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Original Research Paper

Physiology

NORMATIVE DATA OF COGNITIVE ASSESSMENT BY AUDITORY P300 EVENT RELATED POTENTIAL, MONTREAL COGNITION ASSESSMENT AND CHOICE REACTION TIME AND ITS VARIATION WITH AGE AND GENDER IN UTTARAKHAND REGION OF INDIA.

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ABSTRACT

Background: Tests like auditory P300 event related potential, neuro-psychometric pen pencil Montreal Cognition Assessment Test (MOCA) and Choice reaction time have been used as indexes of cognitive function. Thus this study has been planned with the aim to evaluate cognitive ability of a normal adult to find out normative data and its, variation with age and gender in Uttarakhand region of India.

Materials and Method: This cross-sectional study was carried out in the department of Physiology of AIIMS, Rishikesh on 52 healthy with ages ranging from 20 to 40 years, equal number of male & female volunteers with the ability to understand test procedures. Following tests were performed in the given order for uniformity during 11-1 pm timing of a day:
1. Event Related Potential-P300 2. Neuro-psychometric assessment (Hindi Montreal Cognitive Assessment -HMOCA test) and 3. Choice Reaction Time.

Results and Conclusion: Mean of P300 Latency is 310 ± 37.14 msec, mean of P300 Amplitude is 14 ± 7.5 uv (from Cz electrode site), mean of Montreal Score is 24.81±3.25, and mean of CRT is 584.5 ±84.06 ms in all the subjects. All the parameters are better in younger age group. All the parameters are better in male except MOCA score.

KEYWORDS : Cognitive assessment, Auditory P300, MOCA, CRT

INTRODUCTION

Event-related potentials (ERPs) are objective and non-invasive indicator of cognitive functions that represent time locked EEG and reveal the summed activity of postsynaptic potentials produced when a large number of similarly oriented cortical neurons fire in synchrony while processing information in response to variety of cognitive, sensory and motor events or stimuli (1).

ERPs generated in later parts specifically P300 wave reflects the manner in which the subject evaluates the stimulus and are termed 'cognitive' or 'endogenous' ERPs as they scrutinize level of information processing as correlate with attention, working memory and decision making (2).

P300 (P3) can be obtained in an 'oddball' paradigm when a subject detects occasional auditory or visual 'target' stimuli (low probability task) in a regular train of auditory or visual standard stimuli (high probability non target task) respectively by a given motor reaction, e.g. to button pressing. The P300 wave develops if the subject is actively engaged in the task of detecting the targets that is attention and decision making (3).

P300 is evaluated in terms of latency and amplitude. The latency is usually inferred as the speed of stimulus classification resulting from discernment of one event from another. Shorter latencies designate superior mental performance relative to longer latencies. P300 amplitude seems to reflect stimulus information such that greater attention produces larger waves (4).

The P300 that is elicited in the auditory oddball consists of neural activity originating from presumably the prefrontal cortex, the temporo-parietal junction, the primary auditory cortex and possibly more sources (5).

In a meta-analysis of 75 studies, mentions overall mean of P300 latency has been given 316.5 milliseconds (range: 290.0–447.5) and overall mean of P300 amplitude has been given 10.4 microvolts (range: 2.6–37.7) for a mean age of 33.3 ranging from 4 to 95 years (6).

Various neuro-psychometric tests, like Montreal Cognition Assessment Test (MOCA), Wechsler Adult Performance Intelligence Scale (WAPIS) and Mini-Mental State Examination (MMSE) have been used as indexes of cognitive function over a century. In spite of repeated modification and improvisation over decades there are still many limitations and inherent shortcomings in these tests like subjectivity, non-specificity and unknown neural substratum. However, these tests are still popular and valuable in Neuropsychology because of simplicity & ease of application, instantaneous clue and low cost (7).

Reaction time (RT) is also a measure of Information processing speed that can be represented traveling in the following way: Stimulus -> Sensory Neuron ->Spinal Cord and/or Brain -> Motor Neuron-> Response. There are many different types of RT measures, however, two common and useful measures are simple reaction time (SRT) &choice reaction time (CRT). SRT involves making a response as quickly as possible in response to a single stimulus. In the CRT subject is to make appropriate response to one of a number of stimuli (8).

This study aims to evaluate cognitive ability of a normal adult with the different sets of test to find out a normative data and its variation with age and gender.

METHODOLOGY

Study Design and Setting

This cross-sectional study was carried out in the department of

Physiology of AIIMS, Rishikesh on 52 healthy with ages ranging from 20 to 40 years, equal number of male & female volunteers and getting approval from institutional research and Ethics committee for the study as per the inclusion and exclusion criteria's given below.

INCLUSION CRITERIA:
Age between 20 to 40 years, normal hearing ability, and the ability to understand test procedures.

