Assessment of cognitive functions in posterior circulation ischemic stroke

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Abstract: Background: Posterior circulation ischemic stroke refers to ischemic brain insult restricted to vertebrobasilar vascular tree. Cognitive impairment occurs frequently after stroke, commonly involving memory, orientation, language, and attention. The presence of cognitive impairment in patients with stroke has important functional consequences, independent of the effects of physical impairment. **Objectives:** Assessment of cognitive functions by psychometric tests and patterns event related potentials for early management of subtle cognitive impairment in vertebrobasilar ischemic stroke patients. **Methods:** This case-control prospective study included 24 vertebrobasilar ischemic stroke patients admitted to our stroke unit and outpatient clinic during a six-month period and 20 control subjects matched for age, sex and educational level. The patients were divided into four groups according to the ischemic region, which included 8 thalamic, 7 cerebellar, 5 brainstem and 4 occipital stroke patients. Assessments included the Mini-Mental State Examination (MMSE) and Cognitive Abilities Screening Instrument (CASI) for cognition and (P300 and P600) Event-Related Potentials (ERP) waves were conducted. **Results:** Patients with vertebrobasilar stroke had lower MMSE score (P=0.001) and CASI score (P=0.001) than control. 33% of vertebrobasilar ischemic stroke patients have cognitive impairment by psychometric tests. Impaired cognitive domain included attention, memory and visual-spatial abilities. Patients with thalamic infarction have experienced more cognitive dysfunction than other subtypes. Presence of more than one stroke had a negative impact on cognitive functions in vertebrobasilar ischemic stroke. Prolonged P300 & P600 latency and reduced amplitude are correlated with cognitive impairment. **Conclusion:** In vertebrobasilar stroke patients, cognitive impairment is one of the most important manifestations, it occurred in 33 %. CASI is an accurate and reliable test for detecting cognitive impairment in vertebrobasilar ischemic stroke. ERPs (P300 & P600) waves are considered of value in assessment of cognitive dysfunction and can be used for following up patients. Studies of stroke outcome and intervention should take into account both cognitive and physical impairments.

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1. Introduction

Stroke continues to be a major public health problem that ranks in the top four causes of death in most countries and is responsible for a large proportion of the burden of neurologic disorders. One of the leading causes of severe neurologic disabilities is cerebrovascular stroke ***(Stebbins and Nyenhuis, 2008).*** In fact, it is the second leading cause of cognitive disabilities and dementia ***(Mok et al., 2005).*** Calculation, executive functioning (the integration of multiple and complex processes), and visual perception/construction are the cognitive areas most often affected during the first several weeks after a stroke **(Nys et al., 2005).** The frequency of impairment is similar because of either isolated brainstem or isolated cerebellar infarct, and similar tocognitive impairment with cerebral hemispheric lesions ***(Hoffmann and Schmitt, 2004).*** Event related potentials are neurophysiological measurements that provide a valuable estimation of cognitive function. Event-related potentials (ERPs) measure brain activity during cognitive processing have useful information on stroke-related cognitive decline. A promising prospect within this field is the use of long latency or endogenous ERPs such as the P600 because of their association with cognitive constructs and processes ***(Nunez-Pena et al., 2004).*** Studies differ with each other whether P300 and P600 has the same neuronal origin or not. The P600 normally found for a broad range of syntactic anomalies appears to be 'just' a P300-like component in the sense that it reflects the same process of detecting a task-relevant and unexpected event. The finding that the generation of the P600 is dependent on basal ganglia and cingulate gyrus which do not play a role in eliciting a P300 response is an evidence for the assumption that we deal with two different components **(*Tylor, et al., 2007*). *Frodl-Bauch et. al., (1999)*** suggested that thalamus is considered as possible location of the P300 generators.

Subjects and Methods

The study was carried out at Al-Hussein hospital, Al-Azhar University to assess cognitive functions by psychometric tests and patterns of event related potentials for early management of subtle cognitive impairment in vertebrobasilar ischemic stroke patients.

They were divided into two main groups:

Group I: included twenty-four (24) patients with vertebrobasilar ischemic stroke and this group included 15 males and 9 females. Their ages ranged between 48 and 66 years (with a mean 57.644 ± 4.995 years).

