High resolution analysis of Contingent Negative Variation in Children and Adolescents with primary Headache

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http://www.med.uni-heidelberg.de/psychia/psych/forschung/sektionen/exp_psych/index.html

Introduction:

The understanding of the pathophysiology of migraine has changed within recent years. Today it is assumed that migraine is a cerebral disorder and that the vascular response is a secondary process. The prevalence of headache among children is high, especially after they have started school. Recently, evidence has emerged that maturation processes might play an important role in migraine pathophysiology. Increased CNV amplitudes reflecting cortical hyperexcitability have been described for migraineurs by various authors; however, the cerebral sources which account for differences in CNV amplitude have not been revealed yet.

Methods:

In order to address this question we examined 123 children with primary headache (diagnosis according to the criteria of the International Headache Society) and 81 healthy control children aged 6-18 years in a contingent negative variation (CNV) paradigm using 64-channel high resolution DC-EEG. Diagnose-related group differences were tested for initial (iCNV) and late CNV (lCNV) as well as for the postimperative negative variation (PINV), for motor and non-motor areas of interest (pre/primary motor cortex, supplementary/cingulate motor area, posterior parietal cortex).

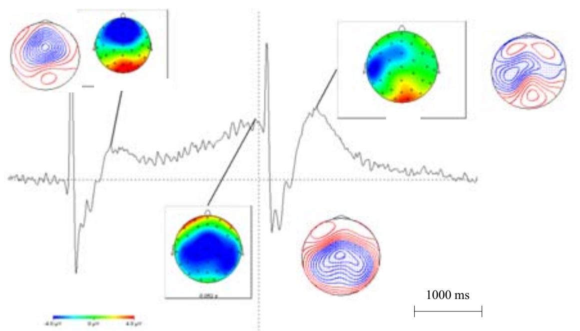

Figure 1:
Time course of CNV in healthy 12-18-year-old subjects at C3 and colour / isopotential-line maps illustrating topography of CNV components (early and late CNV as well as postimperative negative variation). Please compare figure 2 (difference headache patients minus healthy subjects) and figure 1 (normal mature CNV).

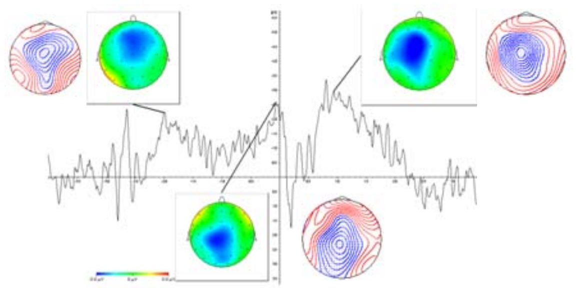

Figure 2:
Time course of the difference wave 6-11-year-old headache patients minus healthy subjects at Cz and colour / isopotential-line maps illustrating the topography of the diagnose-related differences. Please compare to figure 1 (physiological topography of CNV-components) and note that the diagnose related differences follow the same time course as physiological CNV and to a certain amount the differences between the groups adjust to the topography of the physiological components (during early CNV more frontal, during late CNV more posterior maximum). These facts point towards a **general hyperactivation/-excitability**.
However, for all three components, differences are most pronounced in the area near the vertex pointing towards a **qualitatively different, area-specific hyperactivation**.

Results:

The ANOVA with the between-subject factors age group (6-11 and 12-18 years), diagnose (healthy, migraine without aura, migraine with aura, tension type headache), area of interest (see methods) and the repeated measurement factor CNV-component (iCNV, lCNV and PINV) yielded a significant interaction between age, diagnose and area of interest (F=1.83; p=0.04; see figure 4). Post hoc tests revealed that this was due to an area-specific increase in negativity for migraineurs without aura over the supplementary/cingulate motor area (SCMA) for 6-11-year-old children (6-11 year-old subjects suffering from migraine without aura differed from healthy controls of the same age over SCMA, Tukeys HSD p=0.01; see figure 2). 6-11-year-old migraineurs showed a PINV over the vertex which was absent in normal children and paralleled motor PINV at C3 [2] (see figure 3) and also presented an elevated late CNV. As a consequence, migraine children lacked age-dependent development of late CNV [1]. No differential diagnostic differences between headache groups were found, results turned out to be statistically different between the two largest groups - healthy controls and migraine without aura.

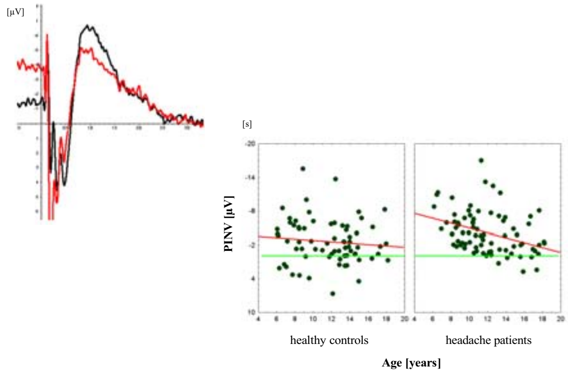

Figure 3:
Top: Time course of physiological motor postimperative negative variation (PINV) at C3 (black line) and the time-course of the increased negativity over the vertex (electrode Cz) in 6-11-year-old headache subjects (red line).
Bottom: Scatterplot showing the age-dependent elevation of PINV in all children suffering from headaches.

