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P300 EVENT RELATED POTENTIAL IN NORMAL HEALTHY CONTROLS OF DIFFERENT AGE GROUPS

R.SHUKLA, J.K.TRIVEDI, R.SINGH, Y.SINGH & P.CHAKRAVORTY

ABSTRACT

P300 event related potential was recorded in 115 healthy controls with a mean age of 35.9±14.81 years and a male : female ratio of 72 : 43. There was significant difference in the P300 latency in <40 years as compared to ≥ 40 years group (p<0.001). There was no significant difference between males and females. There was a strong positive correlation between age and P300 latency (p<0.001). The regression equation for P300 latency was Y=287.9+1.492x with an SEE of 20.2 (where Y is the P300 latency in ms, x is the age in years, SEE is the standard error of estimate). There was a negative correlation between age and P300 amplitude which was significant in < 40 years age group while in ≥ 40 years age group it was not significant.

Key words : Event related potentials, P300

P300 is a long latency event related endogenous potential which was first described by Sutton et al. (1965). It is an objective method of cognitive evaluation and can be generated by any form of stimulus, however the auditory odd ball or beep-boop paradigm is the most commonly used.

P300 is recorded by a target detection task. The subject is presented with two kinds of stimuli at different rates which are slightly different from each other with respect to certain parameters (e.g. pitch variation in case of auditory stimulus) and he is expected to respond only to the infrequently placed stimulus with a certain task (Duncan & Donchin, 1977) P300 can be recorded by averaging the electrophysiological response to the infrequently placed target stimuli. It occurs as positive wave after about 300 ms of the stimulus and is recorded from midline Fz, Cz & Pz electrode (Picton,1990). It can be divided into two components P275 or P3a and P300 or P3b (Squires,1975). The former is better recorded from the frontal region while the latter from the centroparietal region.

Event related potentials (ERPs) result mainly from the summation of cortical excitatory and inhibitory postsynaptic potentials triggered by the release of neurotransmitters like gamma amino butyric acid (GABA) and glutamate into the synaptic cleft (Mitzdorf, 1994) ERP amplitude can therefore directly reflect functional aspects of these neurotransmitters. Furthermore, ERP parameters can indirectly reflect modulatory effects of neuromodulators (e.g serotonin, acetylcholine) which have more global and tonic effects on cortical function (Hegerl et al.,1996). No ethnic differences have been reported in the P300 event related potential however as only a few studies in normal controls have been done in our country (Tandon,1990; Jha et al ,1995) so the present study has been undertaken to evaluate the P300 latency and amplitude in healthy subjects of various ages belonging to both the sexes.

MATERIAL AND METHOD

One hundred and fifteen healthy controls

belonging to both sexes were the subjects for the present study They were taken from the resident doctors, paramedical staff and relatives of patients admitted in the neurology and psychiatry department. The mean age was 35.87±14.83 years (range 10 to 70 years) with a sex ratio of 72:43 . None of the subjects included in the study were suffering from hypertension, diabetes, epilepsy or any psychiatric disorder. There was no history of head injury, ear discharge, intake of ototoxic drugs in the past, alcohol intake or use of psychoactive substances. A detailed neurological examination was done in all the subjects and found to be normal. Cognitive evaluation was done using the Folstein's minimental status examination (MMSE) (Folstein et al., 1975) and Raven's progressive matrices for intelligence quotient (IQ) assessment. The mean MMSE score was 27.03±1.67 (range 23 to 30) and IQ was 102.12±7.94 (range 90 to 120).

