Assessment of Cognitive Dysfunction in Arteriosclerotic Patients in relation to Cerebral Blood Flow (Cerebral Perfusion)

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ABSTRACT

The aim of our work is to observe the changes in cognition and cerebral blood flow of patients with arteriosclerosis and multiple cerebral infarctions compared to healthy control subjects. Cognitive dysfunction in patients, reflected by P300 Long Latency evoked potential wave changes, is also meant to be correlated with cerebral blood flow velocities in both anterior and posterior circulations. Twenty-four patients with arteriosclerosis and multiple subcortical cerebral infarctions, and twenty healthy control subjects were included in the study with mean age 60.3 years and S.D. ±8.8. Cognitive functions were evaluated by the Mini-Mental State Scale Examination score (MMSSE) and the P300 long latency evoked potentials was checked in all cases. Also, the mean cerebral blood flow velocities (CBFV) were measured in all subjects, both patient and control groups. For the anterior circulation, the middle cerebral arteries (MCA), and anterior cerebral arteries (ACA) on both sides have been considered, and for the posterior circulation, the posterior cerebral artery (PCA) and vertebral artery (VA) on both sides as well as the basilar artery (BA) have been examined. The correlation between the mean blood flow velocity changes and the cognitive changes was evaluated. The results of the study revealed the presence of significant negative correlation between the P300 latencies changes and blood flow velocities changes in (PCA), (VA), and the (BA) in the patient group; the more delay in latency the more diminishing in the mean blood flow velocities. Also, significant negative correlation with the MMSSE and the mean blood flow velocities in the left (MCA) and (PCA) is found. We concluded from this study that there is correlation between the cognitive changes in the brain of arteriosclerotic patients with multiple subcortical infarctions and the diminished state of blood flow velocities in all blood vessels particularly the left (MCA) and the (PCA), (VA), and (BA). (Egypt J. Neurol. Psychiat. Neurosurg., 2006, 43(1): 295-301)

INTRODUCTION

The P300 latency has been used to evaluate the cognitive function but its source of generation has not yet been elucidated. The correlation between the P300 latency and the regional cerebral blood flow has not been yet fully investigated. In a recent study in 2005, it was reported that there are some changes in the P300 correlated with abnormality of the brain blood supply in the arteriosclerotic patients. A general cognitive dysfunction may occur in cases of arteriosclerosis and multiple subcortical ischemic lacunar infarctions, and the vascular cognitive impairment could be improved with the early diagnosis and secondary prevention and treatment.

PATIENTS AND METHODS

The 44 cases: 24 cases of multiple cerebral infarctions and 20 cases of healthy controls were included in the study with the mean age of 60 years ±8.8. The patients with multiple cerebral infarctions who had small infarcts in the territory of perforating arteries or in the deep white matter and/or periventricular lesions of high intensity on magnetic imaging were studied more than one month after the onset of cerebral infarction. The cognitive function was evaluated by using the MMSSE Score, and by measuring the P300 latency in both the patient and the control group.
Assessment of the mean cerebral blood flow velocities in the anterior circulation in the MCA, and the ACA bilateral, and the posterior circulation in the PCA, VA bilateral and the BA was done to correlate the cognitive changes with the changes of CBFV and to evaluate its possible source of generation.

METHODS

Recordings of P300 Long Latency evoked potentials were made in a sound attenuated room - with subject seated in a reclining chair. Bipolar recordings were made between silver-to-silver chloride electrodes at three midline sites: frontal (FT), central (CZ) and parietal (PZ), according to the 10-20 electrode system of the International Federation. A ground electrode was positioned at FPZ and indifferent ear - clip electrodes were attached to both ear lobules. The electrode impedance was less than 2 kilo - ohms.

Sounds were delivered binaurally through headphones. Tones were presented in a random sequence. Eighty five percent of the stimuli (frequency) were low-pitched tones of 1000 Hz and 50 milliseconds duration. The other fifteen percent of the stimuli (oddball) were high-pitched tones of 2000 Hz and 50 milliseconds duration. The ratio of high to low pitched tones was 1: 10 / sec. Intensity was 60 dB above hearing level (SPL) with a rise - fall time of 10 milliseconds. The EEG was amplified by 10000 (2 MK Counterpoint - Dantec amplifier) and the response of frequent and rare tones were averaged separately. We used a bandwidth of 0.5 - 40 Hz and a sensitivity of 20 UV.

A total of 500 epochs were averaged and data was monitored by a software procedure as it was sampled, and any data containing high voltage artifacts was automatically reflected. Prior to processing, all data were smoothed with a bi-directional digital filter.

Latencies and baseline - to - peak amplitudes of the individual components of the ERP curve were measured. These were designated N1, P2, N2 and P3.

