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Assessment of cognitive functions using cognitive evoked potential in patients with arterial hypertension

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Summary

Objective

To assess the possibility of cognitive dysfunction diagnosis using cognitive evoked potential in patients with arterial hypertension.

Material and methods

The study included 186 patients. The average age was 47.9±6.4 years. Cognitive function in all patients was evaluated using neuropsychological testing. Quantitative assessment of cognitive function was determined by the method of cognitive evoked potential (CEP).

Results

Patients were divided into two groups. The first group included 92 healthy individuals. The second group consisted of 94 patients with arterial hypertension (AH). The groups were comparable with respect to age and sex. The group of patients with hypertension was characterized with significant increase in the duration of the CEP (346.17±18.37

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and 335.78±16.57 msec respectively; p<0.01) and reduced amplitude (10.4±4.3 and 16.2±5.7 μV respectively; p<0.01), comparing with group of healthy persons. According to the test results, the hypertension group demonstrated decrease of memory (p<0.01) and cognitive functions in general (p<0.01).

Conclusion

The analysis of cognitive evoked potentials is an accurate method to complement clinical neuropsychological examination in the diagnosis of cognitive disorders in middle age patients with arterial hypertension. The study of cognitive evoked potential can be used for early diagnosis of cognitive impairment in these patients.

Key words

Arterial hypertension, cognitive impairment, cognitive evoked potential

Introduction

Due to increased lifespan number of patients with dementia evidently increases worldwide. Up to 7.7 mln new dementia cases are diagnosed each year. Knowing this, it becomes very relevant to perform diagnostics of predementia states. Light and moderate vascular cognitive disorders are considered to precede dementia in the majority of cases [1, 2]. Neuropsychological methods are traditionally used for the diagnostics of cognitive impairment. The protocol of neuropsychological study can become more complex in order to increase its sensitivity, but it can have some negative consequences. Interpretation of the results of complex neuropsychological techniques can often be ambiguous. During the last years more attention is paid to the techniques that can provide more objective information about cognitive disorders.

Investigation of brain electric reactions to external stimuli has been performed since the moment of the first electroencephalogram registration. In 1875 Russian researcher Vasily Danilevsky and English doctor Richard Caton had independently reported weak electric currents of animal brain registered with galvanometer and had observed their changes under sensory stimulation.

The first distinct registrations of cognitive evoked responses in human were performed by American doctors and audiologists Hallowell and Pauline Davis. British scientist George Dowson had further developed this technique up to its modern form [3]. Evoked potentials (EP) are bioelectric signals that appear at regular time intervals after definite external stimuli. Investigation of brain EP is based on the registration of brain electric response on exogenous stimuli (visual, acoustic, sensory) and endogenous events related to expectation, identification, decision-making and motor response initiation [3]. EP are registered using electrodes placed on patient's head. Brain electric response on visual, acoustic and sensory stimuli is estimated according with the change of main EP parameters like amplitude and latency of different components of the response [4]. The main method of endogenous events' detection that advanced the analysis of cognitive processes is the investigation of cognitive evoked potentials (CEP) or P300. Temporal limbic and brainstem reticular structures participate actively in the realization of this process in human brain [5]. P300 is a part of difficult potential that appears in the model of directed attention while carrying out a cognitive task [6]. The process of significant stimulus selection includes simply sensory part related to physical parameters and mainly reflected in the characteristics of early EP components. The next step is primary identification and classification of stimuli that is the most distinctly reflected in negative deviation 96-250 msec after the start of the stimulus and is called N2 (N200). It's further followed by final identification of the stimulus requiring its comparison with the memory template and decision-making in relation to action associated with it. P300 potential is connected with these events [7].

Distinct correlation between CEP and age has been identified in several studies [8]. These changes of P300 time-amplitude parameters are related to normal aging process accompanied with reduction of dendritic spines' number and synaptic contacts' density at the level of cerebral neurons [8]. Objectivity of obtained data and possibility to detect early cognitive disorders (CD) are significant advantages of this technique. This method can be used not only for cognitive dysfunction diagnostics, but also for differential diagnostics between CD and functional disorders like depression [9, 10].

This method is commonly used in neurology for patients with evident abnormalities [11]. Wide prevalence, high social significance and restricted therapy possibilities make the problem of CD early diagnostics in patients with cardiovascular risk factors very relevant.

The objective of this study was to evaluate the possibility of CEP use for CD diagnostics in patients with AH.

