Intensity dependence of auditory evoked cortical potentials in migraine. Changes in the peri-ictal period

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Summary
The presence of premonitory symptoms in about 20% of patients suggest that the migraine attack is initiated long before the occurrence of the aura or headache symptoms. Recording of evoked and event-related potentials has revealed a strong intensity dependence of auditory evoked potentials (IDAP) in migraine with and without aura. We studied changes in IDAP in the peri-ictal period in 63 migraine patients (55 presenting migraine without aura, four migraine with aura, and four both types) and compared findings with interictal controls. The results of this study indicated that cortical processing of sensory information tends to normalize just before and during an attack. The normalization of IDAP may reflect an increase in central serotonergic activity. The study has been published in Cephalalgia (Áfra J, Sándor PS, Schoenen J. Cephalalgia 2000;20:714-719)

KEY WORDS: auditory evoked potentials, intensity dependence, migraine disorders, peri-ictal period.

Materials and methods

Introduction
Migraine is a disease with repeated attacks of headache accompanied by nausea/vomiting and/or photo/phono-phobia. In about 20% of patients premonitory symptoms (changes in mood, behaviour, wakefulness, appetite, bowel activity or fluid balance) precede attacks by up to 24 hours (1), suggesting that the attack is initiated long before the occurrence of the aura or headache symptoms. The pathomechanism of migraine has been extensively investigated over the past decades and one of the methods frequently used in these studies was electrophysiology. This seems to be a very useful tool to study migraine as it is non-invasive and provides a functional approach. Among the methods used, evoked and event-related potentials have been recorded in migraine patients during the interictal period, and the findings suggested that cortical information processing was abnormal compared to healthy volunteers. For instance, a strong intensity dependence of auditory evoked cortical potentials (IDAP) is characteristic of migraine with (MA) and without aura (MO) patients (2), which might be a consequence of reduced central serotonergic transmission (3) and decreased cortical preactivation levels. That IDAP can be considered a surrogate marker of central serotonin neurotransmission, has also been demonstrated previously in healthy volunteers and migraine patients with the administration of acute and prophylactic drugs (4,5).

In the light of these studies and clinical observations we studied changes in IDAP in the peri-ictal period.

For IDAP recordings 1000 Hz tones (50 ms total duration, 10 ms rise and fall times) were delivered binaurally through earphones at a random repetition rate of 0.53 to 0.61 Hz at four intensities (40, 50, 60 and 70 dB) above sensation level in a randomized order. The EEG was recorded with a needle electrode at Cz and referenced to linked mastoids. The amplifier system used was always the same Cadwell 8400 apparatus; filters were set at 1 Hz low- and 20 Hz high-cut. For each stimulus intensity 100 artefact-free sweeps were averaged over a 400 ms epoch.

Data analysis
N1 (between 60 and 150 ms post-stimulus) and P2 (between 120 and 200 ms post-stimulus) components were identified for each averaged recording of 100 responses. Peak-to-peak amplitude of N1-P2 was measured for


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each stimulus intensity and the linear amplitude/stimulus intensity function (ASF) slope (expressed in µV/10 dB) was calculated for each recording session.

**Results**

In all recordings N1 and P1 visual evoked potential (VEP) peaks as well as N1 and P2 components of auditory evoked potentials (AEPs) were clearly identified. There were no significant latency or mean amplitude differences in VEPs or AEPs between groups (Fig. 1). The day before the attack (n=8) and during the attack (n=21) AEP ASF slopes were flat (0.22±1.13µV/10dB and 0.37±1.35 µV/10dB, respectively) (Fig. 2), and thus markedly different from the mean ASF slope of the group of 71 MO patients recorded between attacks, but comparable with those recorded in healthy volunteers. One day after the attack (n=22), ASF slopes were higher (0.82±1.43µV/10dB). On day 2 after the attack they became as steep as in migraine patients between attacks (n=12) (1.25±1.07 µV/10 dB).

**Discussion**

This study indicates that cortical processing of sensory information as measured by IDAP tends to normalize just before and during an attack. It has to be taken into account, however, that recordings were collected from a number of patients who consulted a headache clinic and were at different time points in relation to their attack. Habitation and intensity dependence of evoked cortical potentials are probably to a great extent controlled by subcortical serotonergic afferents to the cortex (3,7). Serotonergic neurons in the raphe nuclei might tune cortical excitability (8). Low plasma levels of serotonin (9) might reflect low central serotonergic activity in migraine patients between attacks. This would explain the high intensity dependence of AEPs (2). The normalization of IDAP might thus reflect an increase in central serotonergic activity. Interestingly, during attacks of migraine without aura hyperperfusion was found in a brain stem region encompassing the dorsal raphe (10).

**References**