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Original Article

Auditory Event Related Potential and PennCNP Neuropsychological Test Battery to Measure Aspects of Cognition in Young Adults : A Correlation Study

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Abstract

Introduction: There are a number of ways to assess cognitive functions. The two most important and routinely done tests are neuropsychological battery and event related potentials. The present study examined the relationship between conventional neuropsychological tests assessing various domains of cognition and an event related potential (P300).

Methods: Subjects were 60 neurologically normal healthy adults 20-30 years old with no history of neurological, neurosurgical, or psychiatric disorders. We administered a neuropsychological test battery (Penn CNP) assessing reaction time, visual memory and logical reasoning and recorded event related potential, P300 using auditory oddball paradigm in all subjects.

Results: A correlation test was run and pearson's analysis revealed that there was a positive correlation between reaction time on neuropsychological test battery and P300 wave latency. No relationship was found between other tests on neuropsychological test battery and P300 wave characteristics i.e., latency or amplitude.

Conclusion: We therefore conclude that P300 measurements cannot be replaced by neuropsychological tests or vice versa; rather, higher cortical functions should be evaluated by both methods.

Introduction

Cognition is an umbrella term which includes memory, attention, executive function, reasoning and other higher mental processes (1). It also facilitates human beings to work in a goal-oriented fashion, and continuously challenge these control processes when attempting to accomplish multiple goals simultaneously (2). Cognitive functions get affected in response to alteration in physiological functions like ageing, stress and sleep disturbance as well as in a number of medical conditions like hypertension, dementia, Parkinson's disease, diabetes, and in different psychiatric illnesses such as schizophrenia

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and bipolar disorders (3). Decline in cognition leads to a number of problems like decreased attention and concentration abilities, increased distractions, increased reaction time, altered responses, behavioural disinhibitions, learning and memory deficits which are critical for day to day functioning (4).

Assessment of cognitive functions can be done in a number of ways. The two most commonly used methods are Neuro-Psychological (NP) Tests and Event Related Potentials (ERP- P300) (5). Neuro-Psychological tests are specifically designed tasks to measure a psychological function known to be linked to a particular brain structure or pathway (6). These tests usually involve the systematic administration of clearly defined procedures in a formal environment (7). Testing of pre frontal cognition, most precisely includes battery of tests assessing reaction time, memory and reasoning ability. Reaction time involves fast decision making, motor planning and execution (8), whereas visual memory keeps a track of attributes or dimensions of the visual stimulus that the individual sees (9), and logical reasoning measures the ability to form concept and apply reasoning to various stimuli presented (10). Evaluation of these cognitive functions are used for research purposes and in clinical settings for the diagnosis of deficits (11). In essence, PennCNP - which is a web-based computerized neuro-psychological test battery, measures performance accuracy and speed on specific neurobehavioral domains using tests assessing various cognitive abilities (12). The psychometric properties of PennCNP is well established (13), therefore, it is considered as a valid and reliable method to assess various aspects of cognition and alterations in the same, if any.

Another way to objectively evaluate pre frontal cognition is by using its electrophysiological correlates via electroencephalography (EEG). Event Related Potential (ERP), in particular P300, an endogenous positive deflection in voltage with a latency of around 300 ms, have been used extensively to assess aspects of cognition in a rare target stimuli detection task using auditory or visual oddball paradigm (14). During the procedure, the subject detects an occasional 'target' stimulus in a regular train of standard stimulus. P300 latency and amplitude are often considered to be importantly related to higher cortical functioning.A decrease in amplitude and increase in latency corresponds to cognitive slowing (15). Thus, the P300 reflects human cognitive processes and has been used to examine higher order mental abilities in various cohorts.

As both these measures evaluate cognition, a few researchers have also focussed on finding out the association between ERPs and NP tests (16, 17, 18). However, data defining the relationship between P300 wave characteristics and cognitive function is inconclusive and scarce, with only a handful of heterogeneous researches being published on the same. Therefore, in the present study,we correlated the results of conventional neuropsychological tests with characteristics of ERP (P300) in young healthy population of India.

