Title:

Correlations between neuropsychological test results and P300 latency during silent-count and button-press tasks in post-traumatic brain injury patients

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Abstract:

To evaluate the correlations between memory function and intelligence and event-related potential, the P300 component for different tasks was studied for 30 post-traumatic brain injury patients (mean age 31.6 ± 13.7 years; 23 male and 7 female). Memory function, intelligence, and depression were measured by using the Mini-Mental State Examination, the revised Wechsler Adult Intelligence Scale and the Self-Rating Depression Scale, respectively. P300 latency was measured during silent-count and button-press tests at three midline scalp (Fz, Cz, and Pz) sites for all subjects by using an auditory 'odd-ball' paradigm. Neuropsychological memory score was predicted by intelligence score, but neurophysiological P300 latency was predicted by memory score for the silent-count test and by intelligence score for the button-press test. These results show that the P300 event-related potential component is sensitive to the diverse nature of cognitive deficits in post-traumatic brain injury patients during different types of discrimination tasks. However, future research is necessary to replicate and extend these findings.

Key words: P300 latency, silent-count, button-press, memory score, intelligence score, post-traumatic brain injury patients.

(Text)

Introduction: Traumatic Brain Injury (TBI) is due to accidents, falls, and various types of violence. After recovery from an acute phase of TBI, patients usually receive rehabilitation at a hospital in order to reduce the disability. Neurological disabilities such as cognitive and attention deficits occur frequently as a common result of TBI.

Cognition may be divided into domains such as memory, intelligence, attention, and executive functions. Memory is the cognitive part that is usually impaired in a traumatic brain injury patient, and this impairment may persist for several years [1]. Many batteries exist to evaluate neuropsychological and neurophysiological tests among TBI patients, such as MMSE, WAIS-R, and SDS, which are thought to reflect the cognitive processes of memory function, intelligence, and affective disorders neuropsychologically. Furthermore, event-related potentials (ERPs) are thought to be a neurophysiologic sign of those cognitive processes. The Intelligence Quotient (IQ) as a measurement of cognitive level has a limited use although IQ has been established as the basis for measuring defective brain performance especially correlated with low intellectual efficiency [2]. Barrett and Eysenck have sought the correlations between IQ scores and the parameters of evoked potentials [3].

Auditory evoked potentials have been widely studied in patients with severe traumatic brain injury [4, 5, 6]. Most studies reveal short latency potentials reflecting brain stem activity, but few studies exist on long latency auditory-evoked potentials (LLAEPs), either in the acute phase [7, 8], or in the long term [9,10]. ERP (P300) has received by far the most attention from researchers interested in the neurophysiological correlates of cognitive processes and conscious experience. Several factors have been shown to influence an individual's ERP values. Some journals include studies regarding how the factors of dementia, depression, and intelligence affect ERP amplitude and latency. Major depression is a frequent and important potential sequela of TBI [11]. One study has found a 26% rate of major depression among acute head trauma patients, and of those patients who were not acutely depressed, 27% went on to develop major depressive episodes within one year [12]. Studies have also shown disturbances in auditory event- related potential (ERP) in some patients with major depression [13], but not in all; only a few studies report a prolonged P300 latency in depression [14]. However, ERPs provide important information about central nervous system activity in conjunction with psychological events.

Some studies demonstrating diverse methodologies (e.g. auditory, visual, proprioceptive stimulation, oddball, and single tone to several tones, silent count, and button press) may influence ERP latency and amplitude [15, 16]. The goal of this study, however, is directed toward illuminating how different cognitive conditions correlate across different paradigms or tasks with P300 latency. To our knowledge no document exists on the relationship of dementia and IQ with ERP latencies in two different tasks (silent and button) in post-traumatic brain injury patients. Therefore, by means of recording P300 latency we consider the relationship between P300 latency and tasks (silent-count and button-press) carried out by post-TBI patients.