Materials and methods

All patients underwent clinical examination of such anthropometric parameters like waist circumference (WC), thighs circumference (TC) and body mass index (BMI). Blood sampling for plasma glucose levels detection and lipid spectrum characterization was performed using "Abbott" reagents ("Abbott", Germany) and biochemical analyzer (ARCHITECT C8000, Germany). BMI was quantified using Kettle formula: body mass/height^2 (kg/m^2). This study included 186 patients with the average age of 47.9±6.4 years. 94 patients had AH. AH duration was 6.3±1.5 years. To exclude significant anxiety and depression we used the HADS scale (The hospital anxiety and depression scale). Cognitive functions were estimated using neuropsychological scales: short MMSE (Mini-Mental State Examination) scale was used for psychic state estimation, battery of tests for frontal dysfunction, clock drawing test, and Luria's 10 words test. Schulte test was used to estimate the speed of reaction and ability to concentrate attention. WMS (Wechsler Memory Scale) scale was used for memory evaluation.

Quantitative estimation of cognitive functions was performed using CEP method and electromyogram/EP Nicolet Viking Select approach. P300 study technique is based on "odd ball" – paradigm, when series of two stimuli appear randomly, and between them there are "insignificant"(frequent) ones and "significant" (infrequent) ones, and patient should count the number of the latter ones. To register CEP, we used random event stimulation to acoustic stimuli.

We used auditory click stimulus with different tone for a significant one. We used stimuli with duration of 50 ms, significant stimulus' frequency and probability were 2000 Hz and 20-30%, respectively, and for insignificant ones the frequency was 1000 Hz and probability 70-80%. Stimuli's intensity was 80 dB, time period between stimuli was 1 sec. Binaural stimulation was used. Analysis epoch was 750-1000 ms. Number of averaging was 30-70, it was quantified separately for significant and non-significant stimuli. Frequency band was 0.5-30 Hz. After component verification we estimated P300 component's latency and amplitude.

Statistical analysis of obtained data was performed with Statistica 6.0 software using parametric and non-parametric methods depending on data distribution. The results are presented as M±SD. We considered statistically significant the differences with p-value <0.05.

Results

During the study patients were divided into two groups: group I (control, n=92) made of healthy people and group II (n=94) that included patients with AH (table 1). Groups were matched for age and gender of patients. In the group with AH average systolic blood pressure (SBP) measured in the office setting was 144.06±13.05 mm Hg. Average diastolic BP (DBP) was 89.14±7.55 mm Hg. Patients with AH (Group II) had a tendency to slightly higher blood glucose and total cholesterol levels versus control group: 5.46±0.60 and 5.14±0.51 mmol/L (p>0.01) and 5.69±1.04 and 5.31±1.00 mmol/L (p>0.01), respectively.

Table 1. **Clinical examination and laboratory tests results in two groups(M±m)**

Characteristic	Healthy people, n=92 (Group I)	Patients with AH, n=94 (Group II)
Age, years	47.67±6.43	48.07±5.71
Gender, male/female, abs, %	53(57.6%)/ 39(42.4%)	50(53.19%)/ 44(46.81%)
BMI, kg/m^2	22.93±1.85	23.41±2.09
WC, cm	83.67±8.12	85.40±9.97
TC, cm	98.54±4.62	100.15±8.71
SBP, office measurement, mm Hg	117.91±7.40	144.06±13.05 *
DBP, office measurement, mm Hg	77.26±7.19	89.14±7.55 *
Plasma glucose levels, mmol/L	5.14±0.51	5.46±0.60
TG, mmol/L	1.06±0.47	1.40±0.91
TCh, mmol/L	5.31±1.00	5.69±1.04
HDL Ch, mmol/L	1.54±0.40	1.49±0.34
LDL Ch, mmol/L	1.71±0.42	1.79±0.45

Comment: TCh – total cholesterol; HDL Ch – high density lipoprotein cholesterol, LDL Ch – low density lipoprotein cholesterol, TG – triglycerids; *-p<0.01 comparing with the group of healthy patients.

All examined patients underwent estimation of cognitive functions. Patients with AH had significant increase of CEP latent period duration – 346.17±18.37 vs 335.78±16.57 ms, respectively (p<0.01), and P300 amplitude reduction – 10.4±4.3 vs 16.2±5.7 μV, respectively (p<0.01) comparing with the group of healthy people (table 2).

