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Cognitive evoked potential (P_{300}): a metric for cerebral concussion

R. Pratap-Chand, Malliga Sinniah, F. A. Salem

Department of Medicine, University Hospital, Kubang Kerian, Kelantan, Malaysia

ABSTRACT - Cognitive impairment has been reported to occur in minor head injury (concussion). The value of the P_{300} evoked potential as a measure of cerebral concussion was studied in 20 patients with minor head injury and compared with the data from 20 normal subjects. Significant abnormalities of the P_{300} latency and amplitude were noted in these patients in the post-concussion period. The abnormalities improved completely on repeat testing. The correlation of the P_{300} to other parameters of head injury is discussed. The P_{300} constitutes a simple laboratory test that is a sensitive measure of cerebral dysfunction in concussive head injuries.

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Cognitive impairment following mild head injury (concussion) has been reported to occur in the immediate post-concussion period. Neurophysiological tests have revealed that these cognitive deficits tend to improve completely over a period of 30-35 days (1-3). Cerebral damage in the form of axonal tears has been implicated as the pathology underlying these cognitive deficits as well as the post concussional symptoms like headache, dizziness, loss of concentration, and behavioural changes that these patients frequently complain of (3, 4). Abnormalities in the brainstem auditory evoked potentials in patients with concussion have lent support to this postulation (5, 6).

The P_{300} (P_3) component of the human event related potentials (ERP) is generated in response to infrequent, attended, task relevant stimuli (7, 8). It has been associated with various cognitive functions such as information delivery, orienting, signal detection, stimulus evaluation time and decision making (9, 10). The latency of the P_3 is considered to be a measure of the speed of cognition and has been found to increase with age and in patients with dementing illnesses (11, 12). The P_3 latency is an electrophysiological marker for disorders of cognition. In recent studies on severe head injuries, P_3 abnormalities clearly differentiated demented from non-demented patients. The P_3 was also found to be a sensitive index of subclinical residual brain dysfunction due to head injury (13-15). In the present study, the role of the P_3 as an indicator of cerebral dysfunction was assessed in 20 patients with mild head injury.

Material and methods

A total of 20 healthy subjects aged 14-60 years (12 males and 8 females) were the normal controls for P_3 recordings. In 20 patients with mild head injury, the level of consciousness was assessed by the Glasgow Coma Scale (16) (GCS) and a detailed neurological examination was performed. Criteria for mild head injury were loss of consciousness (LOC) less than 30 min, GCS score between 13-15 and hospitalisation less than 4 days.

The P_3 was recorded in an auditory "oddball" paradigm in normal subjects and in patients (within 4 days of head trauma). The subjects'

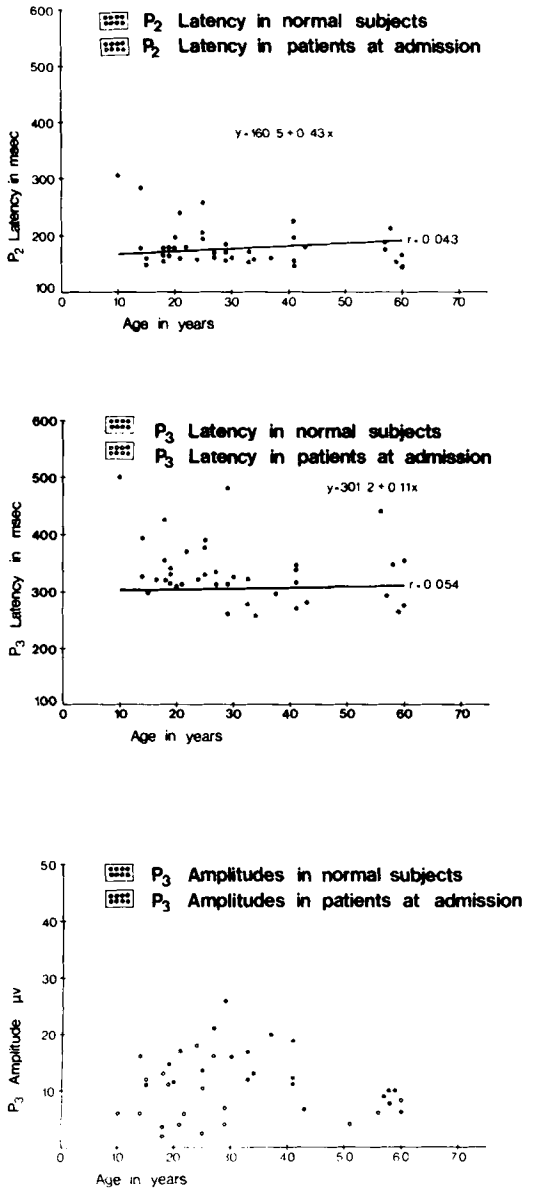

Fig. 1. The scatter of P_2 latencies, P_3 latencies and P_3 amplitudes in relation to age are shown in normal subjects and patients.

