The pattern – reversal visual evoked potentials in children with migraine with aura and without aura

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Abstract

Purpose: Studies of the visual evoked potentials (VEP) in migraine have yielded contradictory results. Several investigators suggested that VEP may be helpful test in diagnosis of a child with headache. The aim of our study was to compare interictal pattern-reversal visual evoked potentials (PR-VEP) in children and adolescents with migraine and tension-type headaches and to evaluate VEP parameters in migraine with and without aura.

Material and methods: The study was carried out in 93 children and adolescents aged 7-18 years with attack headaches.

Results: 51 children had diagnosed migraine. In this group 30 children (59%) had migraine without aura (MO), 12 children (23.5%) migraine with aura (MA) and 9 (17.5%) patients other variants of migraine (MV): hemiplegic, ophthalmoplegic, basilar. In control group 42 children were classified as tension-type headaches. All children had PR-VEP performed in headache – free period, without prophylactic treatment. The P100 mean latency was significantly longer in migraine than in tension-type headache. Amplitudes N1-P100 and P100-N2 were siginificantly larger in migraneurs compared with tension-type headache. The mean amplitudes of N1-P100 and P100-N2 were significantly lower in MA compared with group MO. There were no statistically significant differences of other PR-VEP parameters between MA, MO, MV.

If we compare individual results of each patient with migraine with mean value ± 2 standard deviations (SD) of tension-type headaches group, only 25% have VEP abnormalities of latency or amplitude above 2SD value in tension-type headache group.

Conclusions: The diagnosis of migraine in children actually remains predominantly based on medical history, due to low sensitivity and specifity of electrodiagnostic tests in headaches. However PR-VEP may support the diagnosis of migraine in some cases. VEP could be also helpful method in studying the pathogenesis of different forms of migraine. VEP abnormalities in migraine can be related to a cortical spreading depression and a central neurotransmitter alterations.

Key words: visual evoked potentials, migraine, tension-type headache.

Introduction

Headache is a common complaint in children. The diagnosis and the therapeutic approach is based solely on medical history and physical examination. Electrophysiological techniques of evoked potentials (EP) could be useful to support the diagnosis. The visual function in migraneurs differs from those of normal subjects and patients with other type of headaches. Visual aura is a well-known feature of migraine and the majority of migraine attacks with or without aura are acompanied by photophobia [28]. Migraine patients are more sensitive to enviromental light stimuli [11].

Studies of the cortical visual evoked potentials (VEP) have yielded contradictory results. Several investigators did not find differences between migraneurs and healthy control subjects [4,7,19,29,35,40]. However, others reported changes of VEP amplitudes, latencies and habituation response. Some authors demonstrated increased P100 latencies [13,17] and larger P100 amplitudes [3,6,17,20] in migraneurs. However, some authors showed shorter N75 and P100 latencies in migraneurs [3,20]. Increased amplitudes and P100 response assymetry in migraine with aura in comparison with cases without aura was reported [34]. In the last years disturbances of VEP habituations in migraine were reported [1,2,12,33].

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Table 1. Latencies and peak–to–peak amplitudes of pattern – reversal visual evoked potentials in children with migraine and tension–type headache (mean±standard deviation).

	Migraine (n=51)	Tension-type headache (n=42)
P 100 latency (ms)	109.99±12.63*	106.80±4.42
N1-P100 amplitude (μV)	16.03±5.53*	12.18±4.41
P100-N2 amplitude (μV)	14.65±5.58*	10.08±4.84
N1 latency (ms)	74.33±5.46	73.96±4.43
N2 latency (ms)	152.83±12.23	158.98±7.08

* p<0.05 vs mean value in tension-type headache group

Such studies have been performed mainly in adults. A very few clinical reports of VEPs in migraine in children and adolescents have been published. Lahat et al. [15,16] reported in children significantly larger amplitude between P100 and N2 with migraine compared with other types of headaches. They suggested VEP study may be helpful in diagnosis of a child with headache when symptopms may not be characteristic. However, in other studies there were no statistically significant differences of VEP parameters in children 3-14 years old with different types of headaches [26] and between groups of children with migraine and control subjects [18].

The aim of our study was to compare interictal pattern – reversal visual evoked potentials (PR-VEP) in children and adolescents with migraine and tension-type headache and to evaluate VEP parameters in migraine with and without aura.

Material and methods

The study was carried out on 93 children and adolescents aged 7-18 years with attack headaches, reffered for evaluation to Pediatric Neurology Department between April 2000 and September 2001. Migraine or tension-type headache was diagnosed according to the criteria of Headache Classification Comitee of International Headache Society from 1988. All patients were examined by a neurologist. EEG and CT scan were performed if necessary.

All children were headache – free for at least 2 days before electrophysiologic study. Visual acuity and fixatiom of all subjects were normal. None of patients received prophylactic anti-migraine therapy before electrophysiologic test.

