



From preparation to post-processing: Insights into evoked and induced cortical activity during pre-cued motor reactions in children and adolescents

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ABSTRACT

Introduction: The motor system undergoes significant development throughout childhood and adolescence. The contingent negative variation (CNV), a brain response reflecting preparation for upcoming actions, offers valuable insights into these changes. However, previous CNV studies of motor preparation have primarily focused on adults, leaving a gap in our understanding of how cortical activity related to motor planning and execution matures in children and adolescents.

Methods: The study addresses this gap by investigating the maturation of motor preparation, pre-activation, and post-processing in 46 healthy, right-handed children and adolescents aged 5–16 years. To overcome the resolution limitations of previous studies, we combined 64-electrode high-density Electroencephalography (EEG) and advanced analysis techniques, such as event-related potentials (ERPs), mu-rhythm desynchronization as well as source localization approaches. The combined analyses provided an in-depth understanding of cortical activity during motor control.

Results: Our data showed that children exhibited prolonged reaction times, increased errors, and a distinct pattern of cortical activation compared to adolescents. The findings suggest that the supplementary motor area (SMA) plays a progressively stronger role in motor planning and response evaluation as children age. Additionally, we observe a decrease in sensory processing and post-movement activity with development, potentially reflecting increased efficiency. Interestingly, adolescent subjects, unlike young adults in previous studies, did not yet show contralateral activation of motor areas during the motor preparation phase (late CNV).

Conclusion: The progressive increase in SMA activation and distinct cortical activation patterns in younger participants suggest immature motor areas. These immature regions might be a primary cause underlying the age-related increase in motor action control efficiency. Additionally, the study demonstrates a prolonged maturation of cortical motor areas, extending well into early adulthood, challenging the assumption that motor control is fully developed by late adolescence. This research, extending fundamental knowledge of motor control development, offers valuable insights that lay the foundation for understanding and treating motor control difficulties.

Abbreviations

ACC	anterior cingulate cortex
CNV	contingent negative variation
CSD	current source density
EEG	electroencephalogram
EHI	edinburgh handedness inventory

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ERD	event-related desynchronization
ERP	event-related potential
ERS	event-related synchronization
ICA	independent component analysis
iCNV	initial or early CNV
ICNV	late CNV

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LORETA	low-resolution brain electromagnetic tomography
LRP	lateralized readiness potential
M1	primary motor cortex
MRP	motor evoked potential
PINV	post-imperative negative variation
SMA	supplementary motor area
SSLOFO	current standardized shrinking LORETA-FOCUSS

1. Introduction

Cortical development in childhood and adolescence underlies complex restructuring processes characterized by extensive anatomical (Huttenlocher, 1979; Shaw et al., 2008) as well as functional changes in the cerebral cortex (Thatcher, 1992). Gaining proficient motor skills stands as a key cornerstone in human development; however, there is limited understanding regarding the relationship between brain development and the acquisition of motor abilities.

The motor system engages in various processes when preparing for movement. This includes the selection of the involved muscles, determining the required contraction force, and arranging the temporal sequence of movements. Changes in brain activity prior to a movement reflect neural processes associated with movement preparation and execution (Deecke et al., 1969). Thereby, it was shown that the supplementary motor area (SMA) plays a crucial role in planning and coordinating voluntary movements (Roland et al., 1980; Tanji, 2001) and that SMA activity has a modulatory effect on the output of the primary motor cortex (M1) (Côté et al., 2020).

The maturation of functional activity related to motor network pre-activation can be studied by analyzing age-dependent changes of event-related potentials (ERPs) before the execution of a movement. The negative potential arising between a warning stimulus (S1) and a behaviorally relevant imperative stimulus (S2) is described as contingent negative variation (CNV) and is associated with processes of movement preparation and attention allocation (Rockstroh, 1982; Walter et al., 1964). The imperative stimulus follows the warning stimulus in fixed time intervals and requires a fast motor response. To efficiently process the imperative stimulus, the neuronal network responsible for initiating the chosen response movement must be pre-activated. Since the CNV is based on a predictable, external cue, it allows to temporally disentangle early response selection and preparation processes, i.e., the recruitment and selection processes of the specific neuronal networks required for a fast response (Gomez et al., 2003).

The CNV consists of an early low, negative component that typically follows the warning stimulus with a latency of 550 to 750 ms and a more pronounced negative late component that precedes the behaviorally relevant imperative stimulus. The early CNV (abbreviated as iCNV; initial CNV; “O-wave”) is suggested to reflect an orienting response (Rockstroh, 1982) and to originate from the SMA and the anterior cingulate cortex (ACC) (Cui et al., 2000; Gomez et al., 2001). The late CNV (abbreviated as lCNV; E-wave) is associated with preparatory processes and stimulus anticipation (Rohrbaugh et al., 1976) observed as pre-activation of the contralateral motor areas. Furthermore, the CNV contains a post-movement potential known as post-imperative negative variation (PINV). This slow negative potential can be studied to evaluate processes related to motor performance evaluation (Klein et al., 1996). Previously, the PINV was interpreted as a potential measure of uncertainty regarding the accuracy of motor performance (Werner et al., 2011). While PINV has been extensively studied in various contexts, including neurological and psychiatric conditions, there has been relatively limited research specifically focused on PINV maturation in healthy subjects.