Subjects and Methods:

Thirty patients who had suffered from moderate to severe traumatic brain injury and were undergoing treatment in a rehabilitation hospital were included in this study. Post-TBI patients with the length of a loss of consciousness (LOC) of less than three days, TBI patients who were unable to attend neuropsychological and auditory ERP testing due to aphasia, TBI patients with severe attention deficits, and TBI patients with a history of drug abuse were excluded. One 8 year old TBI patient who did not perform the silent-count paradigm was also excluded. TBI patients who were occasional social alcohol drinkers were included. The patients included 23 males and 7 females with a mean age of 31.6 years ± 13.7. The thirty subjects' descriptive statistics are given in Table 1.

Radiology (MRI) findings

Traumatic brain injury occurs in a variety of forms. There are no satisfactory procedures available for the assessment of brain injury. In this study we assessed the 30 patients into three categories: 1) 17 patients with diffuse axonal injury (DAI), 2) combined diffuse and focal injury of 7 patients (bilateral frontal contusion, left frontal-temporal contusion, two with a left frontal contusion, bilateral frontal-temporal haematoma, right temporal contusion, and left frontal contusion), and 3) 6 patients with focal injury(left temporal contusion, bilateral frontal-temporal contusion, right temporal contusion, right frontal-temporal contusion, left occipital-temporal contusion, and left temporal contusion).

Neuropsychological Tests

The patients were evaluated by the Mini-Mental State Examination (MMSE), which is made up of five subtests: orientation, registration, calculation, recall and language, with a maximal total score of 30. The Wechsler Adult Intelligence Scale-Revised form (WAIS-R) consisting of a verbal scale (VIQ) determined by 6 subtests and a performance scale (PIQ) determined by 5 subtests was used for the measurement of the subjects' intelligence, and the results of the tests were expressed in three forms of Intelligence

Quotients (IQ); the VIQ, PIQ, and full-scale IQ (FIQ). Patients completed the Zung Self-rating Depression Scale (SDS) [17]. The SDS is a validated 20-item questionnaire to assess depressive syndrome. Half the items on the SDS are reverse coded. Individually endorsed items on a four-point scale ranging from “none, or little of the time” to “most, or all of the time”, and these responses are assigned numerical values from 1 to 4, respectively. Scores range from 20 to 80.

Neurophysiologic examination (ERP recordings);

ERP (P300) latencies of all subjects were measured by an ‘oddball paradigm’ wherein the patients were asked to count silently in ‘silent count paradigm target tones (60 dB sound pressure level (SPL), low frequency (20%), high pitched (2000Hz)) presented binaurally by ignoring the standard tones (60 dB SPL, high frequency (80%), and low pitched (1000Hz) non-target tones). The subjects had to tell the examiner the number of the target tones upon completion of the task. The same tests with the same procedure were done at different sessions with the ‘button-press paradigm’. In the button-press paradigm the patients were asked to press a button instead of counting as quickly as possible at the appearance of the target tones by paying no attention to the non-target tones. Tone duration was 100ms with a rise/fall time of 10 ms. Amplifiers had a band pass of 0.1Hz – 50 Hz. The stimulus rate was 0.5 Hz. EEG activity was recorded from the midline (Fz, Cz, and Pz) scalp sites with Ag/AgCl electrodes placed on the sites using international 10/20 systems. Linked earlobe electrodes were used as a reference and the forehead as the ground. 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. Thirty artifact-free potentials were averaged following target stimuli. Waveforms of 100 milliseconds before stimulus were analyzed to refer to the baseline.

Statistics:

All variables were checked for normality, heterogeneity of variance and outliers. P300 differences between silent-count and button-press tactics were ascertained by means of the Wilcoxon Signed Ranks Test. Relationships between variables were assessed with Pearson's correlation coefficients and multiple regression analysis.