N1 (N100) was the point of maximum negativity between 70 - 120 msec and P2 (P200) the maximum positive deflection between 140 - 230 msec in the average response to frequent stimuli. P3 (P300) was the positive wave deflection between 265 and 500 msec in the averaged response in the rare stimuli and N2 (N200) was the negative deflection immediately preceeding P300.

Latencies were measured at the point of maximum amplitude for each component using a cursor on the Counterpoint - Dantec visual display unit and by inspection of the pen-recorded trace. When the deflection did form a single sharp wave, the latency was measured at the point of intersection of the tangents to the up going and down going slopes measured from pen-recorded trace.

Subjects were instructed to count silently high pitched tones and report at the end of the trial how many high pitched tones they had heard. No task was assigned to the subjects.

Transcranial Doppler (TCD) used to detect the changes in the mean blood flow velocities. Using The TCD MDX – TCD-7 software (version 7.3) apparatus multi-channel Doppler operating at 2 MHz, Insonation of MCA, ACA, PCA through trasanstemporal window and VA, BA Insonated through the suboccipital window.

RESULTS

As regard the MMSSE score, there were significant differences between the control (score=30) and the patient group (mean score = 23±3). The other results can be summarized in the following tables and figures.

Table (1) shows that there was no significant difference (P=0.5) between the P300 latency in the patient and control groups yet it is more delayed in the patient group.

Table (2) shows negative correlation between the MMSSE and the P300 latency which means the more decrease in the MMSSE score, the more delay in the P300 latency and vice versa, yet it is insignificant.

Table (3) shows significant negative correlation (between the P300 latency and the MBFV) in the (PCA), (VA), and (BA), denotes the more the decrease in blood flow, the more the delay in P300 latency.

Table (4) shows significant negative correlation between the MMSSE and the MBVF in the left (MCA) and left (PCA), which denotes
the more decrease in the mean blood flow velocity, the more delay in P300 latency. Figure (1) illustrates the negative correlation between the delayed P300 latency and the diminished MBFV in the left MCA.

**Table 1.** Comparison between the P300 latency changes in the patient and the control group.

<table>
<thead>
<tr>
<th></th>
<th>P300 Latency Mean</th>
<th>S.D.</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>330</td>
<td>±59.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Control</td>
<td>318.5</td>
<td>±11.7</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2.** Correlation between the MMSSE score and the P300 latency changes in the patients' group.

<table>
<thead>
<tr>
<th></th>
<th>Mean (S.D)</th>
<th>Number of Patients</th>
<th>Correlation</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSSE</td>
<td>23±3</td>
<td>12</td>
<td>-0.522</td>
<td>0.082</td>
</tr>
<tr>
<td>P300 Latency</td>
<td>330±59.7</td>
<td>12</td>
<td>-0.07</td>
<td>0.800</td>
</tr>
</tbody>
</table>

**Table 3.** Correlation between P300 latency changes and the changes in the mean blood flow velocities (MBFV) in the PCA, VA, and BA.

<table>
<thead>
<tr>
<th></th>
<th>Mean (S.D)</th>
<th>Number of Patients</th>
<th>Correlation</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>P300 Latency</td>
<td>330±59.7</td>
<td>12</td>
<td>-0.07</td>
<td>0.800</td>
</tr>
<tr>
<td>MBFV in PCA</td>
<td>22.60±6.8</td>
<td>12</td>
<td>-0.09</td>
<td>0.661</td>
</tr>
<tr>
<td>MBFV in VA</td>
<td>25.04±2.9</td>
<td>12</td>
<td>-0.28</td>
<td>0.890</td>
</tr>
<tr>
<td>MBFV in BA</td>
<td>26.50±4.6</td>
<td>12</td>
<td></td>
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**Table 4.** Correlation between the MMSSE score and the changes in the MBFV in the left (MCA) and (PCA).

<table>
<thead>
<tr>
<th></th>
<th>Mean S.D.</th>
<th>Correlation</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSSE</td>
<td>23.20±3.03</td>
<td>-0.08</td>
<td>0.69</td>
</tr>
<tr>
<td>MBFV in left MCA</td>
<td>35.50±5.0</td>
<td>-0.06</td>
<td>0.76</td>
</tr>
<tr>
<td>MBFV in left PCA</td>
<td>22.70±4.50</td>
<td>-0.06</td>
<td>0.76</td>
</tr>
</tbody>
</table>
Fig. (1): The delayed P300 latency in relation to the diminished MBFV in the left (MCA) in one of the patients.

