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P300 Evoked Potential in Patients with Mild Cognitive Impairment

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Original paper
ABSTRACT
Aim: The aim of this study is to present differences of amplitude and latency of P300 wave between examinees with mild cognitive impairment and examinees from the control group. **Methods:** A cross-section study was performed between April 1st and July 10th 2012, with the diagnosis of mild cognitive impairment as the main criterion for inclusion. In the twenty-two examinees who participated in the research, mild cognitive impairment was confirmed by neuropsychological testing, following which they were subjected to the examination of auditory evoked potentials. The control group consisting of 22 examinees, for which the lack of the same diagnosis was previously ascertained, was also subjected to the examination of auditory evoked potentials. The main findings were the differences in the latency and amplitude size of P300 wave targeted and non-targeted stimuli. **Results:** The latency of P300 wave targeted stimuli in patients with mild cognitive impairment has, in statistical terms, proven to be significantly longer when compared to the control group. The average latency length in those with MCI amounted to 306.18 ms, whereas the latency in the control group came to 295.95 ms. Similarly, the latency length of non-targeted stimuli turned out to be statistically higher, with the length of 320.00 ms in the former group, and 301.36 ms in the latter. Amplitudes in patients with mild cognitive impairment were lower in comparison to the control group, with extremely low amplitudes recorded in 36.36% of patients. **Conclusion:** In patients with mild cognitive impairment extended latency and lower amplitude of P300 wave are recorded.
Key words: P300, evoked potential, mild cognitive impairment, MCI.

1. INTRODUCTION

1.1. MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI) presents a transitional state in cognitive functions between changes deriving from the aging process and those which classify as dementia and Alzheimer's disease (1). It can therefore be said that MCI as a disease is a precursor to the onset of dementia (2). Most patients suffer gradual cognitive degradation, mostly in connection with memory. However, that degradation does not compromise patients in everyday activities (3). We can distinguish between the amnestic and non-amnestic types of MCI (4). Amnestic MCI is a significant deterioration of memory functions which does however not fulfill all criteria for diagnosing dementia. Patients and their families are more aware of the rising forgetfulness of the patient, but other cognitive abilities, such as administrative functions, use of languages and visuospatial skills are relatively preserved. The non-amnestic type of MCI is characterized by a mild disorder of cognitive functions not related to the use of language, memory, attention, and visuospatial abilities. This type of MCI is probably less frequent than the amnestic type, and can also be a precursor for dementia which is not tied to Alzheimer's dementia – namely the frontotemporal and Lewy body dementia (5). The assumed prevalence of that disease, according to population studies, amounts to 10%-20% in persons older than 65 years (6-10). A few studies have shown that patients with MCI are at greater risk of suffering from dementia (6, 7, 8, 9, 10).

Peterson's criteria are used to confirm a diagnosis of MCI, involving subjective disturbances connected to the individual's memory, non-interference in everyday activities, a test of the global cognitive status, memory disorder and absence of dementia (1). Neuropsychological tests used to evaluate cognitive status are: MoCa (Montreal Cognitive Assessment) test, ROCFT (Rey Complex Figure Test) test, COWAT (Control Word Association Test) test, and AVLT (Auditory Verbal Learning Test) test (11,12).

1.2. AUDITORY EVOKED POTENTIALS

Auditory evoked potentials present changes of brain electrical activity caused by auditory stimulus. They are shown with curves that contain positive and negative waves which follow the auditory stimulus. Important factors for interpreting results are the wave amplitude, expressed in microvolts, and wave latency, expressed in milliseconds. The stimulus contains a chain of tones which must be over the examinee's hearing threshold, but not too loud to be a nuisance (9, 10).

1.3. P300 BRAIN WAVE

The P300 wave is a measurable direct reaction of the brain to a certain sensory, cognitive or mechanical stimulus. It belongs to ERP (event related potentials), which are stereotypical

electrophysical answers to stimulants. P300 wave is presumably of endogenous origin. This wave is also taken as a cognitive neuroelectric appearance, because it turns up in psychological tasks and processes, when an examinee is paying attention and discriminates the stimulus which in a certain perspective differs from others. That discrimination creates a proportionally great positive wave deviation (10-20 μV) with a latency of around 300 ms when it is aroused by an auditory stimulus. Although the P300 wave is mostly referred to in the context of registering cognitive processes, a certain part of wave components' variability depends on the state of an individual's excitement. Investigating the brain of humans with deep electrodes brought along an understanding that a part of P300 wave components occurs in the hippocampal part of the medial temporal lobe of the brain. It is also important to note that a great part of wave components occurs in the temporoparietal brain bonds (13).

P300 components are most easily provoked by a simple discriminating task. The examinee is presented with two randomly repeating stimuli so that one of them is repeating proportionally rarely. In the auditory version of this test (auditory evoked potentials) two different, repeating tones are used, where the targeted stimulus (tone) appears fewer times than the non-targeted stimulus (tone). The examinee must count tones i.e. classify the frequency of the targeted tone (13, 14).