The CNV has been extensively analyzed to study pathophysiological differences between control subjects and subjects with various neurological and mental disorders. However, healthy maturation related to

preparatory brain activity remains largely unexplored in terms of its underlying developmental mechanisms. Electrophysiological studies comparing late CNV potentials of children and adolescents showed increasing negativity over pre- and primary motor areas (Bender et al., 2005; 2002; Gomez et al., 2003). The results were interpreted as immaturity of the frontal cortex. However, it remains unclear if absent or low pre-movement negativity in young children directly reflects activity states of the underlying cortical areas and to what extent the supplementary motor area contributes to early response selection, especially in young children.

EEG research of the early CNV component revealed more contradictory results. It was shown that the early CNV exhibits modality-specific characteristics. Specifically, it shows higher amplitudes in response to auditory warning stimuli (S1) compared to visual warning stimuli. Concerning the maturation of early CNV studies focusing on auditory CNV paradigms have reported decreasing amplitudes over frontal electrodes during childhood and adolescence (Bender et al., 2005), whereas investigations involving visual CNV paradigms have indicated rising frontal early CNV amplitudes within the same age range (Jonkman et al., 2003). These findings suggest that S1 post-processing exhibits a modality-specific contribution to the early CNV, showing stimulus-dependent developmental differences. Simultaneously, an S1-modality independent component results in increasing fronto-central amplitudes during response selection processes (Jonkman, 2006; Jonkman et al., 2003).

Besides electrophysiological ERP data, changes in brain oscillatory activity of different frequency bands can be analyzed to study task-related power changes. Changes within the alpha band are typically observed in motor-related brain areas during processes of motor planning (Pfurtscheller and Lopes da Silva, 1999). The analysis of alpha power enables the modulation of more widespread cortical dynamics and provides complementary information to the analysis of evoked potentials (Claudio Babiloni et al., 1999). A relative increase of frequencies related to the alpha rhythm, commonly assessed in a range of 8 to 12 Hz, refers to alpha band event-related-synchronization (ERS) and is suggested to reflect active processes of inhibition (Jensen and Mazaheri, 2010; Klimesch et al., 2007). Alpha band event-related-desynchronization (ERD) is related to a decrease in oscillatory activity and an increased activity of underlying brain areas (Niedermeyer, 1997). Even though analysis of the alpha rhythm provides additional insights into maturational processes, CNV-induced oscillatory changes have been studied rarely in the context of healthy brain development.

While ERPs and power changes provide valuable information about the timing and general location of brain activity, they lack the spatial resolution to pinpoint the exact source of the electrical signals. To gain a deeper understanding of how underlying neuronal networks contribute to cortical activation, source localization can be applied (Eom, 2023). By incorporating anatomical information about the brain with the EEG recordings, source localization allows to estimate the activity of specific brain regions underlying the recorded changes and to analyze developmental changes in recruited brain areas more precisely.

The primary aim of this study was to investigate maturational changes in attention allocation, motor program pre-activation, and performance evaluation. Each quantifier (CNV, PINV, alpha ERS/ERD) offers unique insights into different aspects of motor control development. While CNV reflects preparatory processes and attention allocation, PINV provides information on motor performance evaluation, and alpha band oscillations offer insights into cortical inhibition and activation patterns in cortico-thalamic loops. Integrating these quantifiers allows for a comprehensive understanding of the maturation of motor-related brain activity during childhood and adolescence.

We hypothesize that both iCNV and lCNV amplitudes will increase with age, reflecting enhanced neural efficiency and maturity of preparatory processes. It is assumed that the lCNV will exhibit stronger pre-activation of contralateral motor areas with age, indicating pre-

activation of cortical areas required for a fast response. We expect the PINV to show an age-related reduction in its magnitude, indicating a developmental tendency for children to exhibit greater uncertainty about the correctness of their performance. Since inhibitory control was shown to increase during childhood (Macdonald et al., 2014), we hypothesize an increase in alpha power desynchronization, reflecting improved (inhibitory) motor control and more efficient neural communication during movement preparation.

These hypotheses will be tested through the analysis of high-density EEG data and movement performances collected from children and adolescents aged 5 to 16 years, using a CNV paradigm. To enhance response selection processes in comparison to other developmental studies, we chose a directional warning stimulus S1 (arrow pointing to the right or left side) that indicated the movement side required for the motor response to the imperative stimulus S2. To prevent overlaps with the cortical activity of auditory post-processing, we used visual stimuli. By employing a multimodal approach that integrates complementary analyses of cortical activation patterns, oscillatory dynamics, and underlying neural sources, we aim to achieve a deeper understanding of the developmental processes that shape motor skill acquisition and motor control in children and adolescents.

2. Material and methods

2.1. Subjects

A total of 46 typically developing subjects in the age range of 5- to 16-years were recruited. For details regarding demographic characteristics, see Table 1. All participants had no history of motor impairments or any neuropsychiatric condition. A diagnostic interview was used for all subjects to assess and exclude neuropsychiatric disorders (Kinder-DIPS; Adornetto et al. (2008)). The study included only right-handed participants (Edinburgh Handedness Inventory, Oldfield (1971)) who had an IQ score of at least 70 (WISC V; Wechsler, D. (2017)). Participants with an individual or a family history of epilepsy, severe or acute psychiatric diseases, and neurological or non-correctable visual impairments were excluded from the study. Subjects were not permitted to take any psychoactive or antipsychotic drugs affecting the central nervous system. Two participants had to be excluded from the analysis due to high artifact levels.