EXCLUSION CRITERIA:
H/O of any neurological & psychiatric disorder, psychotropic medication, any prolonged medication, head injury, consumption of alcohol and caffeine within 24 hours of experimental session.

Procedure:
After taking informed consent, detailed history and physical examination were done to select participants. Following tests were performed in the given order for uniformity during 11-1 pm timing of a day:

1. Event Related Potential-P300 (P300 is preferred with respect to the other components of the ERP being relatively large size and easy to identify).
2. Neuro-psychometric assessment (Hindi Montreal Cognitive Assessment) and
3. Choice Reaction Time were carried out

1. Event Related Potential-Auditory P300: (9)
Subjects were advised for a head bath on the day of testing and abstain from caffeine and alcohol for 24 hours prior to test.

The participant was asked to sit comfortably in the noise free lab. He was explained the procedure and acquainted with all equipment operatives pertinent to him. A practice trial of test for first 15 stimuli was done in all subjects for familiarizing with the test. Using an Electrophysiology dedicated 'Nihon Kohden Neuropack' machine, pure silver disk surface electrodes were placed using Konix EEG paste after cleaning the sites skin with Nuprep gel. The configuration of electrodes was in accordance to the standard protocol of international 10-20 system. These electrodes were put to the forehead (Fpz, ground electrode), Midline skull (Fz and Cz, active negative electrodes-channel 1 and channel 2 respectively, Cz recording values were used for data analysis) and ear lobules (reference electrodes - A1 and A2 positive electrodes). Inter-electrode impedance ≤5 Kohms was ensured prior to testing. Patients were instructed to keep their eyes open (but looking down) throughout test to avoid contamination of response waveform by alpha waves in EEG.

Auditory stimuli were provided via headphones transducers put on to the subject. Stimuli and acquisition parameters settings for auditory P300 recording were as follows:

1. Position: sitting with both arms and back resting, eyes open

Active task: participant needs to press button by right foot at foot pad as fast as he heard sound of each target stimulus

2. Electrode Type: EEG/pure silver disk
3. Leads/Electrode Position: Active: Fz and Cz, Reference: A1 & A2 (ear lobules), Ground: Fpz
4. Auditory stimuli - Odd-ball paradigm -Two categories– Standard &Target
5. Stimuli probability: Standard - 80%; Target - 20%
6. Stimuli Frequency: Standard -1000 Hz-; Target - 2000 Hz
7. Intensity of stimuli (both): 80 dB
8. Presentation of stimuli: Binaural
9. Total number of stimuli: 200
10. Stimulus duration: 50 msec; 10 msec rise/fall
11. Electrode impedance: ≤5kohms
12. Filter setting: Hi- 50-100Hz, Low-0.1 Hz
13. Sensitivity: 20-50 uV/div
14. Analysis time: 100 msec/div
15. Response type: pressing button by right foot
16. Eyes: open

Marking
i. Latencies:
N100: negative peak at around 100msec.
N200: next negative peak between 150msec and 300msec.
P200: positive peak usually between N100 and N200 and before P300 between 100msec and 300msec.
P300: Positive peak after 200msec to 500msec after P200.
ii. Amplitude: voltage difference between N100 and P300

2. Hindi Montreal Cognitive Assessment Hindi (MOCA)

Pen and paper neuro-psychometric test battery was carried out and scores were recorded (10, 11).

3. Choice Reaction Time: (12)

The Choice reaction time was recorded on already validated Deary – Liewald reaction
time software on a computer with Windows™ version 8.1.

STATISTICAL ANALYSIS:
Signal Analysis: All the trials of P300 waves were averaged in each session. Peak amplitudes (micro-volts- V) and latencies (milliseconds-msec) were obtained relative to a pre-stimulus baseline. Data from Cz electrode was considered for analysis. All the values were expressed as mean ±sd. p value <0.05 is considered significant.

All statistics were done with help of SPSS version 21. Unpaired T-test was applied between 2 groups for age-wise, gender-wise comparison. Pearson correlation was applied to see the correlation between the variables. Correlation coefficient was expressed as 'r' value along with p-value.

RESULTS:
1: Mean of P300 Latency is 310 ± 37.14 msec, mean of P300 Amplitude is 14 ± 7.5 uv, mean of Montreal Score is 24.81±3.25, and mean of CRT is 584.5 ±84.06 ms in all the subjects (Table 1).

Table 1: Mean and ± sd of all parameters of all the participants

	P300 Latency msec	P300 Amplitude μV	MOCA Score	CRT msec
Mean	310	14	24.81	584.5
± sd	37.14	7.5	3.254	84.06

2: P300 latency is lesser, amplitude is higher, MOCA score is higher and CRT is lower in lower age group (19-28 years) in comparison to higher age group (29 -40 years) although not significant statistically. There is no correlation was found out of age with P300 latency and amplitude but small correlation was found out with MOCA (fig 1) and CRT (fig 2) (Table 2).