task was to count the number of infrequent (target) 2 KHz tone bursts presented randomly in a sequence of frequent (non-target) 750 Hz tone bursts. The target tone bursts had a probability of 20% in a total number of 300 stimuli. Both

Table 1
P_2 and P_3 in normal subjects

	P_2 latency μv	P_3 latency msec	P_3 amplitude msec
Mean	175.7	305.1	13.8
Range	145-230	256-358.4	6.8-26.2
Standard Deviation	22.9	30.1	5.1

stimuli were presented binaurally through ear phones at an intensity of 90 dB. The subjects were seated relaxed and instructed to avoid eye and finger movements. The recording silver chloride electrodes were fixed to the scalp at C_z with electrode paste and referenced to linked mastoids with FP_z as common electrode (10-20 system). Electrode resistance was kept below 2 Kohms. The recording electrodes were led to a Nicolet C_4 evoked potential system with filter band pass at 1-30 Hz. An oculogram channel with electrodes above and below the eye was used to monitor eye movement artifacts. Averaging epochs contaminated by artifacts were automatically rejected by the averaging computer. The sampling time was 800 ms and stimulus rate was 0.7/s. The ERPs to both target and non-target stimuli were averaged separately. Each test was repeated once for consistency of results. The latencies of the P_2 (P_2L) and P_3 (P_3L) components and amplitude of P_3 (P_3A) were measured.

In the patient group, the ERPs were done on admission (within 4 days of head injury) and repeated at intervals ranging from 30 to 240 days. The intervals differed for patients. The ERP results in patients were compared to those in normal controls. The P_2L and P_3L were defined as abnormal if the absolute latency was more than mean plus 2.5 standard deviations ($P_2L > 228.5$ ms and $P_3L > 383.1$ ms). The results were correlated with the GCS, LOC, post-traumatic amnesia (PTA), outcome and development of post-concussional symptoms (PCS).

Results

Normal subjects

The P_2L, P_3L and P_3L data in normal subjects and their correlation with age are shown in Table 1 and Fig. 1. There was no significant difference in P_2L, P_3L and P_3A between males and females.

Table 2
P_2 and P_3 in patients with concussion

No	Age years	GCS	LOC	PTA	P_2 latency msec		P_3 latency msec		P_3 amplitude μv		Interval days	PCS
					First	Repeat	First	Repeat	First	Repeat		
1	9	15	10	15	304	158	500	230	6.0	7.5	30	Nil
2	14	13	10	15	284	163	393.6	339.2	6.2	14.2	24	Giddiness
3	18	14	15	15	156.8	86.4	252.8	243.2	13.3	14.8	30	Nil
4	22	13	20	30	172	158	370.3	323	5.8	8.6	235	Nil
5	24	14	15	5	156	153	326.4	316.8	18.7	28.1	35	Nil
6	25	15	15	15	192	166.4	329.6	310.4	13.6	17.0	30	Nil
7	25	14	10	10	256.2	264.4	388.6	313.6	10.5	29.1	100	Nil
8	25	15	0	15	201	170	385.2	320.6	2.4	9.4	35	Poor memory
9	27	15	2	5	169.6	160	300.8	278.4	15.8	18.6	250	Nil
10	29	15	5	5	169.6	163.2	300.8	275.2	7.4	8.3	30	Nil
11	29	15	30	30	166.8	156.8	480	313.6	4.5	19.5	195	Nil
12	41	13	10	45	185.6	172.8	345.6	265.6	8.9	18.9	240	Nil
13	60	14	30	30	176.8	156.8	278.4	256	8.6	10.9	100	Nil
14	19	15	5	5	163	153	339.2	281.6	15.0	11.3	53	Nil
15	56	15	0	0	176	172	438.4	275.2	5.9	9.2	45	Nil
16	15	14	5	5	160	140	322	280	12.8	16.8	40	Nil
17	21	14	15	15	240	180	320.2	300	3.9	10.9	50	Nil
18	18	13	20	60	166.4	120	426.4	320	7.12	10.2	35	Nil
19	18	15	20	20	170.2	160.2	340	310	8.5	15	60	Nil
20	51	15	20	20	176	150	320	290	4.5	9	50	Nil

Abbreviations: GCS: Glasgow Coma Scale; LOC: duration of loss of consciousness following head injury in minutes; PTA: post traumatic amnesia in minutes; Interval: interval between first and repeat evoked potential recordings; PCS: post concussional symptoms.

Patients with concussion

These patients' ages ranged 10-60 years; there were 18 males and 2 females. At admission they reported LOC ranging 0-30 min (mean 12.8) and PTA ranging 0-60 min (mean 18). Examination revealed GCS ranging 13-15 and no focal neurological deficits (Table 2). They all recovered completely and were discharged within 4 days. PCS of giddiness and loss of memory respectively were seen in 2 patients on follow up (Table 2). The initial P_2L and P_3L (at admission) were abnormal in 20% and 35% of patients respectively.