The experiments were performed in accordance with the Declaration of Helsinki. In an age-adjusted information letter as well as in a personal briefing, participants and parents were informed about the procedure of the measurements and the possibility of terminating participation at any time without giving reasons. Before participation, participants and their parents signed written informed consent.

2.2. Experimental procedure

The software package *Presentation* (Version 10.3, Neurobehavioral Systems Inc., Albany, CA) was used to generate a task-related program with alternating visual stimuli displayed on a monitor at a distance of 90 cm from subjects. To prevent any distractions, the light was dimmed, and the noise level was reduced to the highest possible minimum. To minimize distracting eye movements, a fixation cross was displayed in between visual stimuli. Subjects sat in a comfortable position on a skid-proof chair, reducing muscle activity as much as possible to prevent interfering contractions.

Table 1
Sample characteristics.

Age Group (Years)	N	Mean age ($\pm$ SD)
5–8	12 (5 m, 7 f)	7.27 ($\pm$ 1.14)
9–12	17 (7 m, 10 f)	10.68 ($\pm$ 1.34)
13–16	15 (7 m, 8 f)	14.72 ($\pm$ 1.13)

2.3. Behavioral CNV task paradigm

Subjects performed a visual CNV (Fig. 1) task with 50 trials, respectively for each response side. The warning stimulus (S1) was presented as a black arrow on a white background pointing to the left or right side. The imperative stimulus (S2) was presented as a colored sheriff on a white background. Both stimuli were displayed for 150 ms, interstimulus intervals were set to 3.05 s, and pseudorandomized intertrial intervals varied from 3 to 6 s. The warning stimulus indicated the side of the required button press, whereby arrows were presented in a pseudorandomized order. Subjects were instructed to respond to the imperative stimulus S2 as fast as possible by pressing either the right or left button on a German standard keyboard (ctrl for left button press, enter on the numeric keypad for right button press) with the left or right thumb.

2.4. Electroencephalography

EEG was recorded using a 64-channel BrainAmp system (BrainProducts, Munich, Germany) and Brain Vision Recorder software (BrainProducts). Elastic EEG caps with direct current sintered Ag/AgCl disc electrodes (BrainProducts) were selected based on head sizes. Electrodes were named based on their location on the scalp, consistent with the international 10–20 system, electrode impedances were kept below 5 k Ω . Additionally, EOG electrodes were positioned under the left and right eye and on the nasion. The sampling rate was set to 5000 Hz, electrode CZ was used as a recording reference.

2.5. Electromyography

Surface EMG (compound muscle action potential) was recorded using self-adhesive silver-silver chloride electrodes in a belly tendon montage respectively for the left and right hand. To record thumb movement, active electrodes were placed on the adductor pollicis muscle, reference electrodes were attached to the exterior proximal phalanx of the thumb. The ground electrode was placed on the inner forearm. The EMG was recorded using the bipolar BrainAmp ExG amplifier (Brain Products, Munich, Germany), which was synchronized with the EEG recordings.

2.6. Signal preprocessing

EEG and EMG data were processed using the BrainVision Analyzer2 software (BrainProducts, Munich, Germany). To reduce large file sizes, data were downsampled to 500 Hz. For ERP analysis, EEG data were re-referenced to an average reference. For the analysis of current source density and alpha ERD, signals were transformed to reference-free data (for details, see section 2.7.4 for CSD and 2.7.6 for alpha ERD). For the analysis of the CNV characteristics, EEG data were segmented into epochs of 7.5 s (from 800 ms before warning stimulus S1 to 3000 ms after imperative stimulus S2), respectively for left and right button press conditions. Only trials with a correct response within the time window of 100 to 1500 ms following S2 were included in further analysis. Muscle artifacts were rejected by visual inspection, and independent component analysis (ICA) was used to remove artifacts evoked by eye movement (Mennes et al., 2010). Baseline correction was set from 500 to 0 ms preceding the warning stimulus (S1), and signals were filtered digitally (50 Hz notch filter). To prevent slow drift effects from affecting EEG data, a linear DC detrend was applied. Visual inspection before and after DC detrending confirmed that there was no systematic effect on the EEG data, preserving the overall shape and characteristics of the signal. Averages were calculated, respectively for each experimental condition and parameter.