Methods

The protocol was approved by Institutional Ethics Committee (IEC), Jamia Millia Islamia and the study was conducted in compliance with the guidelines set out by the IEC. All the participants gave their written consent before the start of the study. They were informed of their right to decline or terminate participation in the study at any time.

Sixty neurologically normal, healthy subjects, of both the genders, aged between 20-30 years were recruited for the study. All the participants reported normal hearing and normal, or corrected to normal, vision and they all had an understanding of basic English language. Participants were excluded if they had a history of any neurological, psychological and psychiatric disorders, use of alcohol, other drug abuse, centrally active medications or if they were taking sleeping pills.

Neuro-Psychological battery

PennCNP test battery was administered individually to a single person at a time working with an examiner

in a quiet office environment, free from distractions. As a first step in testing, the subject was acquainted with the computer and mouse and performed an un-speeded version of the Mouse Practice task. This practice was administered at the beginning of the session to assure the participant has sufficient skills in moving and clicking the mouse. The participants were tested for their reaction time, visual memory and logical reasoning on various cognitively engaging task.

Reaction time

The reaction time task required moving the mouse and clicking as quickly as possible on a green square that disappears after the click. The square gets increasingly smaller owing to an increase in the difficulty level. The median response time was used as the main dependent measure to quantify reaction time.

Visual memory

The face memory test presented 20 digitized faces that were later mixed with 20 distracters. The participant's efficacy score, ranging from 0-40 is calculated, which reflects the number of correctly recognized targets and correctly rejected foils with higher scores indicating better face memory.

Logical reasoning

Subjects were presented with task in which they had to decide which of the 4 objects does not belong with the other 3 based on different sorting principles (e.g., shape, size, line thickness). Sorting principle changed after 10 successive correct responses to increase difficulty. An accuracy score was calculated for the task, with higher scores demonstrating better reasoning ability.

Scoring of tasks

The scores for these cognitive tasks (median response time for reaction time task, efficacy score for visual memory and accuracy score for logical reasoning task) were calculated by the PennCNP website (https://penncnp.med.upenn.edu).

Event related potential P300

Because there is high inter-individual variability in ERP P300, great care was taken to standardize measurement conditions. The ERP was recorded at the same time of the day (10-11 am) for all the participants to avoid circadian variations on the wave. Environmental factors which influence ERP such as temperature, noise, or strong luminosity was controlled during each recording. Moreover, instructions for the last 24 hours were given to the participants to refrain from consuming caffeinated products and excessive physical activity as these can also contribute to changes in P300 wave.

The participant was made to lie comfortably. The scalp was gently cleaned with NûPrepTM skin prepping gel to abrade the dead skin and Ten20TM conductive EEG paste was applied to different locations on the scalp for the placement of electrodes. Ag-AgCl disc electrodes were used for recording. The active electrode was attached on the vertex (Cz), reference electrodes on mastoid (A1), and ground electrode on the forehead (Fpz) (19). The auditory ERPs were recorded during a task involving standard auditory oddball paradigm on RMS Salus 2C machine, India. The sound intensity for auditory stimulus was computed in accordance to hearing threshold of each individual. The subjects were presented with two kinds of sound through headphones, and were instructed not to count the number of (frequent, non-target stimuli) presentations of a low-pitch tone (S1), but to count the number of (rare, target stimuli) presentations of a high-pitch tone (S2). The S1 and S2 sounds were produced at a target: non-target ratio randomly. Subjects were tested twice in this manner. The first test was to familiarize the subjects with the process. The second test was the main test, in which the subjects were given instructions about the measurement process. During the recording of AERPs, subjects were instructed to avoid excessive movement of the face, eyes, and neck (20).