Results:

The significant difference of P300 latency between silent- count and button- press strategy has been observed only at the Cz site, but there was a clear drift of longer P300 latency on silent-count strategy, compared to the button press at all scalp sites (Figure). Table 2 shows the result of a simple correlation between neuropsychological tests and age. The MMSE showed a strong positive correlation with PIQ (r=.545, p=.002) and FIQ (r=.584, p=.001), also showed a positive correlation with VIQ (r=.434, p=.019). Age had a negative correlation with MMSE and a positive correlation with WAIS-R. SDS had a positive correlation with age and a negative correlation with MMSE and WAIS-R, but those correlations were not reached at a significant level. To investigate the effect of MMSE on other factors (Table 1), stepwise regression analysis revealed that PIQ had a significant effect on MMSE (Table 4).

Table 3 shows the correlation coefficients between the regional P300 latency with neuropsychological tests. P300 latency shows a negative correlation with MMSE and WAIS-R at all three scalp sites in both the silent-count and button-press paradigms. P300 latency with MMSE at Fz (r=-0.495, p=.003), Cz (r=-0.361, p=.025), and Pz (r=-0.39, p=.017) sites at the silent-count paradigm reached a significant level. At the button-press paradigm, P300 latency with MMSE at Fz (r=-0.372, p=.022) and Pz (r=-0.33, p=.038) scalp sites reached a significant level. Following stepwise multiple regression analysis, MMSE had a significant effect on P300 latency at Fz and Pz sites only on the silent-count strategy (Table 4). In the provision of P300 latency with WAIS-R, VIQ at Cz (r=-0.323, p=.044) and Pz (r=-0.351, p=.031), PIQ at Fz (r=-0.459, p=.005), Cz (r=-0.322, p=.042) and Pz (r=-0.385, p=.018), and FIQ at Fz (r=-0.371, p=.022), Cz (r=-0.342, p=.032) and Pz (r=-0.385, p=.018) sites show significant negative correlation at the button-press strategy. Later on regression analysis, PIQ at Fz and FIQ at Pz sites had a significant effect on P300 latency by button-press strategy (Table 4). P300 latency also had significant positive correlation with SDS at Fz (r=0.491, p=.022) and Cz (r=0.439, p=.007) scalp sites at silent-count strategy. SDS had no significant effect on P300 latency after regression analysis.

Discussion:

Cognitive changes such as memory, intelligence, and non-cognitive changes such as depression, psychosis, and over-activity occur frequently in post-traumatic brain injury patients. Cognitively deficit patients need more time to process information in their central nervous systems. Event-related potentials latency reflects the impaired information processing in TBI patients [18]. P300 components reflect the amount of cognitive resources devoted to task performance. One of the most widely studied long latency components is the P300, which is related to the processing of signals. According to these findings, it appears that a trend of association of ERP latencies with cognitive function in post-traumatic brain injury patients exists. The negative correlation between MMSE score and P300 latency were found in a study among a control of 118 healthy subjects [19], in Parkinson's disease patients [20], and in another 39 cases (16 cases of multiple cerebral infarction, 11 cases of chronic alcoholism, 5 cases of Alzheimer's disease and 7 cases of healthy control patients) at silent-count strategy [21]. Montserrat Zurron and Fernando Diaz [22] investigated the correlation between long latency auditory-evoked potentials and IQ in both active and passive paradigms; significant negative correlation between IQ and evoked potentials was found only at active oddball experiments similar to other experiments [23, 24]. The focal point of these studies was that impairments resulting from diffuse patterns of cerebral injury may manifest with more complex cognitive processing in complex tasks.

