Maturation of early visual processing investigated by pattern-reversal Visual Evoked Potentials (VEPs) is altered in migraine

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Introduction
Deficient habituation is proposed as principal interictal abnormality in migraine and was found inter alia for Visual Evoked Potentials (VEPs) in adults. During childhood latencies and amplitudes of VEPs change with age, this is supposed to indicate cerebral maturation processes. Recently, evidence for a disturbed maturation of cerebral information processing in migraine came from studies investigating contingent negative variation (CNV) and the auditory evoked potential during childhood (Knopp et al. 1999, Bender et al. 2002). This study is to clarify if age-dependent development is altered also for the processing of visual stimuli in migraine.

Methods
Response to high-contrast pattern-reversal VEPs with 4 different check sizes (60, 30, 15 and 7.5 min of arc) and habituation to a low-contrast pattern reversal VEP (7.5 min of arc) were investigated in children with primary headache in the headache-free interval and healthy controls from six to 18 years. 123 children suffering from primary headache (n=67 migraine without aura (MS), n=32 migraine with aura (MA), n=24 tension-type headache (TH)) and 82 healthy controls (CO) were included.

Age-dependent development of VEP components was investigated as a measure for maturation. Children were divided into two age groups: 6-11 years (late puberty and post puberty) and 12-18 years (early puberty and early puberty). For measuring habituation, a linear regression analysis of the interpeak amplitudes was performed over the 5 blocks in each subject. Habituation was indicated by a negative slope of the regression line, potentiation by a positive slope.

Results
For the high-contrast patterns, age-dependent development was normal for N80 and P100 latency in children with primary headache, but altered for N135 latency as indicated by a significant interaction between the factors diagnosis, spatial frequency and age group (p<0.01) (see fig 1). In headache-free controls, N735 latency reduction between pre- and postpuberty age was most pronounced at high spatial frequency whereas in primary headache, it was less pronounced at high spatial frequency (see fig 2).

For the low-contrast habituation paradigm, a reduction of N180 latency from pre- to postpubertal age was also clearly present in controls but lessened in migraineurs. N180 latency was prolonged in migraineurs without aura from 12 years onwards (see fig 3). Habituation did not differ between groups (see fig 4).

Discussion
The VEP N135 component is prolonged at high spatial frequency in adult migraineurs (Oelkers et al. 1999), this is found in migraine children from puberty onwards (12 years) as well. In younger children, inactivity of the VEP components masks possible differences between groups. The main “decline” of N135 latency with increasing age was shifted to lower spatial frequencies in the headache subgroup. The results give further evidence that sensory maturation is altered in migraine for special subfunctions and quite normal or even advanced for others. The phenomenon of deficient habituation which has been proposed to be characteristic for migraine could not be reproduced in children and adolescents. This might be due to the finding that habituation itself is a subject to maturation and decreases with increasing age during childhood.

Conclusion
• Habituation to visual stimuli undergoes maturation during childhood.
• The habituation deficit which has been described in adult migraineurs may also develop during childhood and adolescence.
• Maturation of visual processing is altered in migraine which gives further evidence for migraine as a maturation disorder.

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