High resolution analysis of Contingent Negative Variation during Childhood and Adolescence

Stephan Bender*, Rieke Oelkers-Ax*, Franz Resch*, Matthias Weisbrod**

* Department for Child and Adolescent Psychiatry
** Section For Experimental Psychopathology, Psychiatric Clinic, University of Heidelberg, Germany

Introduction:

The basic mechanisms of movement preparation, post-movement motor processing and sensory attention as reflected in the contingent negative variation (CNV) paradigm undergo a prolonged maturation during school age and adolescence.

Methods:

We examined a large sample of 81 healthy children and adolescents between 6 and 18 years in an acustic CNV paradigm (3s stimulus onset asynchrony) using 64-channel high resolution DC EEG. Alpha event-related desynchronization (alpha-ERD) was also determined as an indicator of motor cortex activation.

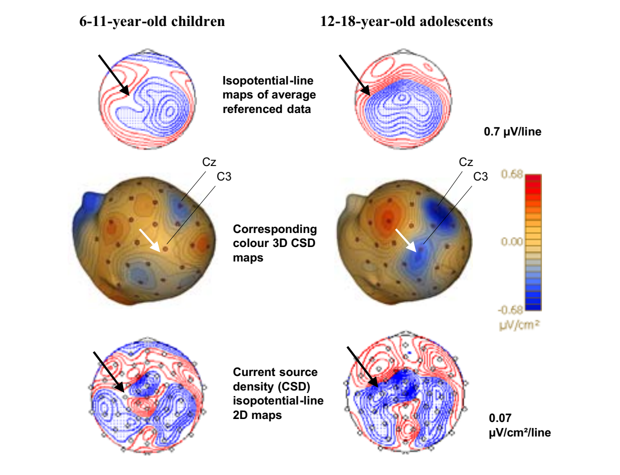

Figure 1: Maps during late contingent negative variation (CNV) for 6-11 (left) and 12-18-year-old subjects (right).
Top: Isopotentialline-maps (BESA) for average referenced data during late CNV. Scaling: 0.7 µV/line. Blue dotted areas indicate negativity, red lines indicate positivity. The arrows indicate that 6-11-year-old children were lacking negativity over the left central area. Please note that in contrast 6-11-year-old children did show right-sided posterior negativity.
Middle: The same data are illustrated as the corresponding 3-D current source density (CSD) colour-maps (BESA). The white arrow visualizes that a dipole oriented perpendicular to the surface of the posterior wall of the precentral gyrus (primary motor cortex) could account for the centro-parietal negativity as well as the fronto-polar positivity in older subjects (12-18 years). Scaling: From dark blue (-0.68 µV/cm²) to dark red (+0.68 µV/cm²).
Bottom: Current source density (CSD) isopotentialline-maps (BESA) for late CNV. Scaling: 0.07µV/cm²/line. Blue dotted areas indicate current sinks, red lines indicate current sources. The arrows indicate that the current sink over the left (contralateral) pre-/primary motor cortex was only present in 12-18 but not 6-11-year-old children.

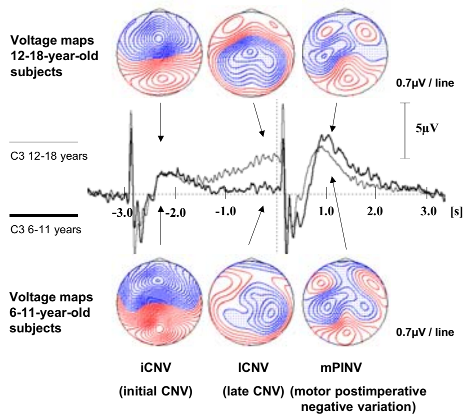

Figure 2: Time-course of CNV at C3 against average reference (contralateral to the response movement).
Please note that missing left central negativity for 6-11-year-old children is specific for the late CNV-interval.

Conclusions:

High resolution EEG and the combination of evoked (CNV) and induced (alpha-ERD) activity can provide important insights into the motor and attentional subcomponents of CNV and their different maturational courses, providing an explanatory model for CNV abnormalities in different pathologies such as ADHD, schizophrenia or migraine.