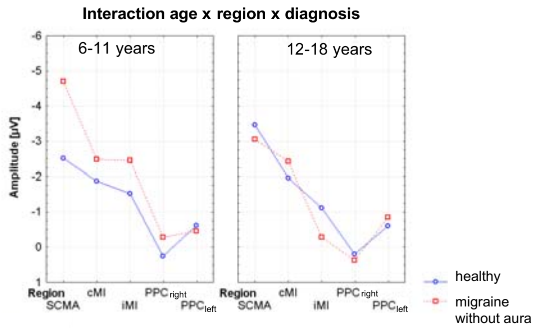

Figure 4:
Interaction age x region (area of interest) x diagnosis. SCMA = supplementary/cingulate motor area; cMI = contralateral pre/primary motor area; iMI = ipsilateral pre/primary motor area; PPC = posterior parietal cortex

Discussion / Conclusions:

Because the CNV difference waves between 6-11-year-old migraineurs without aura and healthy controls followed the same time-course and adjusted to some extent to the topography of physiological CNV components (see figure 1), our findings could be explained by a general (noradrenergic) hyperactivation of the cortex (arising from the locus coeruleus in the brainstem), leading to an unspecific overactivation of all physiologically implicated cortical areas.
However, because the difference waves did NOT entirely follow the normal CNV topography but showed also a specific negativity increase over the vertex, our results could also be accounted for by a specific involvement of dopaminergic influences from the basal ganglia on the supplementary motor area.
In agreement with previous studies showing increased PINV amplitudes in migraine children but not in adult migraineurs, important influences of maturation and/or relative task difficulty could be shown because differences were found only in the prepubertal group.
Further research is needed to clarify whether an area-specific hyperactivation occurs in migraineurs.

References:

[1] Bender S, Weisbrod M, Just U, Pfuller U, Parzer P, Resch F, Oelkers-Ax R. Lack of age dependent development of the contingent negative variation (CNV) in migraine children?, Cephalalgia 22 (2002) 132-136.
[2] Bender S, Oelkers-Ax R, Resch F, Weisbrod M. Motor processing after movement execution as revealed by evoked and induced activity. Cognitive Brain Research 21 (2004):49-58.

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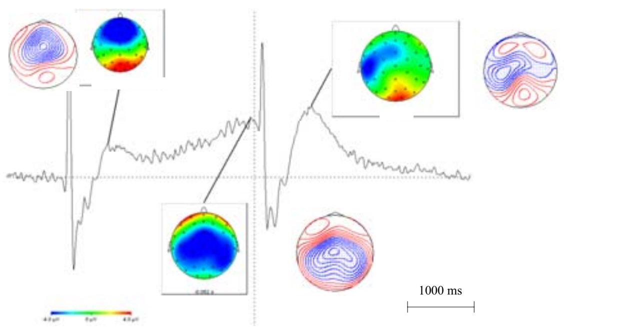

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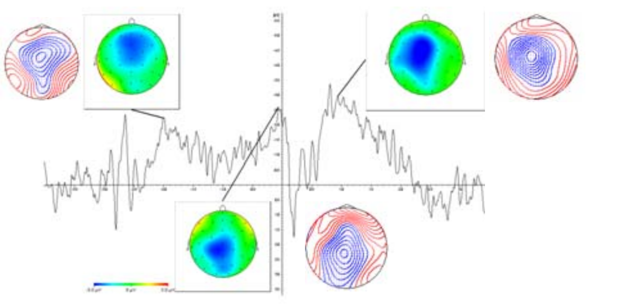

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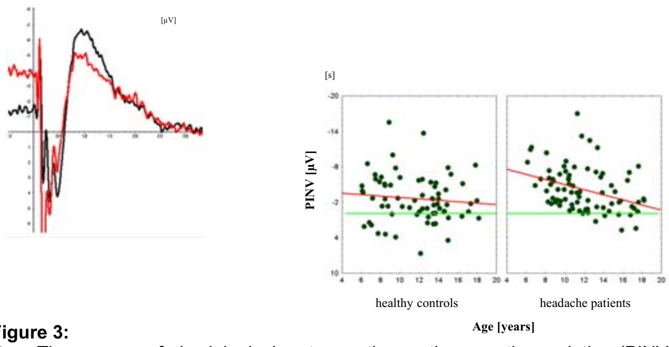

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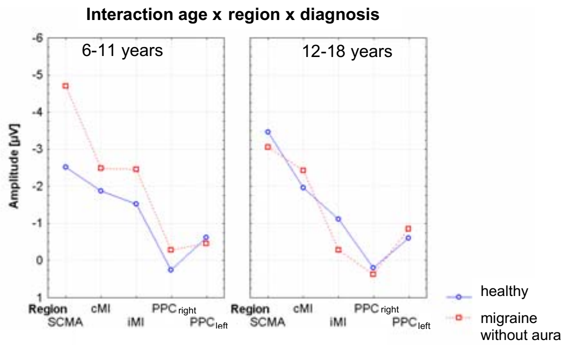

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