MEDELEC Sapphire Premiere was used for VEP recording. Patients were seated 1 metre in front of the TV monitor. Checkboard pattern of black and white squares subtending 16' of arc at reversal frequency of 2 Hz was presented. Subjects with one eye patched were instructed to fixate on the middle of the screen. The responses were recorded from silver chloride electrodes on the scalp in occipital region in points Oi and Oz. The refferal electrode was in Cz. The bandwidth was 1 Hz to 100 Hz. During uninterrupted stimulation blocks of 128 responses were averaged. Analysis time was 300 ms. Peaks N1, P100 and N2 were analysed.

Table 2. Latencies and peak–to–peak amplitudes of pattern – reversal visual evoked potentials in children with migraine without aura (MO), migraine with aura (MA), variants of migraine (MV). (mean±standard deviation).

	Migraine without aura (n=30)	Migraine with aura (n=12)	Variants of migraine (n=9)
P 100 latency (ms)	108.74 ±14.50	114.68 * ±8.11	106.88 ±4.86
N1/P100 amplitude (μV)	17.38 ±5.19*	13.38 ±3.95 #	15.04 ±8.37*
P100/N2 amplitude (μV)	16.45 ±4.81*	10.09 ±4.07 #	14.07 ±6.46 *
N1 latency (ms)	74.48 ±5.05	75.82 ±4.21	71.81 ±7.41
N2 latency (ms)	154.08 ±12.84	151.79 ±11.33	150.03 ±11.43

* p<0.05 vs value in tension-type headache group
# p<0.05 vs value in migraine without aura group

The mean latencies N1, P100, N2 and amplitudes N1-P100, P100-N2 were compared by Student t test for unpaired samples. A „p" value below 0.05 was considered significant.

The study was approved by the Ethics Comittee of Medical University in Białystok (R-I-003/140/99).

Results

51 children aged 12.43±2.86 years: 31 boys and 20 girls had diagnosed migraine. In this group 30 children (59%) had exclusively migraine without aura (MO), 12 children (23.5%) classical migraine with aura (MA) and 9 (17.5%) patients other forms of migraine (MV) with focal neurologic signs: hemiplegic, ophthalmoplegic, basilar. In control group 42 children aged 13.02±2.89 years: 14 boys and 28 girls were classified as tension-type headaches. All patients in this group had episodic tension-type headaches: less than 15 days with headache per month.

The mean latencies and amplitudes of the PR-VEP in group of all cases of migraine (M) and tension-type headache (TH) are shown in *Tab. 1*. The P100 mean latency: (109.99±12.63 ms) was significantly longer in migraine than in tension-type headache (106.80±4.22 ms). Amplitides N1-P100 (16.03±5.53 μV) and P100-N2 (14.65±5.58 μV) were siginificantly larger in migraneurs compared with tension-type headaches, respectively: 12.18±4.41 μV and 10.08±4.84 μV. There were no differences of mean latencies N1 and N2 peaks compared M and TH groups (*Tab. 1*).

The comparison of the PR-VEPs results in different forms of migraine are summarized in *Tab. 2*. There were no statistically significant differences of all PR-VEP mean values of latencies: P100, N1, N2 between migraine with aura, without aura and other migraine variants. However, tendency to longer P100 latencies in migraine with aura was observed. The mean amplitudes of N1-P100 and P100-N2 were significantly lower in migraine with aura compared with group without aura (*Tab. 2*).

We compared also VEP parameters of each patient with diagnosed migraine with mean value +2 standard deviations (SD) in tension-type headache group (TH). 13 children (25%) have P100 latency above 2SD, 13 children (25%) have amplitude N1-P100 above and only 6 (11%) have P100-N2 amplitude value above mean +2SD in TH group.

Discussion

Our study showed that the mean latency of P100 and also the amplitudes N1-P100, P100-N2 are larger in migraine compared with tnsion-type headache. These results correlate cardinally with previous studies in children [15,16]. However, in study of 78 children aged 3-14 years there were no significant differences in the mean values of VEP between different types of headache: migrane with and without aura or tension-type headaches [26]. Earlier studies, which suggested that using VEP is an objective test in patients with migraine [10,13,21,22] were later criticized based on inappopriate choice of study groups [26] and erroneous interpretation of VEP results [36,37].