References:

[1] Bender S, Resch F, Weisbrod M, Oelkers-Ax R. Specific task anticipation versus unspecific orienting reaction during early contingent negative variation. Clin Neurophysiol; 115 (2004):1836-45.
[2] 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.
[3] 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.

This work was supported by the Pain Research Programme (F207040, E1) and the medical young investigator award (the latter for the first author) of the Medical Faculty, University of Heidelberg.

Results:

1.) Unilateral alpha-ERD over the contralateral sensorimotor area early during the initial CNV (iCNV; see figure 4; alpha-ERD lateralization during iCNV is significant) showed that the warning stimulus was sufficient to produce early task specific motor processing and that during iCNV there occurred already movement-specific processes instead of a mere general orienting response [1].

2.) Current source density analysis of the late component of CNV revealed that 6-11-year-old children were nearly completely missing the current sink over the contralateral primary motor cortex and the supplementary/cingulate motor area, while both 6-11 and 12-18-year-old subjects showed a right-sided posterior negativity (see figure 1). Late CNV seemed to consist of two different components, a motor preparation subcomponent with a prolonged maturation (for first results regarding Cz see [2]) and a sensory-attention-component which is visible already at earlier stages.

Dipole source analysis (see figure 3) confirmed that posterior negativity in younger subjects was no projection from frontal (motor) areas but could be attributed indeed to sensory attention and sensory-motor integration because dipoles 3 and 4 (perpendicular to the precentral gyrus) took up considerable activity only in 12-18 year-old subjects.

Significant alpha-ERD before S2 (see figure 4) confirmed that also 6-11-year-old subjects did use motor preparation. Thus the missing centro-parietal negativity in younger children could image the immaturity of a specific subcomponent of the motor system and show how younger children prepare for a fast movement in a different way than adults do.

3.) A postimperative negative variation (PINV) lateralized contralaterally to the response movement side [3] occurred regardless of age providing hints towards a post-movement processing in the motor cortices which followed a different maturational course than the motor preparation subcomponent of late CNV (see figure 2).

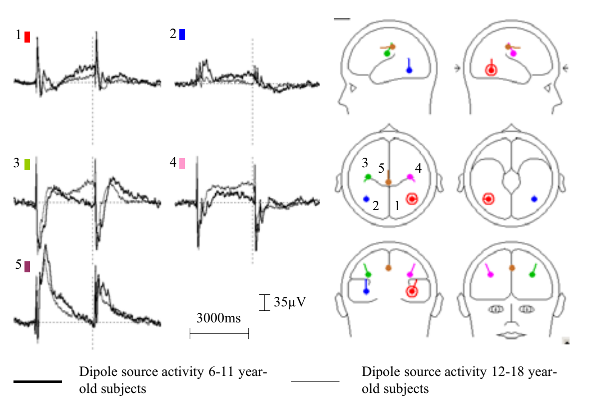

Figure 3: Dipole source analysis.
Right: Dipole model for late CNV (BESA). Dipoles 1 and 2 were fitted on the interval 200ms before the imperative stimulus on the grand average of 6-11-year-old children while dipoles 3 and 4 were fitted on the grand average of 12-18-year-old subjects. Dipole 5 was introduced to model influences from the early component of CNV. Please note, that only dipoles 3 and 4, fitted on the grand average of 12-18-year-old subjects, showed an orientation perpendicular to the precentral gyrus. Please note that all dipoles are equivalent dipoles which come to lie deeper in the brain than the actual active anatomical structures because in contrast to early sensory evoked potentials, widespread cortical areas are activated.
Left: Grand average of the exported source waveforms when the dipole model is applied to the individual averages for 6-11-year-old subjects (thick line) and 12-18-year-old subjects (thin line). The dashed vertical line indicates the time of occurrence of the imperative stimulus. Dipoles 3 and 4 explain the surface potential during late CNV only for 12-18-year-old subjects. For 6-11-year-old subjects a projection from frontal areas does not contribute substantially to right posterior negativity. Please also note that dipole 5 takes up considerable activity only during early but not late CNV.

