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Somatosensory-Evoked Potentials in Vascular Dementia and in Alzheimer's Disease*

Somatosensoryczne potencjały wywołane w otępieniu naczyniopochodnym i w chorobie Alzheimera

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Abstract

Background. The search for sensitive biochemical, genetic, and electrophysiological markers which could be helpful in differentiating dementia continues.
Objectives. The aim of this study was to assess the usefulness of short somatosensory-evoked potentials (SSEPs) in differentiating vascular dementia (VD) and Alzheimer's disease (AD).
Material and Methods. The study covered 34 patients who met the criteria of probable vascular dementia (NINDS-AIREN) and 59 patients who met the criteria of probable Alzheimer's dementia (NINCDS-ADRDA) with similar dementia advancement on the MMSE scale. SSEPs were elicited in response to electric stimulation of the median nerve. The somatosensory responses were recorded hetero- and homolaterally by a Nicolet computer which calculates mean values of data.
Results. The average latencies of N13 responses in both groups of patients with recognized dementia were significantly extended compared with the control group (VD: $p < 0.001$; AD: $p = 0.01$). The latencies of N20 responses recorded contralaterally to the stimulation were also significantly longer on both sides, both in the group of AD patients ($p < 0.001$) and in the VD patients ($p < 0.01$). The central time to the cortex (TTC) was extended in both the examined groups, but it was not statistically significant ($p > 0.05$). The mean latency of the N20 response recorded homolaterally was indeed extended, but only in patients with VD and on the right side ($p < 0.001$).
Conclusions. The extended N13 latency in patients with AD may indicate vascular changes in cervical posterior columns, similar to the changes observed in VD. In the differential diagnosis of dementia, assessment of the latency of the somatosensory N20 cortex response recorded heterolaterally seems of little use. Only the latency of the N20 response recorded homolaterally may indicate the location and advancement of vascular changes in VD (**Adv Clin Exp Med 2007, 16, 2, 263–267**).

Key words: vascular dementia, Alzheimer disease, SSEPs heterolaterally, SSEPs homolaterally.

Streszczenie

Wprowadzenie. Wciąż trwają poszukiwania czułych markerów biochemicznych, genetycznych, a także elektrofizjologicznych, które mogłyby być pomocne w różnicowaniu otępień.
Cel pracy. Ocena przydatności somatosensorycznych potencjałów wywołanych (SSPE) w różnicowaniu otępienia naczyniopochodnego (VD) i alzheimerowskego (AD).
Materiał i metody. Badaniami objęto 37 chorych spełniających kryteria otępienia naczyniopochodnego (NINDS-AIREN) oraz 59 chorych spełniających kryteria otępienia alzheimerowskiego (NINCDS-ADRDA), o podobnym stopniu zaawansowania otępienia w skali MMSE. SSPE uzyskiwano stymulując bodźcem elektrycznym kolejno oba nerwy pośrodkowe. Odpowiedzi somatoczuciowe rejestrowano hetero- i homolateralnie za pomocą komputera uśredniającego firmy Nicolet.
Wyniki. Średnie latencje odpowiedzi N13 w obu grupach chorych z rozpoznaniem otępienia były znamiennie przedłużone w porównaniu z grupą kontrolną (VD: $p < 0{,}001$; AD: $p = 0{,}01$). Latencje odpowiedzi N20 rejestrowanych przeciwstronnie do stymulacji były także znamiennie dłuższe po obu stronach, zarówno w grupie chorych z AD ($p < 0{,}001$), jak i z VD ($p < 0{,}01$). Czas przewodzenia ośrodkowego (TTC) był przedłużony w obu badanych grupach chorych, ale nie wykazywał znamienności statystycznej ($p > 0{,}05$). Średnia latencja odpowiedzi N20 reje-

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grupach chorych, ale nie wykazywał znamienności statystycznej ($p > 0,05$). Średnia latencja odpowiedzi N20 rejestrowanej homolateralnie była istotnie przedłużona, ale tylko u chorych z VD i po stronie prawej ($p < 0,001$).
Wnioski. Przedłużenie latencji N13 u chorych z AD może świadczyć o zmianach naczyniowych w tylnych kolumnach rdzenia szyjnego (*cervical posterior column*), podobnych do zmian obserwowanych w VD. W diagnostyce różnicowej otępień ocena latencji somatoczuciowej odpowiedzi korowej N20 rejestrowanej heterolateralnie wydaje się mało przydatna. Jedynie latencja odpowiedzi N20 rejestrowanej homolateralnie może wskazywać na umiejscowienie i zaawansowanie zmian naczyniowych w VD (**Adv Clin Exp Med 2007, 16, 2, 263–267**).