Table 2: Mean and ± sd of 19-28 years and 29-40 years age groups

Age (years)		P300 Latency msec	P300 Amplitude μV	MOCA Score	CRT msec
19-28	Mean	309.88	14.44	25.5	566.4
	±sd	34.62	7.53	2.59	75.57
29-40	Mean	310.15	13.96	24.1	601.2
	±sd	40.18	7.65	3.72	89.37
	T Test	0.98	0.81	0.16	0.13
	Pearson Correlation Coefficient (r)	0.03 (p=0.83)	0.07 (p=0.62)	-0.13 (p=0.36)	0.14 (p=0.32)

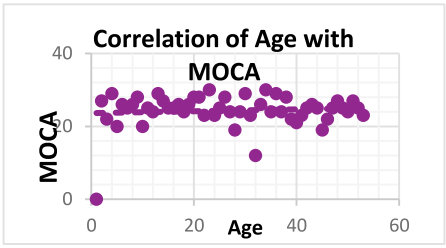

Fig 1: Correlation of age 19-40 years with MOCA Score

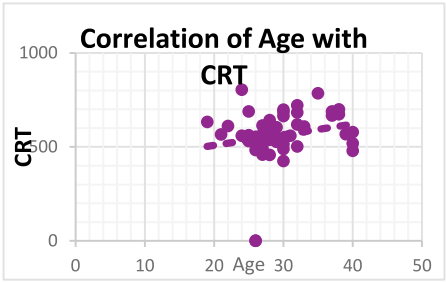

Fig 2: Correlation of age 19-40 years with CRT

3: P300 latency is slightly higher, amplitude is lower, **MOCA score is higher** and CRT is higher in female gender group in comparison to male gender group although not significant statistically (Table 3).

Table 3: Gender wise Comparison: Mean and ± sd of female & male groups

Gender		P300 Latency msec	P300 Amplitude μV	MOCA Score	CRT msec
Female	Mean	312.07	14.05	25.61	591.93
	±sd	41.38	7.13	3.73	81.62
Male	Mean	307.96	14.36	24	577.06
	±sd	33.05	8.03	2.51	87.45
	T test	0.66	0.84	0.09	0.55

DISCUSSION:

In the present study, the normative data mean of P300 Latency is 310 ± 37.14 msec, P300 Amplitude is 14 ± 7.5 uv (from Cz electrode site), Montreal Score is 24.81±3.25, and CRT is 584.5 ±84.06 ms in all the subjects of 19-40 years old.

The normative mean latency value is quite comparable to the study of Polich et al in the 20-40 age groups but value of P300 latency is lesser and P300 amplitude is higher in comparison to study of Uvais et al (13, 14).

It is thought that P300 latency and amplitude divulge different aspects of cognitive performance. Explicitly, P300 latency may be considered as an index of information-processing or neural speed whereas the P300 amplitude might be an index for the amount of cognitive resources or neural power being used (15).

In the present study, all the cognitive assessment parameters are better in younger age group (19-28 years) in comparison to the older group (29-40 years) i. e. P300 latency is lesser, amplitude is higher, MOCA score is higher and CRT is lower in lower age group. Age wise increase in latency and decrease in amplitude but no significant increase in reaction time has been reported by Iragui Vicente J et al. Studies of Salthouse et al and Siegler et al on reaction time tasks showed that young adults respond faster than older adults (16, 17,18).

Consistent with our results, some reports on pen and paper neuro-psychometric test battery MOCA have suggested small to non-existent age differences (19. 20. 21. 22).

So overall on reviewing the findings of the undertaken cognitive parameters, there is an overall reduction of cognitive function status with increase in age but that was very slight from 19 to 40 years of age. There are studies suggestive of age-related slowing due to diffuse cell loss causing longer transmission of neural impulses through indirect pathways to arrive at the same place (23, 24).

In our study there is statistically non-significant increased P300 latency and decreased P300 amplitude (difference of mean = 0.30) in female subjects. These outcomes in latency is similar to Melynyte et al and in amplitude is similar to Lindín et al and Shelton et al (25, 26 27). However, the results of this study showed very small difference in mean i.e. by 4 ms for P300 latency and 0.3 uv for P300 amplitude, this data is comparable to many other studies that do not find any difference for P300 latency and amplitude amongst male and female subjects (28, 29,30).

Effect of gender on MOCA score was similar to Eddy et al and Mittal et al results (31,32).

In the present study, choice reaction time is lengthier in female subjects which is similar to Adam et al and Blough et al but contrary to Landauer et al (33,34,35).

CONCLUSION:

Normative data range of cognitive parameters in this study were quite comparable with other studies. Overall cognitive parameters indicate better results although marginally, in younger age group and in male gender.

Conflict of interest: None

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