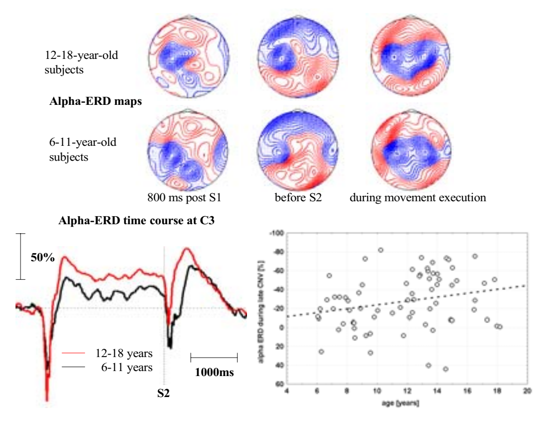

Figure 4: Alpha event-related desynchronization (ERD) during late CNV.
Top: Isopotential-line alpha-ERD-maps for 6-11 and 12-18-year-old subjects early during CNV (800ms after the warning stimulus, left), before the imperative stimulus during late CNV (middle) and during movement execution (right). Blue dotted areas indicate alpha-ERD, red isopotential-lines an increase of alpha power. Scaling: 2.5%/line for iCNV and lCNV for 6-11 year-old children and 4%/line for the rest of the maps. Please note alpha-ERD over the contralateral sensorimotor area in both age-groups though clearly more pronounced in older subjects. While during early CNV and during movement execution additional alpha-ERD over posterior parietal/occipito-parietal areas becomes visible (most likely related to sensory-motor integration), during late CNV a widespread frontopolar alpha-ERD occurred for both age groups.
Bottom left: Time-course of alpha-ERD at C3 during CNV and movement execution. The dashed vertical line indicates the time of occurrence of the imperative stimulus.
According to the faster reaction times in older children, also post-imperative alpha-ERD peaked earlier in 12-18-year-old children.
Bottom right: Scatterplot alpha-ERD at C3 during late CNV against age. It becomes apparent that there is a certain increase in the amount of alpha-ERD during late CNV with increasing age. However, please note that alpha-ERD during movement execution also increased with age (left) suggesting that this increase did rather reflect changes in alpha-background-power than actual changes in the extent of motor preparation.

High resolution analysis of Contingent Negative Variation during Childhood and Adolescence

Stephan Bender*, Rieke Oelkers-Ax*, Franz Resch*, Matthias Weisbrod**

* Department for Child and Adolescent Psychiatry

** Section For Experimental Psychopathology, Psychiatric Clinic, University of Heidfelberg, Germany

Corresponding author: stephan_bender@med.uni-heidelberg.de

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

Introduction:

The basic mechanisms of movement preparation, post-movement motor processing and sensory attention as reflected in the contingent negative variation (CNV) paradigm undergo a prolonged maturation during school age and adolescence.

Methods:

We examined a large sample of 81 healthy children and adolescents between 6 and 18 years in an acoustic CNV paradigm (3s stimulus onset asynchrony) using 64-channel high resolution DC EEG. Alpha event-related desynchronization (alpha-ERD) was also determined as an indicator of motor cortex activation.