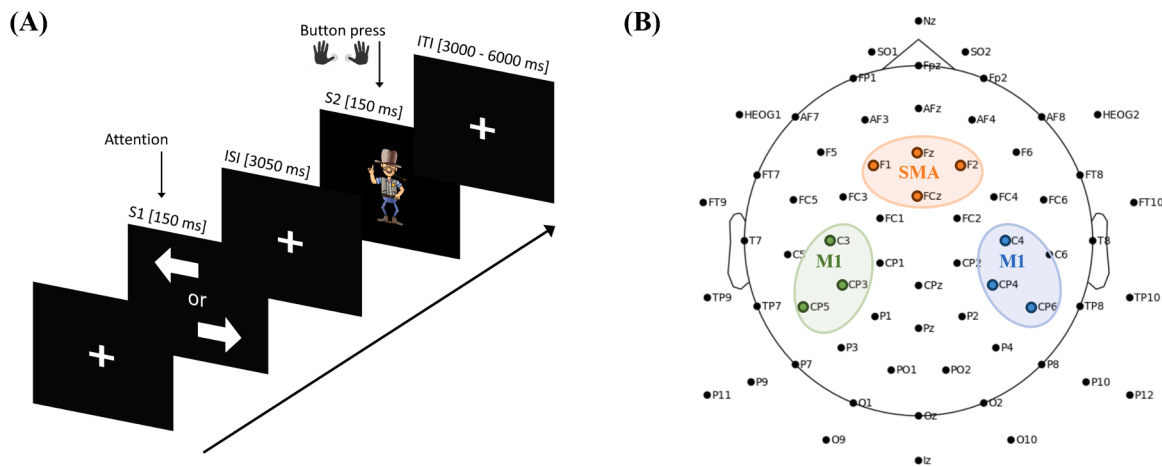


Fig. 1. Experimental design (A) Contingent negative variation (CNV) task paradigm with a directional warning stimulus S1 and a behaviourally relevant imperative stimulus S2. (B) Electrode locations with regions of interest and specific electrodes used for data analysis marked in orange (SMA), green (M1 right), and blue (M1 left). Sensor locations were plotted by using MNE-Python (Gramfort et al., 2013).

2.7. Analysis of parameters

2.7.1. Behavioral data

Reaction times were calculated as the mean time between the presentation of S2 and the button press of correct response trials. Error rates were calculated, based on the recorded 100 trials, as the sum of no or false alarms (button press between S1 and S2) and incorrect button presses in response to S2 (button press on wrong movement side).

2.7.2. Conceptual design: parameters, time windows, and scalp-locations

To gain a deep insight into the development of motor control, changes of evoked potentials (ERPs) and alpha power changes (ERD) were investigated. The analyses were performed separately for each CNV component, after confirming the well-known interaction between the CNV components and scalp areas, which indicates different topographies for the components. Moreover, to investigate generators of cortical activity during early motor-preparation (iCNV) source localization approaches (CSD and SSLOFO) were applied.

The following time windows were used for the analysis of the different components, respectively for left and right response conditions: iCNV was defined as the mean value of a 200 ms time window around the maximum negative amplitude at mid-frontocentral electrodes (Fz, FCz', FC1', FC2') between 550 and 1400 ms following S1 (Bender et al., 2002; Böcker et al., 1990; Kropp et al., 1999). Data inspection and iCNV latency analysis revealed a pronounced, continuous latency shift of the early component, especially in younger subjects (see Fig. 3A). Consequently, the iCNV peak detection time window was extended from 550 - 750 to 550 - 1400 ms after S1 to prevent the shadowing of maturational differences in iCNV amplitudes. The iCNV component was calculated as the mean voltage of the interval of 200 ms preceding the imperative stimulus S2 (Böcker et al., 1990). The PINV was defined as the mean value of a 200 ms time window around the maximum negative amplitude between 500 and 1500 ms following the imperative stimulus (S2).

Electrodes Cz, FCz', FC1', FC2' were used to analyze midfronto-central activity (Cui et al., 2000; Gerloff et al., 1998), electrodes C4, CP4'CP6', respectively C3, CP3, CP5' were used to analyze motor activity over centro-parietal areas related to the right and left primary motor cortex (Gerloff et al., 1998). Fig. 1B shows an overview of the sensor distribution and electrodes used for data analysis.

2.7.3. Event-related potentials (ERP)

To investigate age-related CNV characteristics, ERPs were investigated, respectively for each component. For the analysis of the evoked cortical activity, topographical distribution, CNV waveforms, and

amplitudes were analyzed. To analyze potential differences in the timing of motor preparation and post-processing, iCNV and PINV latencies of the amplitudes were investigated.

2.7.4. Current source density (CSD) analysis

To enhance spatial resolution (Nunez et al., 1994) and identify locations of current sources involved in iCNV generation, we used CSD analysis. This approach is particularly valuable because previous studies investigating developmental differences in early motor preparation using ERPs have yielded inconsistent findings. Given the potential for modality-specific and modality-independent components to contribute to iCNV activity observed in ERP analysis, CSD analysis offers a more precise tool for identifying the true underlying neural sources.

For CSD estimation, EEG signals were transformed into reference-free data, since it enables the estimation of current source generators without relying on a specific reference electrode, thereby minimizing potential biases and artifacts associated with reference choices (Tenke and Kayser, 2005). CSD analysis relies on the relative differences in voltage between neighboring electrodes. The spherical spline interpolation method was applied before surface Laplacian based on the EEG voltage distribution was used. CSD data is indicated as $\mu\text{V}/\text{m}^2$. The topographical distribution of cortical activity over mid-front areas (Cz, FCz', FC1', FC2'), which is likely to originate from the SMA (Pfurtscheller et al., 2003), was analyzed.

2.7.5. Current standardized shrinking loreta-focuss (SSLOFO)

In addition to CSD analysis, the inverse SSLOFO (standardized shrinking LORETA-FOCUSS) algorithm was used to enhance the precision of cortical source reconstruction (Liu et al., 2005) during iCNV. The algorithm combines multiple techniques to improve source localization abilities. Initially, a low-resolution sLORETA image is calculated. To improve spatial resolution, the re-weighted minimum norm of FOCUSS is applied. "Standardization" technique is used to enhance the ability of localization, as in sLORETA. Further insights into the specifics of the SSLOFO algorithm, along with comprehensive performance comparisons against other prevalent algorithms, can be found in Liu et al. (2005).