P300 was recorded on Neuropack- 4 evoked potential machine (Nihon Kohden) according to the method of Barrett (1993). The test was done in a quiet, air conditioned room with the subject lying comfortably on a couch. The auditory odd-ball paradigm was used and pure tone stimuli were applied binaurally at an intensity of 70 dB SPL at a rate of 0.5 Hz. The target tone (20%) was 2000 Hz and non-target (80%) 1000Hz and the order of occurrence was pseudo-random. The rise time and fall time of the tones were 10ms while plateau time was 100ms. The test procedure was explained to the subject and he was familiarised with the frequently occurring non-target and the rare target stimuli. The subject was asked to respond only to the infrequently presented rare target stimuli by lifting the right index finger to indicate his response. Electrode placement was done at Fz and Cz (recording sites), ear lobes A1 and A2 (linked reference) and on the forehead at Fpz (ground) according to the International 10-20 system (Jasper, 1958). Disc electrodes were applied using conducting jelly. The electrode impedance was kept below 5KOhms by rubbing the scalp with special abrasive cream. The EEG was amplified and averaged using a filter bandpass of 0.5 Hz to 50 Hz. Automatic artifact rejection facility was used. A 50 Hz notch filter was not used. A pre-stimulus baseline of 100 ms was obtained and EEG epochs of 900 ms triggered by the target and non-target stimuli were averaged separately. Thirty responses were averaged and two trials were done to ensure reproducibility. The subject was asked to lookup straight in front of him with eyes closed. Experimenter observed the subject to ensure that he/she does not go of to sleep and detected the targets correctly. Correct detections were counted. The accuracy of the subjects response was checked by noting the difference between the number of target stimuli actually presented and those to which the subject responded by lifting his right index finger. A correct detection rate of 80% or more was considered adequate. Smoothening of the response was done and the data was stored on a floppy disc.

The measurements were done at Cz site. P300 peak was recognized as the positive wave after N1-P2-N2 complex and between 265 and 600msec and is followed by a slow negative wave. The latency and amplitude measurements were done by placing cursors on the screen. Statistical analysis was done by computing the mean and standard deviation Regression equation for latency and amplitude of P300 with age was also calculated (Swinscow, 1978).

RESULTS

The P300 could be recorded in all the subjects. The latency and amplitude are depicted in table 1. The mean latency was 361.5±32.9 msec (range 295 to 438 msec) while the mean amplitude was 9.32.±5.11 µV (range 2.47 to 20.41 µV). There was a significant difference in the latency between the two age groups. Males and females did not show a significant difference in P300 latency. The amplitudes were lesser in the 40 years and above age group, however the difference was significant for males only. There

TABLE 1
LATENCY AND AMPLITUDE OF P300

Age group (years)	Sex	n	Latency (msec)	Amplitude (μV)
<40	Male	47	331.3±30.05	10.72±5.50
	Female	28	324.19±21.57	10.60±4.88
	Total	75	328.68±27.28	10.71±5.24
≥40	Male	25	368.80±35.30**	7.49±3.40*
	Female	15	357.93±25.65**	8.59±4.39
	Total	40	364.73±32.12**	7.89±3.77*

Values are expressed as Mean±SD
*p<0.01; **P<0.002 as compared to corresponding <40 age group

was a negative correlation between the P300 latency and amplitude (r =-0.20)

A significant positive correlation was observed between the age and P300 latency (Fig.) while the amplitude of P300 showed a significant negative correlation in less than 40 years age group. The equation for linear regression was also calculated for the two age groups separately with latency and amplitude (table 2).

TABLE 2
CORRELATION BETWEEN AGE AND P300

Age group (years)	Correlation coefficient (r)	Linear regression equation	SEE
P300 latency			
<40	0.48**		
≥40	0.49*		
Total	0.66**	Y=287.9+1.492 x	20.2
P300 amplitude			
<40	-0.78**		
≥40	-0.24		
Total	-0.31*	Y=13.45-0.104 x	5.30

*P<0.01, **P<0.001
Y=P300 Latency in ms/ Amplitude in μV, x=age in years
SEE=Standard error of estimate

RELATIONSHIP OF AGE TO P300 LATENCY

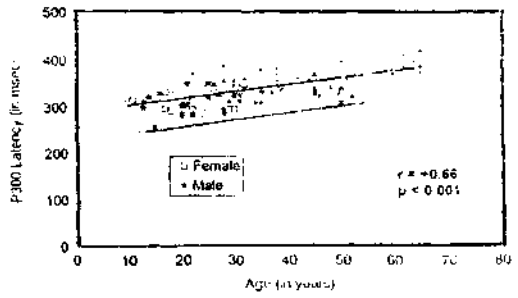

Fig. Scattergram showing the correlation between P300 latency and age

DISCUSSION

P300 is a long latency event related potential recorded over the centroparietal area. It indicates recognition of the stimulus so if the stimulus is perceived but not recognized then the initial short latency evoked potentials are generated but P300 is not generated (Sutton, 1965). It has drawn an increasing attention as a parameter reflecting the cognitive function of the brain, specially in the field of psychology, psychiatry and neurology (Picton et al.,1986).