Group II: included twenty (20) normal healthy volunteers (12 males and 8 females). Their ages ranged between 49 and 67 years (with a mean age 55.156 ±5.215 years). All subjects were matched for age, sex, education level with group I and free of any physical, psychiatric or neurologic impairment including hearing affection.

Exclusion criteria were patients with anterior circulation ischemic strokes, history of prior stroke, hearing impairment, psychiatric or systemic disease affection cognitive functioning, or history of alcohol or substance abuse.

All patients were submitted to:

1-Detailed medical and neurological history.

2-General medical examination.

3-Neurovascular examination.

4-Neuro-imaging as MRI Brain.

5-Neuropsychological assessment:

a-Mini-Mental State Examination (MMSE) is a common widely used method for assessment of cognitive status ***(Folestein et al.1975)***.

b-Cognitive Abilities Screening Instrument (CASI) is more comprehensive than most screening tests of cognitive abilities. The cutoff point equal or less than 67 for dementia ***(Teng et al., 1994)***.

6-Neurophysiological assessment (Event Related Potentials P300 and P600 waves):

P300 and P600 were recorded using an oddball paradigm. Tow tones were presented in a random series at a rate of 0.5/sec. A frequent tone (1000 Hz) was done with intensity of 60 Db. Analysis of the P300 and P600 involve waveform identification, amplitude, latency, and number of peaks of P300 and P600 (***Polich, 2007***).

7-**Statistical analysis:**

The data were analyzed using statistical program for social science (SPSS) to obtain; descriptive data (Mean, standard deviation) & analytical statistics (student "t" test, chi square, Pearson correlation coefficient r and one-way analysis of variance {ANOVA}). (P value less than 0.05 is considered significant and 0.01 as highly significant).

3. Results:

Age has a significant inverscorrelation with CASI (P=0.023) but not with MMSE. The higher educational level the patient receives the higher CASI scores he/she achieves. There is highly significant correlation between neuropsychological tests (MMSE and CASI) in one side and years of education (P < 0.00). No significant difference was found between male and female regarding psychometric tests (MMSE and CASI) and neurophysiological tests (P300 latency and amplitude, P600 latency and amplitude).

The prevalence of cognitive dysfunction (as evidenced by bad performance in psychometric tests {MMSE< 24 and CASI < 67}) in vertebrobasilar ischemic stroke patients was 33.33%. The performance of control was better than vertebrobasilar ischemic stroke patients in MMSE and CASI. There is highly significant difference between patients and control as regard neuropsychological tests (CASI and MMSE) being affected in patients group (table 1). More over thalamic subtype patients performed worse than other subtypes in both tests then occipital, cerebellar and brainstem infarctions respectively.

Table (1): comparison between patients and control regarding neuropsychological tests (CASI and MMSE):

Groups					T-test	
		Range	Mean ± SD		T	P-value
MMSE	Controls	30 - 30	30.000 ± 0.000		6.193	<0.001*
	Patients	17 - 29	24.542 ± 3.934			
CASI	Controls	86 - 97	91.500 ± 3.285		7.574	<0.001*
	Patients	58 - 90	74.625 ± 9.486			

In control group P300 latency ranged between 295 and 317 with a mean (307±5.6 msec.) and P300 amplitude was 24.6±3.5 uV. On other hand P300 latency in patient group ranged between 302 and 440 with a mean (357±42 msec.) but P300 amplitude was 14.6±4.4 uV. Also in control group P600 latency ranged between 615 and 645 with a mean (615 msec.) and P600 amplitude was 9±2.8 uV. On other hand P600 latency in patient group ranged between 603 and 762 with a mean (676±42 msec.) but P300 amplitude was 5±3.9 uV.

There is highly significant correlation between age, years of education and neurophysiological tests. There is highly significant direct correlation between neuropsychological tests (MMSE and CASI) and

neurophysiological tests (P300 and P600) latency but inverse with their amplitude.

There were 10 patients (41.6%) with right sided infarctions (3 thalamic, 4 cerebellar, 2 occipital and 1 midbrain) and 14 patients (58.4%) with left sided infarctions (5 thalamic, 3 cerebellar, 2 occipital, 3 pontine and 1 midbrain).

Attention was markedly affected in brainstem infarction. However, attention was markedly affected in thalamic infarction and to lesser extent memory.

Memory was markedly affected in cerebellar infarction and to lesser extent attention. Visu-spatial abilities was markedly affected in occipital infarction.