The large discrepances between various investigations are probably caused by several factors. Important causes are differences in selection of examined groups: all forms of migraine, migraine with aura or without aura only, migraine equivalents. They were compared to different controls: healthy asymptomatic subjects [18,29,40], non-specific headaches [15,16], tension-type headache [26]. In this study, we chose comparing with tension--type headache and demonstrate prolonged mean P100 latency in group of all children in migraine, but not in common migraine without aura. This result seems to depend mostly on migraneurs with visual aura, where mean P100 latency was significantly longer. However, other incestigators observed that increase P100 latency is not related to the presence or absence of an aura [14]. Second cause of disagreement among various studies is irreproducibility of results because of differences in methods: position of recording electrodes, parametres of stimulation: flash or checkboard pattern, frequency, size of pattern, stimulus intensity. It was confirmed that VEP habituation or potentiation was found for small check stimuli, but not for medium sized checks [29]. Differences in VEP were dependent also on spatial frequency. Only at high frequency 2 and 4 cycles per degree was the latency N2 prolonged in migraine with aura and did it tend to be delayed in migraine without aura [23]. Important factor seems to be duration of migraine. P100 amplitude is increased in cases of short duration, but in addition it showed a sharp decline with duration to below normal in cases with a long history of migraine with aura [14]. There were also found significant correlation between duration of illnes and percentage of VEP assymetries in migraine with aura [34]. However comparing 2 groups of patients with migraine for 2 years or less and other with disease for 10 years and more, Yucesan et al. [41] concluded that migraine duration has no influense on PR-VEP. VEPs are related also on time relationship to attack. Amplitude of PR-VEP in migraine with aura and migraine equivalents increases, when recorded soon after attacks, especially with 10 days [34]. During the attack VEP habitation was less pronounced than the day before and during the 2 days following the attack VEP habitation were replaced by potentiation [12].

The pathnomechanism of VEP alterations in migraine is not clear. They have been interpreted as markers of anatomical lesions of the optic pathway due to ischaemia during the attacks. The changes of P100 amplitude and latency in children with migraine with aura in our study support the hypothesis that visual dysfunction in aura might be secondary to a loss of inhibitory GABAergic interneurons in the visual cortex, due to repeated parenchymal insults during the aura [5]. Because in most studies none correlation of VEP with duration and severity of migraine was found [32,39], some investigators suggests that visual evoked potentials abnormalities are congenital features [1]. The mutation in the gene CACNL1A4 was identified for familiar hemiplegic migraine [24]. Abnormal genes in other types of migraine are possible.

It has been also postulated that electrophysiologic abnormalities can be related to a central neurotransmitter alterations involving the input modulation mechanism: lack of inhibition or increase in excitation [10,38]. Serotonin is thought to play a pivotal role in migraine pathogenesis [8]. So, low interictal activity in the raphe cortical serotonergic pathway could be responsible for the low preactivation level of sensory cortices [33]. The normalisation of VEP just before and during the migraine attack might reflect an increase in the cortical preactivation level due to enhanced activity in raphe – cortical serotonergic pathway [12].

Furthermore, an inverse correlation between increased P100 amplitude and lowered serum magnesium levels was found in children suffering from migraine with and without aura in a headache – free period [3]. Magnesium is known to play an important role in the release of neurotransmitters (serotonin, dopamine, GABA, catecholamines and excitatory amino acids) and in the regulation of calcium channel in neural cells. A reduction of magnesium levels in blood and saliva in juvenile and adult migraineurs has been reported [9,31]. This reduction could be associated with spreading cortical depression, central neurotransmitter release and platelet hyperaggregation [27]. These data seem to support the hypothesis that hypomagnesemia could facilitate transmission in the visual pathway by means of hyperexcitability of neural cells [3].

In studies of sequential blocks of PR-VEP there were found major differences between migraneurs and healthy controls. The potentiation of the response in migraine contrasting with habitation in control subjects is characteristic [1,2,33]. The strong negative correlation between the initial amplitude of VEP and their amplitude increase during subsequent averaging, confirms that the response potentiation in migraine is due to a reduced preactivation level of sensory cortices [2]. Habituation of PR-VEP in healthy humans is maximal after 12 minutes, at the time when there is a decrease of stimulation enhanced by lactate levels in the occipital cortex [30]. Interictal habituation deficit in cortical information processing in migraine may suggest lactate accumulation in sensory cortices during sustained activation [1].

Althought we observed statistically significant changes of mean values VEP parameters in migraine, if we compared inividual results of each patient with migraine with mean value +2 standard deviations (SD) of tension-type headaches group, only 25% have VEP abnormalities above 2SD in tension-type headache group. It suggests very low sensitivity of this test. In

group of children investigated by Lemka [18] 50% patients with migraine had P100 latency more than 2SD above mean value of control healthy subjects. In other study sensivity of VEP in migraine in children was 67%, and the specifity was 83% [15]. The relatively low sensivity may reflect the inability to distinguish, basing on clinical symptoms alone between migraine and other headaches in children.

In conclusion, the diagnosis of migraine in children to remains predominantly based on medical history, due to low sensitivity and specifity of VEP in headache. However PR-VEP may support the diagnosis in some cases. PR-VEP could be helpful method in studying the pathogenesis of different forms of migraine. VEP abnormalities can be related to a cortical spreading depression and a central neurotransmitter alterations.

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