Słowa kluczowe: otępienie naczynioruchowe, choroba Alzheimera, SSEP heterolateralne i homolateralne.

Vascular dementia (VD) constitutes from 9 to 10% of all dementia [1, 2]. In a study by Lobo et al. [3], VD appeared in only 1.6% of the population over 65 years old. Neuropathological changes typical of Alzheimer's disease (AD) are also observed in VD, which is the reason for discussions questioning the existence of a pure form of VD [4, 5]. AD most frequently is a dementia with a neurodegenerative background. The main characteristic of the neuropathological changes in AD is the appearance of senile plaques consisting of β-amyloid, neurofibrillar degeneration, and amyloid deposits on cerebral vessels [6, 7]. The development of neuro-imaging examinations and the methodology of neuropsychological tests allows differentiating dementia types to a large extent. However, sensitive biochemical and genetic markers as well as electrophysiological parameters which allow for an early diagnosis of a dementia process are still being sought.

In the electrophysiological diagnosis of neurological disorders, spontaneous bioelectric activity (electroencephalogram, EEG) and responses evoked by stimuli of various modality (visual, auditory, and sensory) are used. These responses can be recorded at different levels of the nervous system in the form of mean potentials. EEG changes in AD and in vascular dementia are nonspecific and consist of a slowing down of the basic activity, with alpha activity maintained for a longer period by means of electrodes applied to the temporal region [8, 9]. The evoked potentials which are the most frequently applied in clinical practice are visual (VEPs), brainstem auditory (BAEP), and short somatosensory (SSEPs) evoked potentials. They are characterized by frequent recurrence and great sensitivity and enable a noninvasive assessment of the bioelectric activity of the central nervous system.

The aims of this study were 1) an assessment of the latency and amplitude of somatosensory-evoked potentials recorded hetero- and homolaterally, 2) assessment of the transit time to the cortex (TTC), and 3) specifying the usefulness of SSEPs in the differential diagnosis of Alzheimer's desease and vascular dementia.

Material and Methods

The study covered 96 patients divided into two groups. The first group consisted of 34 patients (23 women and 11 men) with an average age of 66.3 ± 5.9 years and with diagnosed vascular dementia. All patients in this group met the NINDS-AIREN criteria of probable diagnosis of vascular dementia [10]. In Hachinski's ischemic test [11] they received more than 7 points. The second group consisted of 59 patients (25 women and 34 men) with an average age of 66.8 ± 7.3 years meeting the NINCDS-ADRDA criteria of probable diagnosis of Alzheimer's disease [12]. In the Hachinski's ischemic test all these patients received fewer than 4 points. Clinical and neuropsychological tests as well as CT or MRI findings were applied in the diagnostics of dementia. The extent of dementia was specified on the basis of the Mini Mental State Examination (MMSE) [13]. The control group consisted of 37 people (18 women and 19 men) with an average age of 63.4 ± 11.4 years without cognitive disorders.

SSEPs were elicited in response to electric stimulation of the median nerve of the wrist with 0.1-ms pulses having sufficient intensity to elicit a small twitch of the thumb. Surface receiving electrodes were placed monopolarly at the height of the cervical vertebra CII (with the reference electrode at the frontal central point Fz) and bipolarly in the left (C3/P3) and right (C4/P4) parietal region, with the response recorded homolaterally and contralaterally to the incited nerve. Five hundred responses were made on average using a Nicolet computer. The analysis time was 20 ms for recording at point CII and 100 ms for recording in the parietal region. The latency and amplitude of the cervicomodullary potential N13, recorded at the level of CII, and the hetero- and homolateral N20 cortex response were analyzed. The transit time to the cortex, TTC (interpeak latency N20–N13), was also specified.

Statistical Description of the Results

Mean values and standard deviations of the examined parameters in the groups of patients

and in the control group were calculated. Verification of the hypothesis of the equality of means in both groups was carried out according to the method of variance analysis by the Bartlett test and, for groups of heterogeneous variance, by the Wilcoxon test. Statistical analysis was carried out using the Statistica computer package of statistics programs.

Results

Mean ages in the examined groups were not statistically significant. The mean score on the MMSE scale was 20.25 ± 3.23 in the group with AD and 21.52 ± 2.47 in the group with VD. These results differed significantly from the value obtained in the control group (29.37 ± 0.75 points; $p < 0.001$). The mean latency of the N13 response in the patients with diagnosed VD was significantly extended in comparison with the control group and it showed great statistic significance ($p < 0.001$). The mean latencies of N13 in the group of AD patients were bilaterally significantly extended compared with the control group ($p = 0.01$), although there were no statistically significant differences between N13 latencies in VD and AD ($p > 0.05$). The average amplitudes of the N13 response in all the examined groups showed no statistically significant changes (Tab. 1).