P300, P600 latencies was significantly prolongedand amplitudes is significantly reduced in patients group (P<0.001) than control group.

P300, P600 latencies is prolonged in thalamic, cerebellar, occipital and brainstem infarctsrespectively.

P300, P600 amplitudes was reduced in thalamic, occipital, cerebellar and brainstem infarctsrespectively.

Patients with lower CASI scores have prolonged P300, P600 latencies and lower P300, P600 amplitudes. Cognitive tests were correlated inversely with ERPs latencies and directly with their amplitudes. P300 wave was significantly affected more than P600 in detecting cognitive decline in vertebrobasilar ischemic stroke.

4. Discussion

Cerebrovascular stroke (CVS) is a risk factor for impaired cognitive functioning. Not only physical handicapping but also cognitive dysfunction after CVS can adversely influence the long-term survival after adjusting other predictors for stroke mortality ***(De Haan et al., 1995, Barba et al., 2000).***

In the present study, demographic determinants for post stroke cognitive impairment included increasing age and low level of education. The risk of post stroke cognitive impairment is increased with aging. Increasing age is an important risk factor for vascular diseases including CVS and vascular cognitive impairment. The decreased cerebral blood flow with age is a factor for brain damage and cognitive decline. It has been recently suggested that an age-related decrease in the buffering capacities of both the vessels and the craniospinal cavity favors cerebral hypoxia and reduction in cerebral arterial inflow (***Ballerd et al., 2002***). Also, patients with low levels of education were more vulnerable to post stroke cognitive impairment than educated patients. Recent reports confirmed a real association between educational attainment and the risk of dementia 50 to 60 years later ***(McDowell et al., 2007).*** It seems that patients with higher educational attainment have larger functional cognitive reserve and differences in lifestyle and risk factor profile which are protective against cognitive decline. Low levels of education were found to be associated with significant decline in incidental memory, psychomotor performance and perception ***(Ngandu et al., 2007).***

The frequency of cognitive impairment after CVS varies between studies. The results of this study revealed that cognitive impairment affects up to 33% of stroke survivors after stroke. In an exploratory effort, ***Tatemichi et al., (1990)*** reported post stroke cognitive impairment in 16% of patients in a stroke cohort aged 60 or more years. Also, they found in a subsequent hospitalized cohort studied three months after stroke, post stroke cognitive impairment was found in 26% which is matched with the present study. This goes in agreement with ***Jonkman et al., (1998)*** who reported that the incidence of cognitive impairment three months after stroke was 35%–37%, ***Pohjasvaara et al., (2000)*** who reported post stroke cognitive impairment in 31.8% and the results of this study come in contrast to ***Madureira et al., (2001)*** who found the frequency of post stroke cognitive impairment to be only 6%. In the opposite extreme ***Kalashnikova et al., (2005)*** found that the presence of post stroke cognitive impairment was as high as 88%. The identified significant difference of post stroke cognitive impairment percentage in this study may b (e related to size & site of infarction, exclusion of patients with anterior circulation ischemic stroke, patients with disturbed consciousness level, other neurologic, psychiatric or systemic disease affecting cognition, study design, population studied, use of certain neuropsychological tests as CASI and MMSE in the diagnosis of post stroke cognitive impairment, demographic characteristics, criteria used for the diagnosis of cognitive impairment, clinical manifestations, the preexisting cognitive level, lesion-related, radiological-associated factors as exclusion of hemorrhage, white matter changes, presence of cerebral atrophy, the time interval between onset of stroke and neuropsychological assessment as well as length of follow-up. In this study, attention was found to be affected in thalamic and brainstem infarctions, being more affected in thalamic infarction. Memory was significantly affected in cerebellar infarction then in thalamic infarction. Visu-spatial abilities are the more affected in occipital infarction. The Mini-Mental State Examination (MMSE) is one of the most popular screens of cognitive functioning however, it is not an ideal test for screening cognitive impairment in vertebrobasilarischemic stroke patients, this may be due to that the item composition of the MMSE does not appear to be well suited to the pattern of cognitive impairment associated with vertebrobasilarischemic stroke. Eight out of twenty-four of patients (33.3%)