2.7.6. Alpha event-related desynchronization (alpha-ERD)

We analyzed alpha band desynchronization to study movement-related changes of cortical oscillations in the frequency range of 8 to 12 Hz. EEG studies in infants have indicated that lower frequency ranges (6-8 Hz, theta rhythm) can be considered comparable to the mu-rhythm observed in adults (Cochin et al., 2001). However, there is no clear

evidence that theta rhythm in infants and mu-rhythm in adults represent equal processes. Furthermore, Berchicci et al. (2011) observed that a shift of “central alpha” activity was most pronounced in the first years of life and reached a frequency of 9 Hz at the age of 4 years. Since our subject sample started at the age of 5 years and to ensure comparability between young children and adolescent subjects, we analyzed common alpha band ERD of 8 to 12 Hz.

Alpha ERD was calculated based on reference-free (current source density) EEG data to minimize the impact of reference-related artifacts on ERD calculations. Moreover, CSD estimation enhances the spatial resolution of EEG data by estimating the underlying neural sources directly, without relying on scalp electrodes. This can provide more precise localization of alpha oscillatory activity and define brain regions involved in power changes more precisely.

The same time windows, trials, and electrodes as in ERP analysis were used for the analysis of alpha ERD, respectively for the iCNV, ICNV, and PINV components. The signal was bandpass filtered in the frequency range of 8 to 12 Hz, subsequently squared, and averaged across segments (Pfurtscheller and Da Silva, 1999). ERD output data was normalized, i.e., baseline corrected and rescaled relative to the mean value within the reference interval of 1000 ms before the onset of the imperative stimulus S1. ERD magnitude at each electrode was expressed as percentage changes of the instantaneous power.

2.7.6.1. Analysis of alpha ERD lateralization during ICNV. Data of alpha ERD during late motor preparation (ICNV), suggested a robust pattern of lateralization across age groups, albeit with shifts of the cortical activity. The analysis of the lateralized portion of the alpha-ERD was included to investigate the overall timing and strength of cortical changes during motor preparation across the age groups, unbiased by the specific cortical regions engaged.

The calculation is known from the double subtraction method of the lateralized readiness potential (LRP, see de Jong et al. (1988)). The method involves subtracting the average ERP/alpha ERD of ipsilateral electrodes (e.g., left centro-parietal area for left response condition and right centro-parietal area for right response condition) from the average ERP of contralateral electrodes (e.g., right centro-parietal area for left response condition and left centro-parietal area for right response condition). Subsequently, the mean of the differences obtained was calculated.

2.8. Statistical analysis

2.8.1. Analysis of age-groups

Statistical analysis was performed using IBM SPSS Statistics 28 software (IBM Corp.; Version 28). To examine maturational changes, data were divided into age groups (5- to 8-year-olds ($n = 12$), 9- to 12-year-olds ($n = 17$) and 13- to 16-year-olds ($n = 15$)). This approach enhances the capabilities to investigate and illustrate *interactions* between age-dependent development and other factors, such as scalp area, especially when data underlies non-linear maturational trajectories. Repeated measurement analysis of variance (ANOVA) with these three age groups was performed since it effectively captures interactions between variables, a capability that linear regression lacks. Dividing the participants into equally sized age groups enables a systematic examination of development across various stages, allowing us to assess effects that are not strictly linear. Expanding the age ranges for each group would likely reduce the resolution of developmental effects, particularly considering the significant differences observed between 5 and 8-year-olds and older children. Meanwhile, increasing the number of age groups would have resulted in smaller sample sizes per group, compromising the statistical power of the analysis.

Repeated measurement analysis of variance (ANOVA) with the within-subject factors movement side (right, left) and scalp area (mid-frontocentral, right and left centro-parietal) and the between-subject

factors age group (5- to 8-year-olds, 9- to 12-year-olds and 13- to 16-year-olds) and gender (male, female) were applied to investigate ERP latencies for iCNV and PINV as well as ERP and alpha-ERD amplitudes for iCNV, ICNV and PINV. The between-subject factor gender exhibited no significant effect or trend toward significance in the data and is consequently not further discussed. This suggests that, overall, gender might not be a major influencing factor. However, it's important to acknowledge the limitations of the analysis due to the small sample size for males in each age group. The possibility of interaction effects between gender and age group cannot be entirely ruled out, even though the results remain consistent in our data when the gender factor is excluded.

Pairwise comparisons of estimated marginal means, including Šídák correction for multiple testing, were integrated into the linear mixed model to test for significant differences across the different age groups and scalp areas. For ANOVA testing and pairwise comparisons of the estimated marginal mean, values of $p < .05$ were considered statistically significant.

Multiple t -tests were used to identify areas with activity that significantly differed from the baseline. To address the issue of multiple comparisons, an alpha correction (Bonferroni correction) related to the tested scalp regions was applied. Due to variations in the number of multiple comparisons across observed parameters, corresponding statistically significant p -values are reported directly with each parameter.