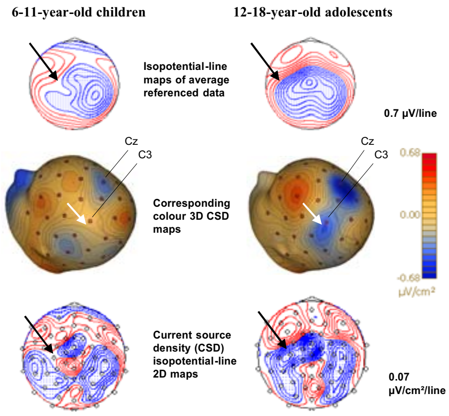

Figure 1: Maps during late contingent negative variation (CNV) for 6-11 (left) and 12-18-year-old subjects (right).
Top: Isopotentialline-maps (BESA) for average referenced data during late CNV. Scaling: 0.7 µV/line. Blue dotted areas indicate negativity, red lines indicate positivity. The arrows indicate that 6-11-year-old children were lacking negativity over the left central area. Please note that in contrast 6-11-year-old children did show right-sided posterior negativity.
Middle: The same data are illustrated as the corresponding 3-D current source density (CSD) colour-maps (BESA). The white arrow visualizes that a dipole oriented perpendicular to the surface of the posterior wall of the precentral gyrus (primary motor cortex) could account for the centro-parietal negativity as well as the fronto-polar positivity in older subjects (12-18 years). Scaling: From dark blue (-0.68 µV/cm²) to dark red (+0.68 µV/cm²).
Bottom: Current source density (CSD) isopotentialline-maps (BESA) for late CNV. Scaling: 0.07µV/cm²/line. Blue dotted areas indicate current sinks, red lines indicate current sources. The arrows indicate that the current sink over the left (contralateral) pre-/primary motor cortex was only present in 12-18 but not 6-11-year-old children.

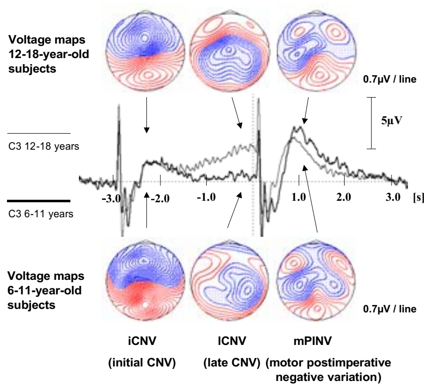

Figure 2: Time-course of CNV at C3 against average reference (contralateral to the response movement).
Please note that missing left central negativity for 6-11-year-old children is specific for the late CNV-interval.

Conclusions:

High resolution EEG and the combination of evoked (CNV) and induced (alpha-ERD) activity can provide important insights into the motor and attentional subcomponents of CNV and their different maturational courses, providing an explanatory model for CNV abnormalities in different pathologies such as ADHD, schizophrenia or migraine.

References:

[1] Bender S, Resch F, Weisbrod M, Oelkers-Ax R. Specific task anticipation versus unspecific orienting reaction during early contingent negative variation. Clin Neurophysiol; 115 (2004):1836-45.

[2] 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.

[3] 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.

This work was supported by the Pain Research Programme (F207040, E1) and the medical young investigator award (the latter for the first author) of the Medical Faculty, University of Heidelberg.

Results:

1.) Unilateral alpha-ERD over the contralateral sensorimotor area early during the initial CNV (iCNV; see figure 4; alpha-ERD lateralization during iCNV is significant) showed that the warning stimulus was sufficient to produce early task specific motor processing and that during iCNV there occurred already movement-specific processes instead of a mere general orienting response [1].

2.) Current source density analysis of the late component of CNV revealed that 6-11-year-old children were nearly completely missing the current sink over the contralateral primary motor cortex and the supplementary/cingulate motor area, while both 6-11 and 12-18-year-old subjects showed a right-sided posterior negativity (see figure 1). Late CNV seemed to consist of two different components, a motor preparation subcomponent with a prolonged maturation (for first results regarding Cz see [2]) and a sensory-attention-component which is visible already at earlier stages.

Dipole source analysis (see figure 3) confirmed that posterior negativity in younger subjects was no projection from frontal (motor) areas but could be attributed indeed to sensory attention and sensory-motor integration because dipoles 3 and 4 (perpendicular to the precentral gyrus) took up considerable activity only in 12-18 year-old subjects.

Significant alpha-ERD before S2 (see figure 4) confirmed that also 6-11-year-old children did use motor preparation. Thus the missing centro-parietal negativity in younger children could image the immaturity of a specific subcomponent of the motor system and show how younger children prepare for a fast movement in a different way than adults do.

