge Department of Physiology, Sri Devaraj Urs Medical College, Kolar for providing the necessary instrument to carry out the study.

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