2.8.2. Regression analysis

To verify that the group cut-offs did not introduce artificial effects, scatterplots, and regression analyses were examined for differences across different age groups and scalp areas, identified by ANOVA. Furthermore, regression analyses were used to investigate the relationship between mid-frontocentral activity and task performance.

Due to developmental trajectories showing curvilinear age effects on certain dependent variables (i.e., more pronounced changes in younger children) (Fietzek et al., 2000; Klein, 2001), regression analysis was performed either as linear regression using age as a predictor ($y = a + b * \text{age}$; y = predicted original data; a = constant; b = regression coefficient) or as non-linear regression using age-1 as predictor (regression equation $y = a + b * \text{age}^{-1}$). An exploratory analysis of the scatterplots was used to determine if data showed a linear relationship between age and a dependent variable, i.e., a constant development of the variable throughout the examined age range of 5 to 16 years, or a non-linear influence of the factor age on the dependent variables, i.e., more pronounced development in younger (or older) subjects. The most suitable regression model (predictors age or age^{-1}) was chosen based on data examination respectively for each variable.

3. Results

3.1. Behavioural task performance (reaction time)

Behavioral task performance across age groups was investigated by analyzing error rates and reaction times. The ANOVA analysis on the dependent variable total response error rate, with the between-subject factors of age group and gender revealed significant differences between the age groups ($F(2, 38) = 5.75, p = .007$). Post-hoc Tukey-HSD comparisons indicated that the oldest age group of 13- to 16-year-olds (3.93 ± 3.33) performed significantly better than the youngest age group of 5- to 8-year-olds ($13.75 \pm 11.01, p = .009$). The middle age group of 9- to 12-year-olds ($10.76 \pm 8.25, p = .056$) exhibited only a trend toward increased errors compared to the oldest age group and no significant differences compared to the youngest age group. The most frequent error observed was a button press during the intertrial interval, occurring between the warning stimulus S1 and the imperative stimulus S2. Only trials with a correct response to S2 were included in further analysis.

Regarding reaction times, ANOVA analysis with age group and

gender as between-subject factors showed a trend toward differences among the age groups ($F(2, 38) = 2.96, p = .064$). Tukey-HSD posthoc comparisons indicated that the youngest age group (443.02 ± 117.42 ms) showed slower reactions compared to the middle (342.03 ± 112.91 ms, $p = .046$) and a trend compared to the oldest age group (369.83 ± 114.12 ms, $p = .05$).

3.2. Early orienting response and motor preparation (initial contingent negative variation)

3.2.1. Latency of iCNV component

The initial component of the CNV potentials was used to investigate developmental changes during childhood and adolescence related to early movement preparatory processes.