3.) A postimperative negative variation (PINV) lateralized contralaterally to the response movement side [3] occurred regardless of age providing hints towards a post-movement processing in the motor cortices which followed a different maturational course than the motor preparation subcomponent of late CNV (see figure 2).

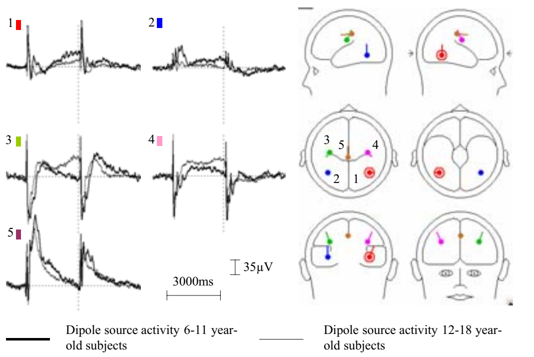

Figure 3: Dipole source analysis.
Right: Dipole model for late CNV (BESA). Dipoles 1 and 2 were fitted on the interval 200ms before the imperative stimulus on the grand average of 6-11-year-old children while dipoles 3 and 4 were fitted on the grand average of 12-18-year-old subjects. Dipole 5 was introduced to model influences from the early component of CNV. Please note, that only dipoles 3 and 4, fitted on the grand average of 12-18-year-old subjects, showed an orientation perpendicular to the precentral gyrus. Please note that all dipoles are equivalent dipoles which come to lie deeper in the brain than the actual active anatomical structures because in contrast to early sensory evoked potentials, widespread cortical areas are activated.
Left: Grand average of the exported source waveforms when the dipole model is applied to the individual averages for 6-11-year-old subjects (thick line) and 12-18-year-old subjects (thin line). The dashed vertical line indicates the time of occurrence of the imperative stimulus. Dipoles 3 and 4 explain the surface potential during late CNV only for 12-18-year-old subjects. For 6-11-year-old subjects a projection from frontal areas does not contribute substantially to right posterior negativity. Please also note that dipole 5 takes up considerable activity only during early but not late CNV.

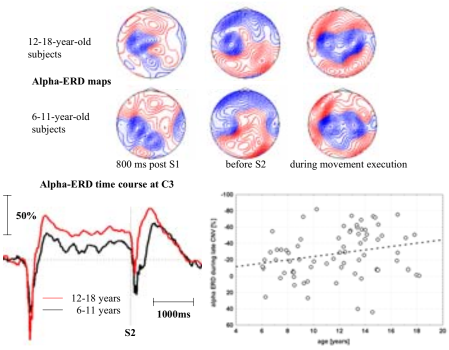

Figure 4: Alpha event-related desynchronization (ERD) during late CNV.
Top: Isopotential-line alpha-ERD-maps for 6-11 and 12-18-year-old subjects early during CNV (800ms after the warning stimulus, left), before the imperative stimulus during late CNV (middle) and during movement execution (right). Blue dotted areas indicate alpha-ERD, red isopotential-lines an increase of alpha power. Scaling: 2.5%/line for iCNV and lCNV for 6-11 year-old children and 4%/line for the rest of the maps. Please note alpha-ERD over the contralateral sensorimotor area in both age-groups though clearly more pronounced in older subjects. While during early CNV and during movement execution additional alpha-ERD over posterior parietal/occipito-parietal areas becomes visible (most likely related to sensory-motor integration), during late CNV a widespread frontopolar alpha-ERD occurred for both age groups.
Bottom left: Time-course of alpha-ERD at C3 during CNV and movement execution. The dashed vertical line indicates the time of occurrence of the imperative stimulus.
According to the faster reaction times in older children, also post-imperative alpha-ERD peaked earlier in 12-18-year-old children.
Bottom right: Scatterplot alpha-ERD at C3 during late CNV against age. It becomes apparent that there is a certain increase in the amount of alpha-ERD during late CNV with increasing age. However, please note that alpha-ERD during movement execution also increased with age (left) suggesting that this increase did rather reflect changes in alpha-background-power than actual changes in the extent of motor preparation.