Latencies of N20 responses recorded contralaterally to the stimulus were bilaterally significantly longer in the VD ($p < 0.01$) and AD ($p < 0.001$) groups compared with the control group. The average amplitudes of the N20 response did not show statistically significant differences. Average TTC was indeed extended bilaterally in both groups of patients compared with the control group, but it did not show statistical significance ($p > 0.05$) (Tab. 1, Fig. 1). The relative latencies and amplitudes of the N20 cortex responses recorded contralaterally were not statistically significant. The average N20 latencies recorded homolaterally in the group of patients with VD were bilaterally extended, but only on the right side was the difference statistically significant ($p < 0.001$) (Fig. 2). In patients with AD the average latencies of the homolateral N20 response were bilaterally longer, but did not show significant differences from the results obtained in the group with VD and in the control group.

Table 1. Latencies and amplitudes of somatosensory-evoked response recorded hetero- and homolaterally in the groups of patients with AD and VD and in the control group

Tabela 1. Latencje i amplitudy somatosensorycznej odpowiedzi wywołanej rejestrowanej hetero- i homolateralnie w grupie chorych z AD i VD oraz w grupie kontrolnej

	Control group (Grupa kontrolna) n = 37	Alzheimer's disease (Chorzy na otępienie alzheimerowskie) n = 59	Vascular dementia (Chorzy na otępienie naczyniopochodne) n = 34
Mean age of patients – years (Średni wiek pacjentów – lata)	63.4 ± 11.4	66.8 ± 7.3	66.3 ± 5.9
MMSE	29.37 ± 0.75	20.25 ± 3.23	21.52 ± 2.47
Heterolateral (Rejestracja heterolateralna)			
latency N13 (ms) left	14.14 ± 1.10	14.90 ± 1.39*	15.22 ± 1.15*
latency N13 (ms) right	14.29 ± 1.03	15.02 ± 1.41*	15.34 ± 1.23*
N20 latency (ms) left	21.98 ± 1.60	23.63 ± 2.82*	23.50 ± 1.93*
N20 latency (ms) right	22.27 ± 1.46	23.83 ± 2.60*	23.70 ± 2.12*
N13–N20 latency left	7.80 ± 1.63	8.65 ± 2.58	8.28 ± 1.59
N13–N20 latency right	8.01 ± 1.38	8.80 ± 2.45	8.29 ± 1.47
N13 amplitude left	1.68 ± 2.30	1.03 ± 0.67	1.02 ± 0.66
N13 amplitude right	1.48 ± 1.76	0.74 ± 0.58	0.60 ± 0.38
N20 amplitude left	4.30 ± 3.75	4.45 ± 4.90	3.34 ± 3.43
N20 amplitude right	3.89 ± 3.80	3.33 ± 4.86	2.98 ± 3.46
Homolateral (Rejestracja homolateralna)	n = 22	n = 34	n = 18
N20 latency left	23.28 ± 1.74	24.31 ± 2.40	23.86 ± 2.92
N20 latency right	23.23 ± 1.65	24.42 ± 2.43	25.08 ± 3.15*

* Statistically significant.

* Istotne statystycznie.

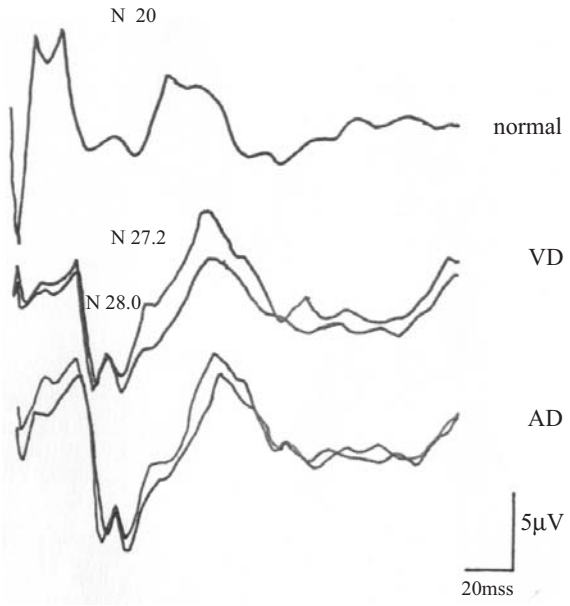

Fig. 1. N20 latency of the cortex response of SSPE in patients with VD and AD and in the control group recorded heterolaterally

