Contingent Negative Variation (CNV) in migraine patients during childhood and adolescence: Lack of age-dependent development

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Abstract:

Objective: Increased negativity of CNV in adult migraineurs is thought to reflect cortical hyperexcitability. Recently CNV was shown to decrease with age in healthy adults but not in migraineurs. Our study investigates age-dependency in younger age.
Methods: 76 healthy controls and 61 children with migraine (IHS criteria) between 6 and 18 years were examined by 64-channel EEG recording using an acoustic S1-S2-CNV-paradigma with 3s interstimulus interval.
Results: Healthy controls showed an increase of CNV amplitude with age whereas in migraine children amplitudes didn't change. Young migraineurs show already a significantly more pronounced negativity of CNV amplitude over central areas than controls. These group differences disappear during adolescence.
Conclusions: 1.) Increased CNV negativity might reflect a biological vulnerability to migraine rather than being a result of chronification.
2.) Migraineurs seem to lack age-dependent development of CNV also during early age which supports the hypothesis of migraine as a maturation disorder.

Introduction

Why is migraine relevant for child and adolescent psychiatry?

The prevalence of headache among school children ranges from 5 to 25%. In psychiatric patients it is even higher. To treat those patients adequately it would be helpful to understand the interactions between pain and the cognitive system.

Evoked potentials reflect cerebral hyperexcitability in migraine: The amplitude of the contingent negative variation (CNV) - the negative shift between a warning stimulus S1 and a target stimulus S2 which requires a response - is increased in adult migraineurs with respect to healthy controls during the headache free interval. This increase is well established, yet it is unclear if it is caused mainly by the late (lCNV, Böcker et al 1990) or the early component (iCNV, Kropp et al 1999).
Though there are first studies concerning children (Besken et al 1993, Kropp et al 1999), age-dependent development of CNV in children with migraine has not been investigated yet.
The aim of the current study was to examine whether children with migraine without aura (MO) differ from healthy controls (CO) in CNV parameters (iCNV, lCNV, total CNV tCNV) during the headache free interval. Special emphasis was put on the question if age-dependent development is altered in migraine.

	Amplitude [µV]			age slope [µV/y]				
	CO	MO	p	CO		MO		diff.
	N=71	N=55		coef.	p	Coef.	p	p
iCNV	-3.83 ± 1.04	-5.12 ± 1.04	0.209	-0.63	0.040	-0.13	0.746	0.305
lCNV	-6.74 ± 0.73	-8.89 ± 0.83	0.001	-0.90	0.000	0.07	0.787	0.006
tCNV	-4.55 ± 0.50	-6.32 ± 0.58	0.010	-0.45	0.004	0.04	0.828	0.049

Table 1. Mean amplitudes and age slopes

Mean amplitude (+/- standard error of the mean) and age slope (coefficient and significancy level of the regression) of iCNV, lCNV and tCNV are presented for healthy controls (CO) and children with migraine without aura (MO).

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Methods

61 children suffering from migraine without aura (MO - IHS classification code 1.1, mean age 10.3 +/- 2.89 (SD) years, 35 male / 26 female) and 76 healthy controls (CO 11.1 +/- 3.32 years, 43m / 33f) were included into the study following these criteria: MO disease duration > 1 year and at least 3 attacks within the last three months. 5 children had to be excluded from analysis because of headache attacks after the recording. We recorded 20 CNV trials using a warning stimulus S1, 1000 Hz, duration 50 ms, and an imperative stimulus S2, 2000 Hz, 50 ms. The interstimulus interval (ISI) was 3 s, the intertrial interval (ITI) varied randomly from 10 to 15 s. Linked mastoids served as reference channels and recordings 1 s before S1 as baseline. 6 subjects of 132 had to be excluded because they did not respond properly or produced unremovable artefacts. The amplitude of iCNV, tCNV and lCNV was calculated as the mean amplitude of the intervals according to Böcker 1990. Multivariate regression analysis procedures were calculated to evaluate the influence of diagnosis, age, sex and the interaction between diagnosis and age (to detect group differences in age-dependent development).

Results

Group differences in amplitude: Children with MO showed significant higher amplitudes of lCNV and tCNV than CO (p= 0.001 and 0.010, table 1). These differences were particularly found at early age (see figure 1 and age-dependency below). The early component (iCNV) showed more variability due to inhomogenous latency and a tendency to increase already at a younger age in controls, no significant differences were found between groups.
In both groups **reaction time** (RT) decreased significantly with age (CO p<0.001 and MO p<0.001). There were no significant differences between CO and MO children (p= 0.988).
Age-dependency: Linear regression showed significant age-dependency (table 1) of tCNV (age slope coef.= -0.45, p= 0.004), lCNV (coef.= -0.90, p<0.001) and iCNV (coef.= -0.63, p= 0.040) for CO at Cz. MO children did not show this development: tCNV coef. = 0.04 (p= 0.83), lCNV coef. = 0.07 (p= 0.79) and iCNV coef = -0.13 (p= 0.75).
The age slopes of CO and MO differed significantly between groups for tCNV (p<0.05) and lCNV (p <0.01) but not for iCNV (p= 0.305).