had bad performance in the test most of them are of thalamic stroke subtype, this was near to results of ***(Khedr et al., 2009)*** who reported a sensitivity of the test to stroke-related cognitive impairment of 28%. The Cognitive Abilities Screening Instrument (CASI) is a more popular, recent and standardized test that assesses intelligence and cognitive abilities. Cognitive Abilities Screening Instruments (CASI) consists of 25 test items and provides quantitative assessment on attention, concentration, orientation, memories for past knowledge and present input, language abilities, drawing and writing abilities, list generating abilities, abstract thinking and judgment. The CASI is more comprehensive than most screening tests of cognitive abilities. In this study, control performed better in CASI test than vertebrobasilarischemic stroke patients, as there was direct correlation between MMSE and CASI. This goes in the same line with ***Sachdev et al., (2004)*** who proved decline in cognitive abilities in vertebrobasilarischemic stroke patients in comparison with healthy control using CASI. Attention, orientation, calculation, language, and motor skills, logical memory, associate learning, visual reproduction, drawing, and abstract thinking were significantly involved in post stroke cognitive impairment, there is affection of all cognitive domains to varying degrees between posterior circulation ischemic stroke subtypes. This goes in agreement with ***Kalaria et al., (2001), Ballard et al (2002), Claesson et al., (2005), Rasquin et al., (2005), Hachinski et al., (2006). Tay et al., (2006)*** who suggested that there is no consistent phenotype for stroke-related cognitive dysfunction because strokes can strike any region of the brain. If selected single impaired cognitive function is considered, 50%–75% of stroke patients are found to be affected**.** The Intracerebral origin of the P300 is most likely reflecting the summation of multiple, simultaneously occurring cognitive and brain processes that are engaged during the active processing of behaviorally significant stimulus events and functionally linked to one resource allocation and memory updating operations in the brain. These structures are important for learning and memory. P300 latency has been found to increase as the cognitive impairment symptoms increase. P300 latency is considered a consequence of attention process, speed of reaction, and immediate memory. The shorter P300 latencies indicate superior mental performance relative to longer latencies ***(khedr et al., 2009).*** P300 latency was prolonged and amplitudewas reduced in posterior circulation stroke patients than control. This delay appears to be due to a disorder in the processing of change in temporal sound patterns, this may be conceived as an extra time taken to compare the incoming sound with the contents of a temporally ordered sensory memory store (the long auditory store or echoic memory), which generates a response when the next expected frequency change fails to occur. This was in agreement with the study of ***Tylor JR, Olichney JM, (2007) and Khedr et al., (2009***) as bad performance in psychometric tests (MMSE and CASI) were associated with prolonged P300 latency.

On the other hand, P600 did not studied before especially in vertebrobasilar strokes; in this study, all of the patients were found to show prolonged P600 latency and reduced P600 amplitude which raises the possibility of association between vertebrobasilar ischemic stroke and memory functions. In this study, the ERPs was of benefit in detecting cognitive disability in vertebrobasilarischemic stroke patients even in subtle cases but P300 wave was more significant and more accurate in detecting the deficit than P600, thus the P300 is a fruitful tool in clinical research to identify abnormalities of cognitive processing especially when cognitive deficits may be subtle and less frank than in later stages. The size, location of lesion (s) with particular reference to the extent of white matter damage, vascular territory involvement, hemispheric and cortical involvement are known as important determinants of cognitive dysfunction ***(Pohjasvaara et al., 2000).*** Large sized infarctions are expected to produce more cognitive impairment compared to small sized infarction unless the small infarcts are in strategic locations e.g., thalamus even when they are lacunar as identified also in this study and this is in agreement with ***Tay et al., (2006). Vinters et al., (2000)*** described three pathogenic concepts of vascular dementias based on pathological and functional imaging data as follow: accumulated cortical infarcts, strategic subcortical infarcts and functional cortical disconnection. Hemispheric dominance involvement was more frequent in patients with post stroke cognitive impairment. Several studies suggest that intelligence or cognitive efficiency relies heavily on the integrity of language processing and hemispheric dominance. Although many studies have been conducted for identification of vascular risk factors for post stroke cognitive impairment, their findings were inconsistent and controversial ***(Stebbins et al., 2008).***

Conclusion:

Cognitive impairment is one of the most important manifestations of vertebrobasilar stroke patients, it occurred in 33 %. CASI is an accurate and reliable test for detecting cognitive impairment in vertebrobasilar ischemic stroke. ERPs (P300 & P600) waves are considered of value in assessment of cognitive dysfunction and can be used for following up patients. Studies of stroke outcome and

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