Results

A sample of sixty students (28=females and 32=males) with demographic characteristics (mean age = 23.6±2.43 years, mean height = 163.813±9.37 cm, mean weight = 58.7±6.32 kg and mean BMI = 21.86±1.28 kg/m²) was assessed for the ERP P300 characteristics and various tests on neuropsychological test battery (Table I).

TABLE I : Mean and SD scores for Neuro-Psychological tests (Reaction time, Visual memory and Logical reasoning) and Event Related Potential (P300 amplitude and P300 latency).

Test	*Mean*	*SD*
RT	866.89	147.13
VM	31.57	4.11
LR	20.70	2.00
P300 lat	312.83	9.19
P300 amp	4.50	1.56

Abbreviations- SD= Standard deviation, RT=Reaction Time, VM=Visual memory, LG= Logical Reasoning, P300 amp=P300 amplitude, P300 lat=P300 latency.

We computed Pearson's correlation (Table II) to assess the relationship between different domains of cognition on neuropsychological test battery (reaction time, visual memory and logical reasoning) and electrophysiological correlates of cognition i.e., P300 characteristics (wave latency and amplitude). The relationship between P300 amplitude and RT was computed but it did not show any association [r = -0.2096, p = 0.1080; Fig. 1 (A)]. Similarly, a correlation analysis was also done for P300 amplitude and visual memory [r = -0.08209, p = 0.5329; Fig. 1 (B)] and P300 amp and logical reasoning [r = -0.1119, p = 0.3947; Fig. 1 (C)], but no association was found in any of the analysis.

TABLE II : Correlation analysis between Neuro-Psychological tests (Reaction time, Visual memory and Logical reasoning) and P300 wave characteristics (amplitude and latency).

	P300 lat	*P300 amp*
RT	0.3283*	-0.2096
VM	-0.1636	-0.0820
LG	0.1532	-0.1119

Abbreviations- P300 amp=P300 amplitude, P300 lat=P300 latency, RT=Reaction Time, VM=Visual memory, LG= Logical Reasoning.

Interestingly, a positive linear correlation was found between the latency of P300 wave and median response time on reaction time task on neuropsychological test battery [r = 0.3283*, p = 0.0104; Fig. 2 (A)], demonstrating that participants who performed better on reaction time task showed an optimal latency values for P 300 wave, and those who took a longer time to perform reaction time task, also had their latencies increased when analysed for P300 wave. However, when P300 latency was analysed for relationship with visual memory [r = -0.1636, p = 0.2116; Fig. 2 (B)] and logical reasoning [r = 0.1532, p = 0.2425; Fig. 2 (C)], no correlation was found in any of the analysis.