Ryc. 1. Latencja N20 korowej odpowiedzi SSPE u chorych z VD i AD oraz w grupie kontrolnej rejestrowana heterolateralnie

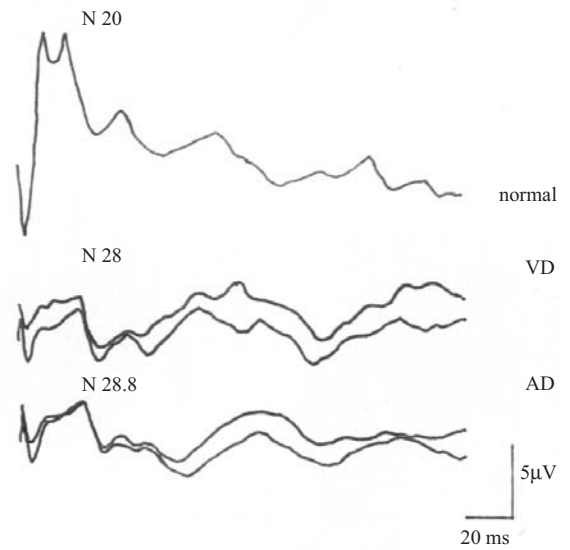

Fig. 2. N20 latency of the cortex response of SSPE in patients with VD and AD and in the control group recorded homolaterally

Ryc. 2. Latencja N20 korowej odpowiedzi SSPE u chorych z VD i AD oraz w grupie kontrolnej rejestrowana homolateralnie

Discussion

SSEPs recorded contralaterally to the stimulated median nerve come from the thalamus, thalamocorical tract, and also from the sensory projective cortex. Cortex somatosensory potentials are registered homolaterally in relation to the incited nerve and are the result of secondary incitement of homolateral sensory areas coming through the commisura magna from the primary excited contralateral hemisphere. The average SSEP latency extensions in patients with VD can be connected with the subcortex location of ischemic foci causing damage to central sensory neurons. Abbruzzese et al. [14], assessing SSEPs in a group of 54 patients with VD, showed, similarly to this research, significant extension of N13 latency and cortex N20 response. The authors suggested that the extension of latency of N13 in the group of patients with VD is probably connected with disorders in transiting the posterior tract damage in chronic spinal ischemia. Similar results were obtained in 2001 by Tsiptsios et al. [15]. The extension of the latency of N13 response observed in the group of patients with AD of the present study can therefore prove that vascular changes in the posterior part of the transiting tract of the spine co-exist. Kato et al. [16], comparing a group of patients diagnosed with vascular dementia with a group of patients with multifocal vascular damage of the brain without dementia features, showed significant extension of the TTC in the group with VD. The latency of the TTC clearly correlated with changes of leukoaraiosis character in the group of patients with VD. The TTC in this test was indeed extended, although it was not statistically significant. These results are different from those presented in subject literature [14, 16]. Perhaps it is connected with the extent of advancement of vascular changes in subcortical areas or with improper qualification of patients to the VD group. Tachibana et al. [17] did not find significantly extended CCT in a group of patients with AD in comparison with a control group.

In Ito's study [18] the latency of the somatosensory cortex response N20 was significantly extended in 24 patients with recognized VD. In a group of patients with AD and also in Parkinson's disease, such independence was not present. In the present study the average N20 latencies were bilaterally significantly extended in both the VD and the AD groups of patients. This results from vascular damage to subcortical structures in VD. The extension of N20 latency in AD can be evidence of more advanced dementia resulting from exacerbated neuropathological changes in the brain cortex. An interesting observation is the bilateral extension of latency of the N20 wave recorded homolaterally, with a clear dominance on the right side ($p < 0.001$), in the group of VD patients. This can be an electrophysiological index of vascular changes in the hetero- and homolateral hemisphere and/or of the dominance of changes typical for AD in the cortex of the homolateral hemisphere.

The authors conclude that the results of investigating SSEP latency in AD and VD indicate central electrophysiological changes in a medium-advanced form of vascular and Alzheimer's dementia. The extension of N13 latency in both groups of patients probably takes place because of vascular changes in the posterior area of the cervical medullar transit. The lack of clear differences in medium N20 latency in the groups of patients with AD and VD makes it impossible to use SSEPs in differentiating VD from AD. A more useful parameter which differentiates primary dementia features from symptoms resulting from advanced vascular changes in the brain may be the latency of the cortex N20 response recorded homolaterally.

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