(A) ERP; right response side

(B) ERP; left response side

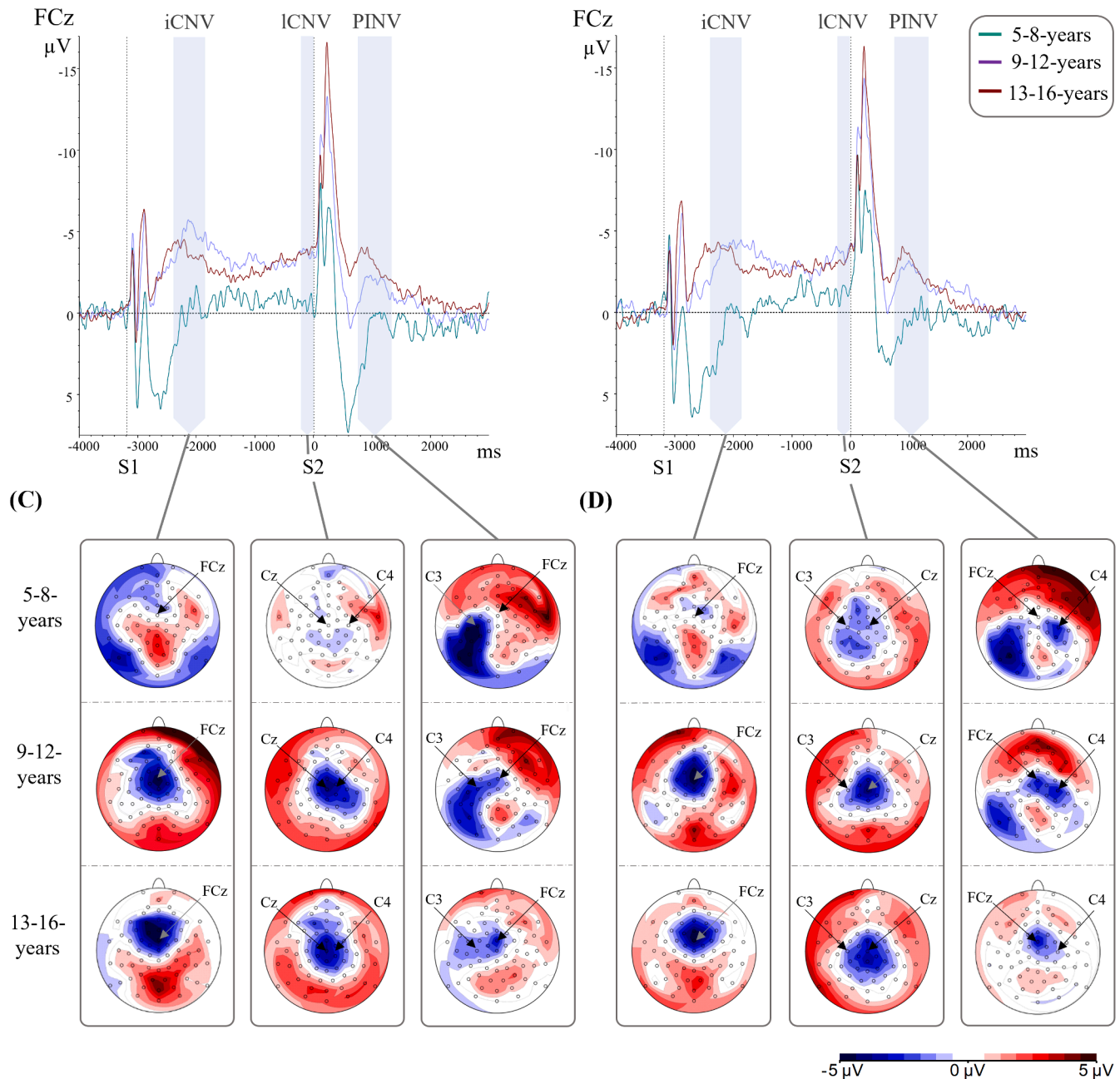


Fig. 2. Grand average CNV waveforms and topographic voltage maps, separately displayed for each age group to demonstrate maturational differences. (A) CNV course of the right and (B) left response condition at FCz (right), respectively for 5- to 8-year-old subjects (green line), 9- to 13-year-old subjects (purple line), and 13- to 16-year-old subjects (red line). The first vertical dashed line indicates the presentation of the warning stimulus S1 (directional arrow), and the second vertical dashed line indicates the presentation of the imperative stimulus S2. Time windows for iCNV, ICNV, and PINV are highlighted in light blue. Please note that voltage scales are presented upside down with negative values going upward. See for more detailed amplitude values supplementary material, [Table 1](#). (C) Voltage maps of each CNV component for the right and (D) left response condition, displayed as the average of 5- to 8-year-old (top), 9- to 12-year-old (middle) and 13- to 16-year-old subjects (bottom). Maps are scaled from $-5 \mu\text{V}$ (blue) to $+5 \mu\text{V}$ (red). Older subjects showed increasing negativity of mid-frontocentral areas in each component. Most pronounced differences were observed between the age group of 5- to 8-year-old and 9- to 12-year-old subjects.

The repeated measures ANOVA revealed a significant effect of the factor age on iCNV latencies ($F(2, 38) = 4.84, p = .013$). The delayed onset of early mid-frontocentral negativity in younger subjects is illustrated in Figs. 2A, 2B, and 3A. For mean latencies with standard deviations, see supplementary material, Table 2.

3.2.2. ERP amplitudes of iCNV component

The CNV topography of evoked cortical activity showed significant age-related developmental changes, most pronounced between the age range of 5- to 12-years. Fig. 2 illustrates the stimulus-locked ERP waveforms for each group (for mean amplitudes with standard deviations see supplementary material, Table 1).

Comparing the evoked amplitudes of the early CNV component, the repeated measures ANOVA showed a highly significant interaction between scalp areas and age group ($F(4, 76) = 6.76, p < 0.001$).

Pairwise comparisons of estimated marginal means indicated significant differences in the activation of the mid-frontocentral area between the youngest age group of 5- to 8-year-olds ($0.16 \pm 2.78 \mu\text{V}$) and the two older age groups of 9- to 12-year-olds ($-3.66 \pm 3.09 \mu\text{V}$; $p < 0.001$) and 13- to 16-year-olds ($-2.78 \pm 2.03 \mu\text{V}$; $p = 0.01$). Mid-frontocentral negativity of the youngest age group was shown not to differ significantly from baseline (see supplementary material, Table 1). In addition, no significant differences were observed when comparing the two older age groups. Centro-parietal scalp areas were found to exhibit no significant age effect during early movement planning.

To investigate the correlation between the early increasing mid-frontocentral activity and improved task performance, regression analyses were performed. The data showed a trend towards a curvilinear dependence between the mid-frontocentral activity and reaction time (RT^{-1} : $R^2 = 0.115$, $F(1, 42) = 5.48, p = .024$), however there was no significant correlation between mid-frontocentral activity and the performed errors (error rate: $R^2 = 0.104$, $F(1, 42) = 4.88, p = .033$; significant at $\alpha < 0.0125$).

3.2.3. Alpha-event-related desynchronization during the iCNV component

Analysis of the alpha band event-related desynchronization (ERD) was conducted to investigate developmental differences of mu rhythm attenuation related to motor behavior planning and whether children aged 5- to 8 years showed early motor preparation, even when significant frontal ERP activity was not observed. Repeated measurement ANOVA revealed a main effect for the factor age group ($F(2, 38) = 5.82, p = 0.006$).

Pairwise comparison of estimated marginal means demonstrated an increase of alpha ERD with increasing age, as indicated by significant amplitude differences, observed between the youngest age group of 5- to 8-year-olds ($-19.41 \pm 4.4 \mu\text{V}$) and the oldest age group of 13- to 16-year-olds ($-38.35 \pm 3.89 \mu\text{V}$; $p = 0.008$) as well as between the middle age group of 9- to 12-year-olds ($-24.72 \pm 3.81 \mu\text{V}$) and the oldest age group ($p = .049$).