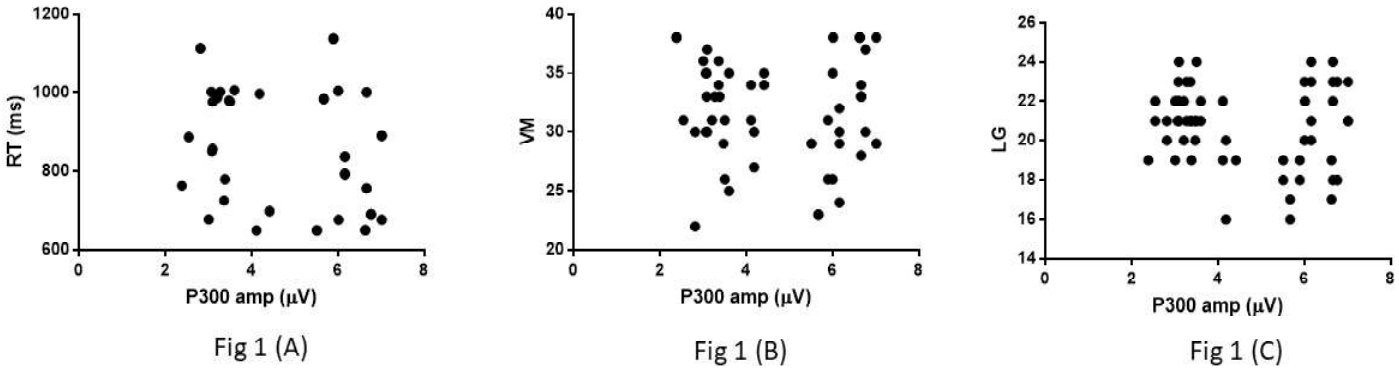

Fig. 1 : (A) Pearson correlation coefficients between the P300 amplitude and reaction time showing no association (r = -0.2096, p = 0.1080).
(B) Correlation analysis between the P300 amplitude and visual memory signifying no relationship with each other (r = -0.08209, p = 0.5329).
(C) Analysis between the P 300 amplitude and logical reasoning showing (r = -0.1119, p = 0.3947) showing no correlation.

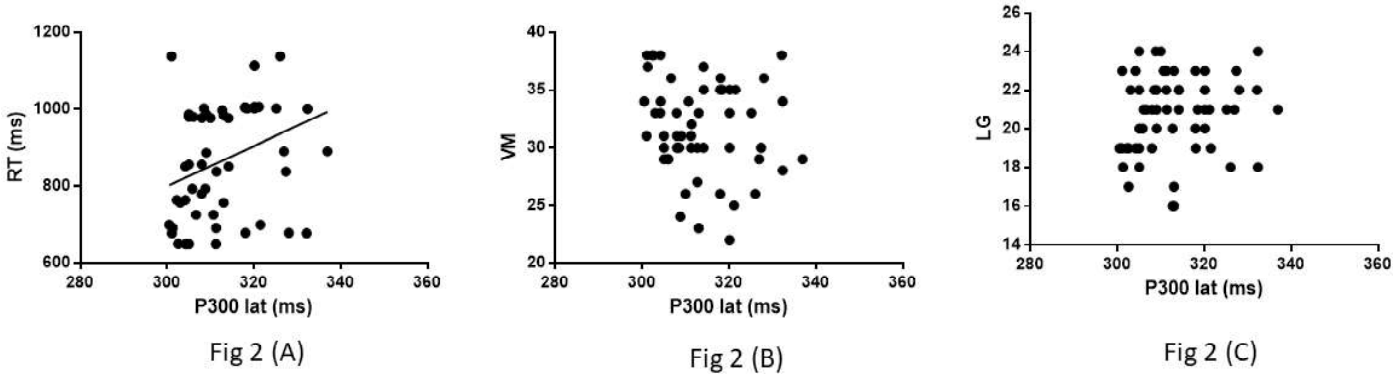

Fig. 2 : (A) Pearson correlation coefficients between the P300 latency and reaction time showing a positive linear relationship ($r = 0.3283^*$, $p = 0.0104$).

(B) Correlation analysis between the P300 latency and visual memory demonstrating no relationship with each other ($r = -0.1636$, $p = 0.2116$).

(C) Analysis between the P300 latency and logical reasoning showing no correlation ($r = 0.1532$, $p = 0.2425$).

Discussion

Different procedures are available to test cognition like simple pen paper tests (21), neuropsychological batteries in which different tests are designed to assess various domains of cognition (22), electrophysiological techniques such as event related potentials (23) and imaging techniques like fMRI (24). Although fMRI is more specific, but because of its high cost it cannot be used in clinical setup on a regular basis. The two most common and specific biomarkers to assess cognition are neuropsychological battery and ERP P300, which can be done regularly in clinics (25).