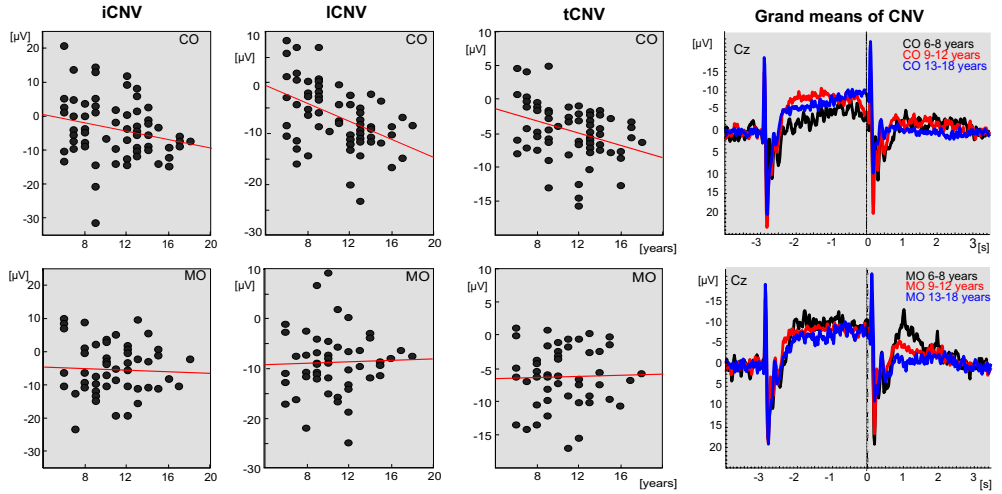

Figure 1. Age development of lCNV

Scatter plots showing age-dependent development and variability of iCNV, lCNV and tCNV in CO (healthy controls) and MO (children with migraine without aura). CO show a significant increase of lCNV and tCNV amplitude with age whereas MO don't.

Discussion

1. Like adults do, young MO children also show increased CNV amplitudes with respect to CO. Thus, differences in late and total CNV amplitude rather represent vulnerability than result from long-term chronification. As CNV represents focused attention and expectancy, its increased amplitude might reflect a disposition to suffer from migraine due to differences in attention and information processing.

2. Healthy children show increase in tCNV and lCNV amplitude with age. The rise in CNV amplitude in CO might reflect natural development of catecholaminergic systems. Migraine children fail to show this development maybe due to a ceiling effect. Maturation processes might be altered in migraine. Altered maturation may be the cause that some but not all patients continue to suffer from headaches during adulthood.

Conclusion

Childhood headache could result from a disposition to a cerebral "over-involvement" in information processing - and on the other hand alter itself again the development of the brain: Results give evidence for a disturbed cerebral maturation. Proper treatment could be the key to avoid sensitization and chronification.

References

1. Böcker KB, Timsit-Berthier M, Schoenen J, Brunia CH. Contingent Negative Variation in Migraine. Headache 1990; 30:604-9.
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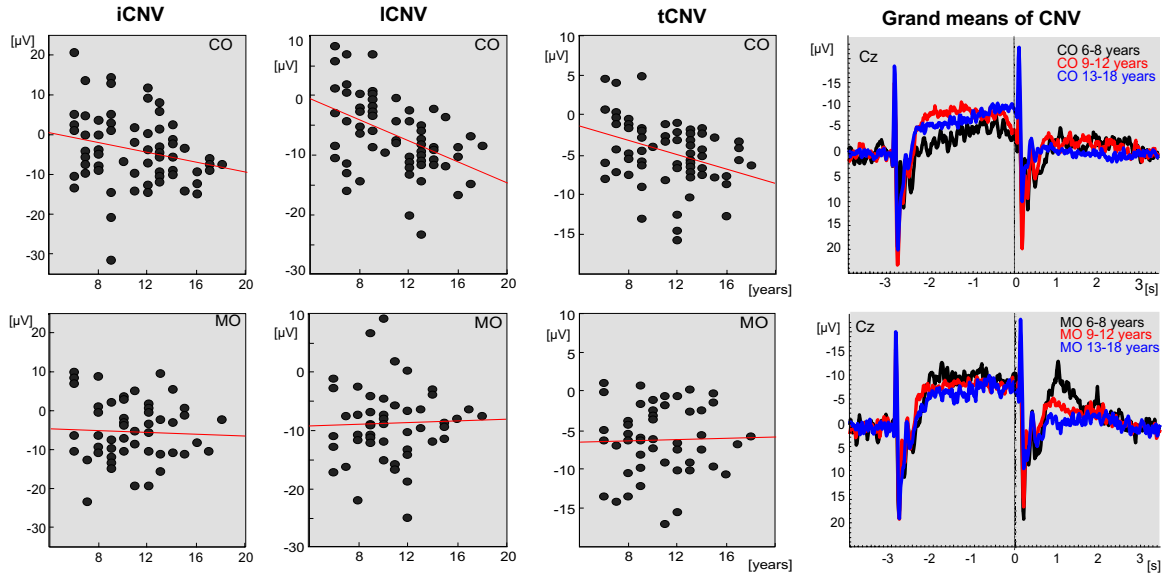

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