A reproducible well defined wave form of P300 was recorded in all the subjects of the present study with age ranging from 10 to 70 years. Jha et al. (1995) on the other hand recorded it in 100% young (20-25 years), 80% middle aged (40-50 years) and 10% aged (75-80 years) male subjects. Age is the most important variable affecting the latency of P300. The P300 latency has a significant positive correlation in both age groups while the amplitude shows a significant negative correlation with age particularly in the less than 40 years age group. Several studies have showed a positive correlation of age with P300 latency (Smith et al. 1980; Brown et al. 1983; Picton et al. 1984; Pfefferbaum et al. 1984; Sklare & Lyon 1984) while the correlation between age and P300 amplitude is uncertain because of conflicting findings (Goodin,1978; Beck et al.,1980; Brown et al., 1983; Pfefferbaum et al.,1984; Picton et al.,1984). There is an increase in mean latency by approximately 1.5 msec per year and the standard error of estimate (SEE) was 20 msec. Goodin (1978) has reported a latency increase of 1.8 msec per year after the age of 20 years while the SEE has ranged

from 20 to 50 msec in various studies.

A significant correlation has been reported between the amplitude of N2 and latency of P300 wave and the scores obtained from the State - Trait Anxiety Inventory Test and Middlesex Hospital Questionnaire suggesting that some personality features can slightly modify the acoustic P300 wave (Raudino,1993). The latency of P300 depends upon the distractability of the frequent and infrequent stimuli while the amplitude varies with the probability of the target stimuli (Fein & Turetsky, 1989). There is a decrease in the amplitude of P300 as a result of repeated stimulation due to habituation of the response (Ivey & Schmidt, 1993). The latency of P300 is a measure of the stimulus evaluation time which is supposed to reflect the brain activity as a whole. By using P300, it is possible to divide the total reaction time to the stimulus into two parts, stimulus processing and recognition time (P300) and the response selection or execution time (Barrett,1993).

The generator site of P300 is not known with certainty, however potentials recorded by depth electrodes from the medial temporal lobe have many similarities to P300 (Halgren et al., 1980). However there may be other generator sites as temporal lobectomy for intractable epilepsy does not significantly change scalp recorded P300 (Johnson, 1988).

Based on the findings of the present study prolonged latency, taken as the predicted value for that age as determined by the regression equation +3 SEE, can be taken as a criteria for abnormality. Amplitude cannot be taken as a criteria as the predicted value minus 3 SEE values are either close to zero or in the negative. An absent waveform however cannot be used as a criterion for abnormality because if the patient is uncooperative or unattentive, then the P300 would not be elicited. It is well known that if during the recording the patient is given a book to read and the auditory targets are ignored the P300 would not be generated.

Extrapolating the regression equation obtained from the present study to that of Jha et al. (1995) the P300 latency for young, middle aged and elderly subjects gives an overestimate of 16.72 ms and 12.53 ms for the first two groups and an underestimate of 3.38 ms for the last group. The estimated value of P300 latency is 9.31 ms greater than those reported by Tandon (1990) in their study of P3 event related potentials in young adults. thus providing external validity to the present study.

The P300 may be a useful objective clinical adjunct to behavioural measures of cognitive processes. It is, however, important to control for behavioural function since patients with altered cognition including inattention may not perform the task accurately and this by itself, may produce alteration in P300. In addition, one needs to be aware of the high variability amongst normal subjects of the P300 latency and amplitude.

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R.SHUKLA,MD. Professor. Department of Neurology. J.K TRIVEDI,MD. Professor. R.SINGH. Resident Department of Psychiatry. Y.SINGH. Resident. P CHAKRAVORTY. Resident. Department of Neurology. K G 's Medical College. Lucknow - 226003*

** **Correspondence***