Event related potentials are stimulus processing measures that are used by many researchers to quantify cognitive functions in normal and pathological cases (26-28). These tests have reached a degree of standardization sufficient to make them gold standard for higher mental function assessment. On the other hand, a few researchers have also used PennCNP, a popular and user friendly neuropsychological battery to assess various cognitive domains. Neves and colleagues (29) assessed sensorimotor performance in euthmic bipolar disorder patients using the motor praxis test of the same battery. Similarly, researchers have explored the difference in executive performance profile of students using the tests of executive function and abstraction on PennCNP (30). In the same lines, Ferriera in 2018, also used Penn CNP tests to demonstrate the relationship between different types of memory including verbal, face and working memory with emotional regulation in college students (31).

In this study, we evaluated the relationship between ERP P300 and neuropsychological tests in healthy adult subjects using PennCNP battery. Our results indicate that P300 wave latency was associated with reaction time on cognitive task. The finding of the present study shares similarities with previous studies, demonstrating that there is a positive relationship between reaction time task on neuropsychological test and latency of P300 wave (32). Our results are also in agreement with studies done by other researchers (16, 33) showing associations between long latency responses and choice reaction tasks. This shows that participants having prolonged wave latency show increased reaction time, and those having optimal P300 latency take less time to react to a particular stimulus on reaction time task. Reaction time task measures general alertness and motor speed through delivery of a known stimulus to a known location to elicit a known response, the only uncertainty is regarding when the stimulus will occur, by having a variable interval between the trial response and the onset of the stimulus for the next trial (34). This, therefore, tests the minimal time needed to respond to a stimulus, and is a basic measure of processing

speed. On the other hand, latency of P300 wave is considered to reflect the speed of neural events underlying perception and discrimination of a target stimulus (35). In physiological terms, both these tasks measure the same underlying neural aspect.

We also tested for association between ERP P300 wave characteristics and neuropsychological tests. No correlation was found between P300 wave variables (amplitude and latency) and other domains of cognition which were tested i.e., visual memory and logical reasoning. Also, the P300 wave characteristics were normal in some cases in whom the neuropsychological tests were abnormal and vice versa. Similar results were found in the study done by Maeshima and group (16), in which healthy participants were subjected to neuropsychological tests and ERP and no correlation was reported between the measures of ERP and neuropsychological tests, however mild to moderate correlations were evident between age and cognitive parameters demonstrating decrease in the efficiency of human cognitive processes with ageing. Moreover, studies with pathological cases like Alzheimer's also share similar findings demonstrating no association between ERP characteristics and performance on NP tests including memory and reasoning tasks (17). While, in literature, P300 amplitude and latency has been correlated with performance on neuropsychological tests, which aspects of cognitive function are reflected in the observed relationships is not clear. Moreover, several studies have reported the relationships of ERPs with psychological tests like matrices, block design and digit span (31), but these studies have worked with neurological and psychological patients rather than healthy adults.

The results of the present study imply that ERP P300 and neuropsychological tests probably reflect and assess different processes involved in cognition. Therefore, any of the test cannot be replaced by the other, and higher cortical functions should be evaluated by both the methods in research and clinical settings. Parra and colleagues (36) too suggested that combined use of neuropsychological tasks, and the analysis of the P300 may offer a very useful method for the assessment of cognitive functions.

The main limitation of the study was that we did not examine gender differences in the present study whereas previous researches have shown some, although mild, gender-based differences in cognitive abilities (37). For better understanding, future researches can also incorporate questionnaire-based psychological tests, and other tasks on neuropsychological test battery measuring different domains of cognition and correlate them with ERPs. These are important issues which should be considered in future studies.

In spite of these limitations, our study has many potential strengths. The present study used a novel approach to evaluate the neuropsychological and electrophysiological measures of cognition together. The study also attempted to establish the relationship between the neuropsychological tasks and P300 components in young healthy participants. Also, the testing procedures applied in the present study are in accordance with the gold standard equipment, and standardized protocols are used as per guidelines. Considering all these facts, the present study implies that although, ERPs and neuropsychological tests are considered specific for cognitive testing but the standardized testing procedure should make use of both the measures, as one measure cannot predict the result of other.

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