The wave is registered on the head skin of the examinee, namely on 3 specific points set on the medial line. From the frontal to the occipital side these points are marked as: Fz, Cz, Pz (13). The two components that this wave consists of are the P3a component which is connected to brain activity during attention directing time, and the P3b, connected to cognitive processes, namely those tied with information processing (13).

2. EXAMINEES AND METHODS

2.1. EXAMINEES

The examination involved 22 examinees in which we have, by neuropsychological testing, proven the existence of an MCI diagnosis, which presented the criterion for inclusion in the research. The criteria for being excluded from the research were other neurological illnesses which have cognitive impairment as a consequence. The control group consisted of 22 examinees, for which the lack of the MCI diagnosis was established by using the same neuropsychological testing. All examinees had given informed consent.

2.2. RESEARCH LOCATION

The research was carried out at The Clinic of neurology of the University Hospital Split, the reference center for evoked potentials of the Ministry of Health of Croatia.

2.3. COMPILATION METHODS AND DATA ANALYSIS

The data was compiled by a direct measurement and analysis of the examinees' medical history. We extracted the list of patients from the medical documentation of The Clinic for neurology of the University Hospital Centre Split. After the inclusion and exclusion criteria were analyzed, selected participants were invited for examination. A neuropsychological testing was conducted together with examinations of auditory evoked potentials. The control group was selected randomly from non-hospital population, taking into account the compatibility with the first group of examinees by sex and age. For the examinees in the control group the lack of an MCI diagnosis was established by conducting neuropsychological testing, a detail anamnesis and by applying basic checks for the existence of other pathological states which were excluded. We have then conducted the examination of auditory evoked potentials on examinees from the control group.

2.4. MAIN ENTRY DATA

The following parameters were analyzed for every examinee: age, sex, MCI diagnosis confirmed by neuropsychological testing, latency of the P300 wave targeted and non-targeted stimuli, P300 wave amplitude.

2.5. MAIN FINDINGS

The main findings encompass the difference in latency lengths of P300 wave and the difference in amplitude between examines with MCI and examinees from the control group.

2.6. STATISTICAL ANALYSIS

The results of this research were statistically analyzed in the SPSS Statistics program ("IBM SPSS Statistics", IBM Corporation, USA), whereby the T-test of independent samples was applied in order to prove latency differences. For comparing amplitudes the $\chi 2$ test was used. The sample contained a total of 44 examinees: 22 examines with MCI and 22 healthy examinees from the control group.

3. RESULTS

Epidemiological traits of both groups are shown in table 1. The research design is shown on Figure 1.

We have first analyzed the length of latency of the P300 wave targeted auditory stimulus. We have compared latencies of 22 examinees with diagnosed MCI with latencies of 22 examinees from the control group. Latencies from the group of patients with MCI were greater than latencies of examinees from the control group. The average value of latency from the group of examinees with MCI amounted to 306.18±20.620 ms, while the average value of latency in examinees from the control group amounted to 295.95±5.028 ms. The result of latency differences has shown to be statistically significant (P=0.048).

Characteristics	Examinees with MCI (n, %)	Control group (n, %)
Age (years) ±SD	73,9±7,4	70±5,8
Female gender	18 (82)	18 (22)
Male gender	4 (18)	4 (18)

Table 1. Epidemiological characteristics of examinees with diagnosed MCI (n=22) and of examinees from the control group (n=22).

In the next stage the length of latency of the P300 wave non-targeted auditory stimulus was analyzed. We compared the latencies of 22 examinees with diagnosed MCI with latencies of 22 examinees from the control group. Latencies from the group of patients with MCI were greater than latencies of examinees from the control group. The average value of latency from the group of examinees

with MCI amounted to 320.00±16.048 ms, with 301.36±4.226 ms as the average latency of the control group. The result of latency length difference has shown to be statistically significant ($P<0.001$).

Finally, the amplitudes of the P300 wave non-targeted auditory stimulus were analyzed. We compared amplitudes of 22 examinees with diagnosed MCI with amplitudes of examinees from the control group. The amplitudes were classified as regular, mildly lower, low and extremely low. 31.81% of examinees from the group of patients with MCI displayed mildly lower amplitudes, 31.81% of them low amplitudes, while 36.36% displayed extremely low amplitudes. Examinees from the control group mostly demonstrated regular amplitudes, namely 90.90%, while 9.09% had mildly lower amplitudes.