The initial prolongation of P_2L was insignificant (P 0.16) and P_3L was significant (P 0.002) by Student t test. A significant initial attenuation of P_3L was also seen in comparison to normals (P 0.003).

However, repeat testing revealed improvements (return to normal values) in P_2L, P_3L and P_3A in all patients (Table 2). The P_2L, P_3L and P_3A improved by mean 32.6 ms, 72.5 ms and 6.3 μv respectively. Paired t tests showed these improvements to be significant $P = 0.002$, $P = 0.0005$ and $P = 0.0003$ respectively for P_2L, P_3L and P_3A. The repeat tests were done after intervals ranging from 30-240 days. The improvements in these parameters were not significantly different between those tested after 30 days and those tested much later. These parameters and their correlation to the neurological assessment are shown in Table 2. Abnormalities of P_2L, P_3L and P_3A did not show significant correlation with the GCS, duration of LOC and PTA or development of PCS.

Discussion

The normal values for P_2L, P_3L, and P_3A are similar to those reported by others (16, 17). However a positive linear correlation with age was not seen in our subjects (Fig. 1). The significant abnormalities of P_2L, P_3L and P_3A in patients at admission and return to normalcy on repeat testing indicate that these are sensitive

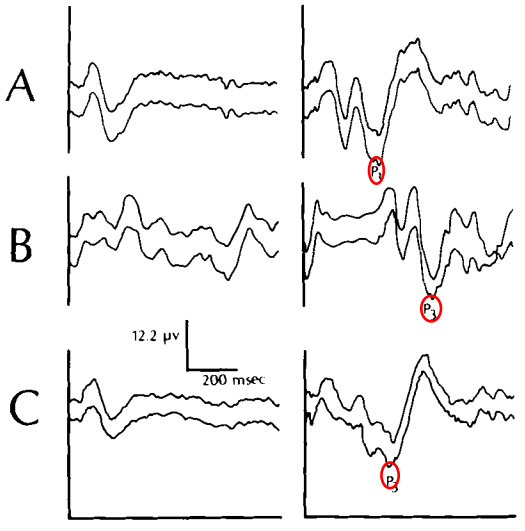

Fig. 2. The P_{300} in (A) normal subject, (B) patient after concussion, (C) the same patient after 30 days. Each test has been done twice for consistency. Note the prolonged P_{300} in latencies in B and return to normal in C.

parameters in detecting the cerebral dysfunction that occurs in concussive head injuries. Of the three, P_3L is the most sensitive parameter on account of its abnormality in a larger number of patients and a greater degree of abnormality. In their study on patients with severe head injury, Olbrich et al 1986 found the P_3 to be a sensitive indicator of cognitive impairment that correlated well with findings on neuropsychological tests. In their patients, repeat testing after 5-6 months showed that while cognitive abnormalities returned to normal, prolongation of P_3L persisted, suggesting residual cerebral dysfunction (14). In contrast, in the present study all parameters returned to normal limits indicating the short-lived cerebral dysfunction in cerebral concussion. This fact has been reported by Gentilini et al (1985) who found that cognitive impairment did not persist after one month after minor head injury (3). The abnormalities in P_2L, P_3L and P_3A did not correlate well with parameters of head injury such as LOC, PTA, GCS or development of PCS. A similar lack of correlation between cognitive impairment (on neuropsychological testing) and these parameters in minor head injury has been documented (2).

Studies of the scalp distribution of the auditory N_1-P_2 complex in normals, suggest the primary auditory cortex of both hemispheres as the neural generators of these components (19, 20). Intracranial depth electrode and extracranial magnetic recordings have provided evidence that the N_2-P_3 components are generated by amygdala and hippocampus (21, 22). These ERPs are thought to be time-locked synchronous neural electrical activity that arises from these structures in association with the processes of perception and cognition (7). The abnormalities of these ERPs in the present study indicate dysfunction or damage to these structures consequent to cerebral concussion. The improvement in the ERPs denotes the transient nature of the dysfunction/damage. Rather than the absolute values of the ERP latencies and amplitudes, the abnormality (cerebral dysfunction) is better characterised by the degree of improvement on repeat testing. It is of interest to note that recent studies strongly suggest a cholinergic role in the generation of the P_3 potential (23). Anticholinergic drugs abolish and cholinergic drugs restore the P_3 (24). Amongst other factors, cholinergic depletion has been postulated as the possible pathophysiology of cerebral concussion (25). A link between P_3 abnormalities and cerebral concussion based on cholinergic dysfunction is a possible hypothesis and a field for future research.

In conclusion, the P_3 constitutes a simple laboratory test that is a sensitive and objective measure of cerebral dysfunction in concussive head injuries and we recommend its regular use for this purpose.

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Address
Dr. Pratap-Chand
Department of Medicine
University Hospital
15990 Kubang Kerian
Kelantan
Malaysia