Fig. (2): Illustrates the relation between the delayed P300 latency and the diminished MBFV in the left (VA).
**DISCUSSION**

The P300 long latency evoked potentials is considered to reflect information processing in the brain and P300 latency has been used to evaluate the cognitive function. Multiple areas in bilateral cerebral hemisphere, the medial part of temporal lobe, hippocampus, and temporoparietal junction, prefrontal area infarction parietal lobe, mid brain, thalamus and basal ganglia has been considered to play a role in P300 generation[^6]. In the current study our results showed that there were more delay in P300 latency in the patient group than the control group, in spite that it is insignificant difference. As well as were the results of MMSSE which showed low score in the patient group more than the control group, considering that the selected patients were not complaining of clinical symptoms of cognitive changes but there was detection of subclinical cognitive affection by different tools. The current study revealed also negative correlation between the P300 latency and the MMSSE score. The less the score the patient has the more delay in P300 latency and this is in agreement with previous studies[^4].

In our study, it was found that there is a significant negative correlation between the P300 latency and the mean blood flow velocities mainly in the PCA, VA, and the basilar artery. This goes with the previous studies which explained that the thalamus has nerve fiber connections with the cerebral cortex, the limbic system, the basal ganglia and the decreased thalamus blood blow may be related to cognitive dysfunction[^4]. Other studies, reported the blood flow in the putamen and the thalamus were decreased more in multiple infarctions with severe dementia than in mild dementias[^9].

There is also significant correlation between the MMSSE and the mean blood flow velocity and the left MCA. This is in agreement with a study which found that the velocities of left MCA was remarkably decreased than in the control group[^5], and other study mentioned that the mean flow velocities in MCA bilateral were significantly diminished in comparison to control group[^3]. Other previous studies investigated correlation between P300 and positive emission tomography (PET) in various neurological diseases and suggested that the blood flow in the right parietal lobe, bilateral temporal lobes and thalamus is related to the problem of P300 latency[^7].
The P300 and cold xenon C.T. were investigated in neurological patients in some studies which suggested that lesions in the right cerebral hemisphere and thalamus are related to the prolongation of P300 latency. These results indicate that multiple cognitive domains are affected in cases of arteriosclerosis with multiple subcortical infarcts.

Clinicians should be aware that although cerebrovascular strokes usually show patchy cognitive deficits, general cognitive dysfunction may occur in mild cases. Such a concept of “vascular cognitive impairment” will improve the early detection of subclinical cognitive changes in patients with arteriosclerosis and multiple lacunar infarctions and this, of course, will promote better secondary prevention and treatment.

REFERENCES


الملخص العربي

تقييم الخلل المعرفي في مرضى تصلب الشرايين، وعلاقته مع معدل الارتواء الدماغي

صممت هذه الدراسة للوقوف على التغيرات التي تطرأ على الوظائف المعرفية ومعدل الارتواء الدماغي لمرضى تصلب الشرايين والاختلالات الدماغية المعتدلة، وعينت أيضا هذه الدراسة تحديد العلاقة بين الخلل المعرفي في المرضى من جهة (تمتала في التغيرات التي تنشأ على الموجات طويلة المدى للجهد المستفز والمعرفة باسم ب–300). ومعدل الارتواء الدماغي في كل الدورة الدموية الأمامية والخلفية من جهة أخرى.

أشمل البحث على أربعة وعشرين مريضاً من بينهم من مرضى تصلب الشرايين والاختلالات الدماغية تحت التقريرية المتعددة، بالإضافة إلى عشرين شخصاً أصحاء كعينة ضابطة.

وتم اختبار الوظائف المعرفية عن طريق فحص الحالة العقلية المصغر، بالإضافة إلى فحص الموجات طويلة المدى للجهد المستفز ب–300 في كل من العينة المريضة والعينة الضابطة. أما بالنسبة إلى معدل الارتواء الدماغي فقد تم قياسه في الدورة الدموية الأمامية من متصلة في الفردين الدماغي الأمامي والأوسط على الانتهاء، والدورة الدموية الخلفية ممتثلة.

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في الشريان الدماغي الخلفي والشريان الفقاري على اللاحقين، بالإضافة إلى الشريان القاعدي وأعقب ذلك تحليل مدى الارتباط بين التغييرات في معدل الارتداء الدماغي والتغييرات المصاحبة في الوظائف المعرفية.

أظهرت النتائج وجود ارتباط عكسي (نلاب) ذي دلالات إحصائية بين التغيرات في وقت ظهور الوجوه طويلة المدى للجهد المستمر، من جهة، وسرعة تدفق الدم في الشريان الدماغي الخلفي للعينة المريضة. من جهة أخرى، الموجودة نفس الارتباط العكسي أيضا بين درجات اختبار فحص الحالة العقلية المصغر وسرعة تدفق الدم في الشريان الدماغي الخلفي وأيضا الشريان الدماغي الأوسط على الجهة اليسرى.

ما تقدم يمكن استنتاج وجود نوع من الارتباط بين الخلل المعرفي ونقص الارتداء الدماغي (خاصة الشريان الدماغي الأوسط على الناحية اليسرى والشريانين الخلفي) في مرضى تصلب الشرايين والاحتشاءات الدماغية (تحت القشرة) المتعددة.