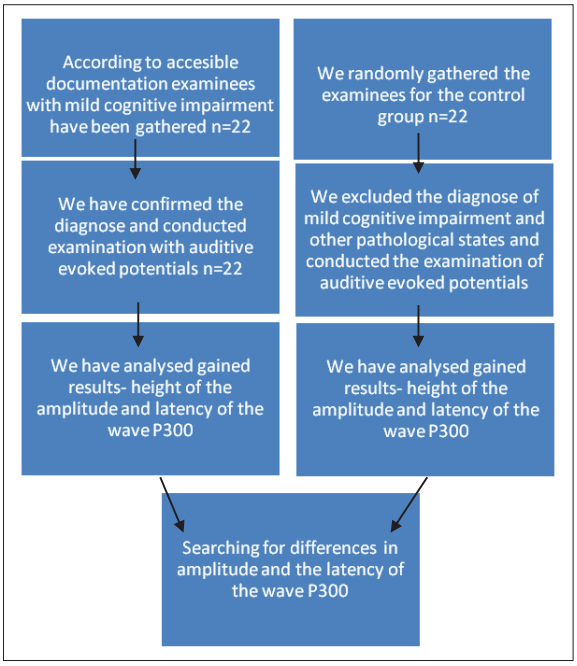

Figure 1. Research design

4. DISCUSSION

This research has proven that patients with MCI demonstrate changes in latency and amplitude of the P300 wave. The results undoubtedly show that examinees from the group with MCI display extended latencies of the P300 wave after examination of auditory evoked potential. With regard to the latency length of targeted stimulus, it was shown that the extension of latency, which is statistically significant, is greater in examinees from the MCI group than in examinees from the control group. The average length of latency in examinees from the MCI group was 306.18±20.620 ms, in comparison to examinees from the control group, where it amounted to 295.95±5.028 ms.

Similar results are obtained even during researching latencies of non-targeted stimuli. The difference between the latencies in patients with MCI and examinees from the control group proves to be statistically significant. The average length of latency in a patient with MCI came to 320.00±16.048 ms, with 301.36±4.226 ms as the average length in examinees from the control group. By analyzing the amplitudes of non-targeted stimuli we reached a conclusion that patients with MCI display lower amplitudes than examinees from the control group. Following the classification of amplitudes as mildly lower, low and extremely low, in the greatest number of patients extremely low amplitudes were registered, as much as 36.36%, while low amplitudes were registered in 31.81% of patients. 31.81% of patients displayed mildly lower amplitudes.

Amplitudes	Examinees with MCI n (%)	Examinees from the control group n (%)
Extremely low	8 (36.36)	0 (0)
Low	7 (31.81)	0 (0)
Mildly lower	7 (31.81)	2 (9.1)
Regular	0 (0)	20 (90.9)
Total	22 (100)	22 (100)

Table 2. Differences in amplitudes of non-targeted stimuli. $\chi 2=44$, $P<0.001$.

The main flaw of this research is a small number of examinees, which could not have been increased due to the fact that this is a relatively rare diagnosis. These results correspond with the results from the research of Papaliaglos and associates (14), which also included 22 examinees with MCI, with one of the conclusions that the latency of P300 wave targeted and non-targeted stimuli was extended in examinees with MCI.

The results of our research could contribute to the improvement of the diagnostic procedure for MCI, at first as a supplement for neuropsychological tests which are conducted today in the diagnostics of the given disorder. The method of examining auditory evoked potentials and measuring the changes of P300 wave components can surely be used as a screening test for MCI in groups which are at risk of the onset of this disease. Examining auditory evoked potentials and the P300 wave has shown important for patients with MCI, which implies that this exami-

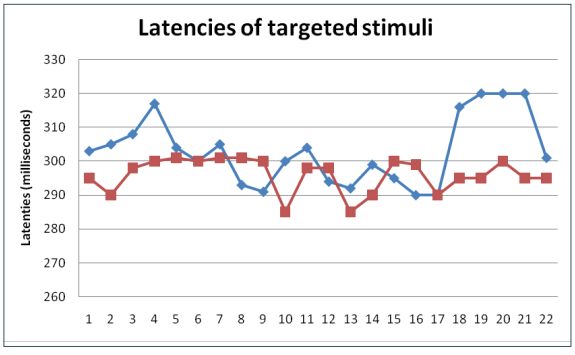

Figure 2. Comparison of latency of the P300 wave's targeted stimulus in examinees with MCI and examinees from the control group. The blue line marks latencies of P300 wave targeted stimulus in an examinee with MCI. The red line marks latencies of P300 wave targeted stimulus in an examinee from the control group. T-test=2.039, P=0.048.

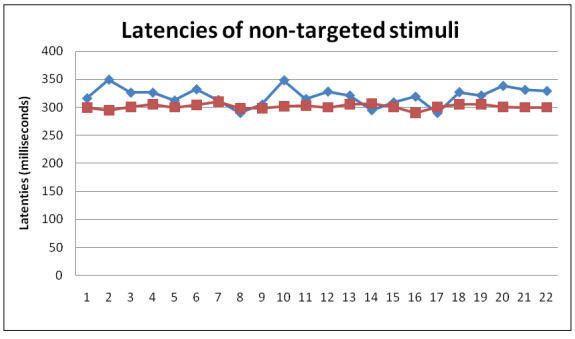

Figure 3. Comparison of latencies of P300 wave non-targeted stimulus in examinees with MCI and examinees from the control group. The blue line marks latencies of P300 wave non-targeted stimulus in examinees with MCI. The red line marks latencies of non-targeted stimulus of the P300 wave in examinees from the control group. T-test=5.267, P<0.001.

nation should be applied more often in the future.

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