The specific effects of button-pressing on P300 obtained by pure tones are not well known [16]. A button-pressing strategy results in an shorter P300 latency along the midline comparative to a silent-counting strategy, as has been depicted by Polich in 1987; and Barret et al., in 1987, in a group of 27 healthy subjects [15, 25]. Likewise the shorter P300 latency on button-pressing tasks relative to the silent-counting strategy has been examined in the 30 post-traumatic brain injury patients in this study (Figure). Between the two different tasks, the silent-counting tasks were comparatively more difficult than the button-pressing tasks because in the silent count the subjects had to remember the target tones. Thus increasing the cognitive load in task demands causes increase in P300 latency [26]. Prolonged ERP latencies have been found in normal aging [27], and P300 latency increases with age at a rate of 1-2 ms every year from adolescence or early adulthood [28, 29]. In this study the positive correlation between P300 latency and age are found in silent-count strategy although not reaching a significant stage. Of interest, however, is a negative correlation between P300 and age observed on the button-press strategy although not reaching a noteworthy level. A probable explanation for this negative correlation is that on the button-press, the task load is decreased when compared to the silent-count for the same group of patients. A prolonged P300 latency has also been reported in few studies on depression [30]. In terms of a positive correlation between SDS and P300 latency in the silent-count paradigm in this study may include similar mechanism that increased load increases latency.

Observing the distribution of P300 ERP component latency values in Table 3 obtained from both the silent-count and the button-press paradigm, it appears that two cognitive functions, memory and intelligence, have negative correlations with ERP latencies. The MMSE is developed for the assessment of memory function, and it includes subtests on registration and recall [31] and WAIS-R is the most widely used tests to measure individual intelligence. To uncover which tasks correlate better with the two cognitive functions, memory and intelligence, the two tasks; silent-count and button-press were done. Memory score (MMSE) correlated with P300 in both the silent-count and the button-press paradigm while the intelligence score (WAIS-R) correlated with P300 components at the button-press strategy. Following regression analysis, there was a significant effect of memory score on P300 latency in the silent-counting tasks and a significant effect of the intelligence score on P300 latency in the button-pressing task, while WAIS-R and MMSE significantly correlated positively with each other, and PIQ had a significant effect on MMSE (Table 4). If the patients in this study, however, share a discrepancy in memory and intelligence due to widespread brain injury, then during the silent-counting strategy, we may presume that cognitive (memory) deficits prevent the patients to overcome the task difficulties. On the other hand cognitive (intelligence) deficits is acceptable to overpower the task demand during the button-press paradigm, since memory function is weighted down by mental count and remembering the oddball target tones. This phenomenon is indicating some different neurobiological procedures motivate the different tasks in two cognitive deficits. The precise elucidation of this phenomenon is intricate. In general, in the button-press strategy the cognitive load is decreased, since the subjects do not need to memorize mentally the current count, but in the neurally-damaged subjects, the intelligence function might be loaded as a cognitive resource to maintain the task by giving additional attention to the motor output, thus they press the button as early as possible when the target tones are presented, which may be an alternative reason for this incident. The neuropsychological memory score was predicted by an intelligence score, but neurophysiological P300 latency was predicted by a memory score on silent-count strategy and by an intelligence score on the button-press strategy. The results indicate that the P300 ERP component is sensitive to the diverse nature of cognitive deficits in post-traumatic brain injury patients during different patterns of discrimination tasks. However, future research requires replicating and extending these findings.

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Figure: P300 latency differences between silent-count (white column) and button-press (black column) tasks

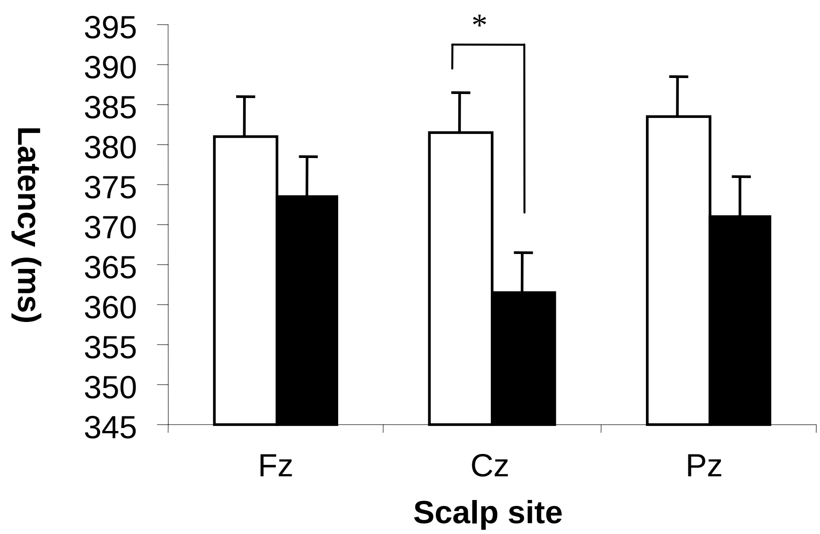

Table 1. The descriptive statistics of thirty post-traumatic brain injury patients