Table 2. **CEP characteristics in patient groups (M±m)**

Characteristic	Healthy people (n=92) (Group I)	Patients with AH (n=94)(Group II)
P300 latent period, ms	335.78±16.57	346.17±18.37 *
P300 amplitude, μV	16.2±5.7	10.4±4.3*

Comment:*-p<0.01 comparing with the group of healthy people

Correlation analysis revealed connection between CEP and BP levels. The correlation between P300 latent period and DBP levels has been found ((r=0.51; p<0.01).

Neuropsychological testing demonstrated that the group of patients with AH had several characteristics significantly different from the control group. MMSE test results were significantly lower in patients with AH comparing with the group of healthy patients – 26.97±2.13 versus 28.9±1.78 points, respectively (p<0.01). The results of the clock drawing test had no significant differences between two groups – 9.34±0.92 vs 9.76±1.44 points, respectively (p>0.01). FAB questionnaire did not reveal significant differences between the groups – 17.2±0.83 vs 17.3±0.89 points, respectively (p>0.01). There was significant reduction of short-term and long-term memory in the group of patients with AH comparing with the control group: 6.24±1.11 vs 8.22±0.44 points (p<0.01) and 110.87±10.63 vs 135.13±12.18 points (p<0.01), respectively. Patients of AH group demonstrated also lowered speed of reaction and ability to concentrate attention comparing with the healthy patients - 197.23±23.78 vs 150.03±21.24 points (p<0.01), respectively. We identified association between SBP (r=–0.34; p<0.001), DBP (r=–0.27; p<0.001) levels and MMSE test results. We also registered statistically significant correlation between SBP levels (r=0.2, p<0.001), AH duration (r=–0.21, p<0.001) and short-term memory characteristics.

Comparison of neuropsychological tests and cognitive functions quantitative estimation results revealed tight connection between them. There was association of CEP latent period and MMSE test results (r=–0.31, p<0.01), clock drawing test (r=–0.24, p<0.01), Wechsler Memory Test (r=0.34, p<0.01), Luria's 10 words test (r=–0.35, p<0.01), FAB-test (r=–0.32, p<0.01), Schulte test (r=0.48, p<0.01).

Discussion

CEP is a complex potential that appears in directed attention paradigm and reflects the process of target stimulus selection [12]. Early CEP components, reflecting its sensory part related to stimulus' physical parameters, are caused by activation of specialized systems of information reception and processing. The stage that corresponds to final stimulus identification requiring its comparison with memory template and decision making in relation to the associated action (ignoring, memorizing, and specified action) has the biggest meaning for clinical use of this technique [13]. P300 potential is related to these events, and processes of directed attention and short-term memory have a particular meaning. But P300 amplitude and temporal parameters aren't connected just with one quality or characteristic of brain or its region. They reflect organization of whole complex of mechanisms responsible for information processing in central nervous system providing various forms of cognitive and perceptive-motor activity of human. P300 generation is realized through complex spatio-temporal interaction of brain cortex, thalamic and hippocampal structures. CEP latent period extension by 20-58 ms strongly correlates with neuropsychological tests results, degree of ventricles dilatation, severity of periventricular leukoaraiosis in computer tomography imaging, but not with the amount of brain infarction loci [14]. Hypothalamus, thalamus, frontal brain cortex are considered by researchers to be a possible area of CEP generation [15]. All mentioned above structures play important role in realization of education and memory processes [16]. This study revealed association of CEP latent period and MMSE test results (r=-0.31, p<0.01), long-term memory and short-term memory parameters (r=–0.34, p<0.01 and r=-0.35, p<0.01, respectively) that proves the results of previous studies.

AH is one of the main pathogenetic factors of vascular dementia development [7, 17, 18]. In the Framingham study 1695 patients with AH aged 55-88 years had been observed for 12-15 years. This observation established significant negative reverse correlation between the BP levels and characteristics of aural and visual memory according with the results of neuropsychological tests [19]. Our work demonstrated similar results. Both SBP and DBP levels were tightly connected with the results of the testing reflecting both the condition of cognitive functions in total and short-term memory parameters. Several authors demonstrated that there was no distinct difference between CEP latent period in aged patients with systolic AH and healthy people [8, 20-22]. In the current study we identified not only the increase of CEP latent period and decrease of its amplitude in patients with AH, but also demonstrated that P300 correlated mostly with DBP levels. We detected significant correlation between neuropsychological tests characteristics and CEP in patients with AH.

Conclusions

CEP characteristics are associated with the results of neuropsychological testing in patients with AH.

P300 investigation can be used for early CD diagnostics in patients with AH

Conflict of interests: None declared.

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