	Mean	Std. Deviation	Minimum	Maximum
Age	31.6	13.7	11	66
Onset	46.8	57.8	2	240
LOC	26.2	19.8	3	70
MMSE	26	4.6	9	30
VIQ	87.3	20.6	50	128
PIQ	85.8	22.1	46	123
TIQ	83.8	22.3	46	119
SDS	46.6	9.9	29	70

Age in years, onset (time since injury) in months, LOC (length of loss of consciousness) in days

Table 2. Relationships between age, memory score (MMSE), intelligence score (WAIS-R; VIQ, PIQ and FIQ), and depression score (SDS)

	MMSE	VIQ	PIQ	FIQ	SDS
Age	-.122	.364	.162	.301	.284
	.521	*.052*	*.391*	*.106*	*.128*
MMSE		**.434***	**.545****	**.584****	-.141
		.019	*.002*	*.001*	*.459*
VIQ			**.708****	**.932****	-.180
			.000	*.000*	*.350*
PIQ				**.893****	-.067
				.000	*.724*
FIQ					-.152
					.424

* p<.05, ** p<.01

Table 3. Correlations coefficient between P300 latency and neuropsychological tests at three scalp sites for different tasks

	Silent count			Button press		
	Fz	Cz	Pz	Fz	Cz	Pz
Age	0.269	0.247	0.136	-0.105	-0.22	-0.186
	0.15	*0.187*	*0.475*	*0.58*	*0.244*	*0.324*
MMSE	**-0.495****	**-0.361***	**-0.39***	**-0.372***	-0.289	**-0.33***
	0.003	*0.025*	*0.017*	*0.022*	*0.061*	*0.038*
VIQ	-0.23	-0.123	-0.106	-0.179	**-0.323***	**-0.351***
	0.115	*0.262*	*0.292*	*0.176*	*0.044*	*0.031*
PIQ	-0.229	-0.266	-0.274	**-0.459****	**-0.322***	**-0.385***
	0.112	*0.077*	*0.072*	*0.005*	*0.042*	*0.018*
FIQ	-0.263	-0.208	-0.203	**-0.371***	**-0.342***	**-0.385***
	0.08	*0.135*	*0.141*	*0.022*	*0.032*	*0.018*
SDS	**0.491****	**0.439****	0.273	0.025	0.01	0.006
	0.022	*0.007*	*0.108*	*0.897*	*0.959*	*0.974*

* p<.05, ** p<.01

Table 4. ANOVA table of stepwise multiple regression analysis

Model	Sum of squares	df	Mean squares	F	Sig.	Predictors	Variables
Regression Residual Total	9153.234 30556.007 39709.241	1 27 28	9153.234 1131.704	8.088	.008	MMSE	P300 (at Fz site, count strategy)
Regression Residual Total	9923.032 56913.933 66836.966	1 27 28	9923.032 2107.923	4.707	.039	MMSE	P300 (at Pz site, count strategy)
Regression Residual Total	7418.736 26516.712 33935.448	1 27 28	7418.736 982.100	7.554	.011	WAIS-R (PIQ)	P300 (at Fz site, button press)
Regression Residual Total	17861.782 97046.908 114908.69	1 27 28	17861.782 3594.330	4.969	.034	WAIS-R (FIQ)	P300 (at Pz site, button press)
Regression Residual Total	186.531 369.676 556.207	1 27 28	186.531 13.692	13.624	.001	WAIS-R (PIQ)	MMSE