In addition, there was a main effect of the scalp area ($F(2, 76) = 45.87, p < 0.001$) which was qualified by an interaction between the movement side and scalp area ($F(2, 76) = 25.84, p < 0.001$). Alpha-ERD over contra- and ipsilateral centro-parietal areas but not over mid-frontocentral areas were shown to be highly significant for all age groups, as well as to be more pronounced over the contralateral hemisphere of the movement side (see Table 2). A pairwise comparison of estimated marginal means indicated that centro-parietal areas (right: $-32.17 \pm 2.77 \mu\text{V}$; left: $-32.32 \pm 2.48 \mu\text{V}$) showed significantly more desynchronization than the mid-frontocentral area ($-17.98 \pm 2.33 \mu\text{V}$, $p < 0.001$). Moreover, the movement side had a highly significant effect on alpha ERD over centro-parietal areas of both hemispheres (right, $p < 0.001$, left: $p < 0.001$), showing distinct lateralization to the contralateral movement side (see Fig. 4C to 4F and supplementary material, Table 3). Thus, already 5- to 8-year-old children showed contralaterally lateralized alpha-ERD during early CNV (i.e., a selection of the required response side).

3.2.4. Current source density (CSD) of iCNV component

The qualitatively distinct pattern observed during iCNV in young subjects could also be evoked by strong, overlapping P300 activity masking the anticipated activity that was shown in older subjects. To investigate activity over mid-frontocentral areas in younger subjects more precisely and to reduce the influence of overlapping P300 activity, we conducted a Current Source Density (CSD) analysis.

To assess age effects, we conducted a repeated measures ANOVA, which indicated an interaction between scalp area and age group ($F(4, 76) = 3.13, p = 0.019$), suggesting age-related topographical maturation. Pairwise comparison of estimated marginal means revealed age-related activity differences over the centro-parietal scalp areas between the youngest (right: $-29.48 \pm 9.12 \mu\text{V}$; left: $-23.72 \pm 9.96 \mu\text{V}$) and the oldest age group (right: $4.09 \pm 8.06 \mu\text{V}$, $p = 0.026$; left: $10.0 \pm 8.8 \mu\text{V}$, $p = 0.045$), showing decreasing negativity over left and right centroparietal areas with age. However, CSD map topographies indicated that the topographic maximum related to these current sinks was over occipitotemporal areas, so we did not interpret this activation any further concerning motor processes.

More importantly, the mid-frontocentral area exhibited no significant differences between the age groups. Further examination of CSD map topographies (Fig. 3C, 3D) revealed that even children in the age range of 5- to 8 years exhibited a small current sink over mid-frontocentral areas ($-10.92 \pm 32.9 \mu\text{V}$) which was however not significant ($t(11) = -1.15, p = .27$). Fig. 3B and 3C illustrate that in younger subjects the positivity of the P3-complex and occipitotemporal negativity over visual cortical areas dominated the CSD maps. Conversely, in older subjects, mid-frontocentral negativity became more prominent.

3.2.5. Source analysis (SSLOFO) of iCNV component

SSLOFO analysis, an inverse algorithm to precisely reconstruct underlying sources, was applied to identify closely spaced cortical generators of the mid-frontocentral activity during iCNV of young subjects. Consistent with the findings from CSD analysis (overlapping P3-complex, occipitotemporal current sinks), SSLOFO analysis confirmed the presence of a prominent posterior source in young subjects during early movement planning. However, source analysis indicated that in young subjects aged 5 years, the supplementary motor area is likely to contribute, at least partly, to early negativity observed over mid-frontocentral areas (Figs. 3D and 3E).

3.3. Late motor preparation (late contingent negative variation)

3.3.1. ERP amplitudes of iCNV component

To investigate maturational processes related to direct motor preparation, we focused on the late component of the CNV paradigm. The iCNV topography showed pronounced differences between the age groups (see Fig. 2C and 2D and supplementary material, Table 1). Children aged 5 to 8 years displayed more widespread low ipsilateral negativity, most pronounced over centroparietal areas. In contrast, older subjects (9- to 16-year-olds) exhibited a more centrally localized negativity over mid-frontocentral and central areas, with decreasing activity over ipsilateral centro-parietal areas with age.

The repeated measurement ANOVA revealed significant interactions between scalp area and movement side ($F(2, 76) = 3.59, p = 0.034$) and between scalp area and age group ($F(4, 76) = 3.63, p = 0.009$). A pairwise comparison of estimated marginal means showed that the movement side had a significant effect on the left centroparietal scalp area (right-hand movements: $-0.36 \pm 0.32 \mu\text{V}$; left-hand movements: $-1.48 \pm 0.3 \mu\text{V}$, $p = 0.017$), with more pronounced ipsilateral negativity observed for the left movement side. The right centroparietal scalp area was observed not to be significantly influenced by the movement side.

Furthermore, significant amplitude differences over the mid-frontocentral area were observed between the youngest age group of 5- to 8-year-olds ($-0.74 \pm 0.73 \mu\text{V}$) and the middle age group of 9- to 12-year-olds ($-3.51 \pm 0.58 \mu\text{V}$; $p = .02$). There was also a trend towards

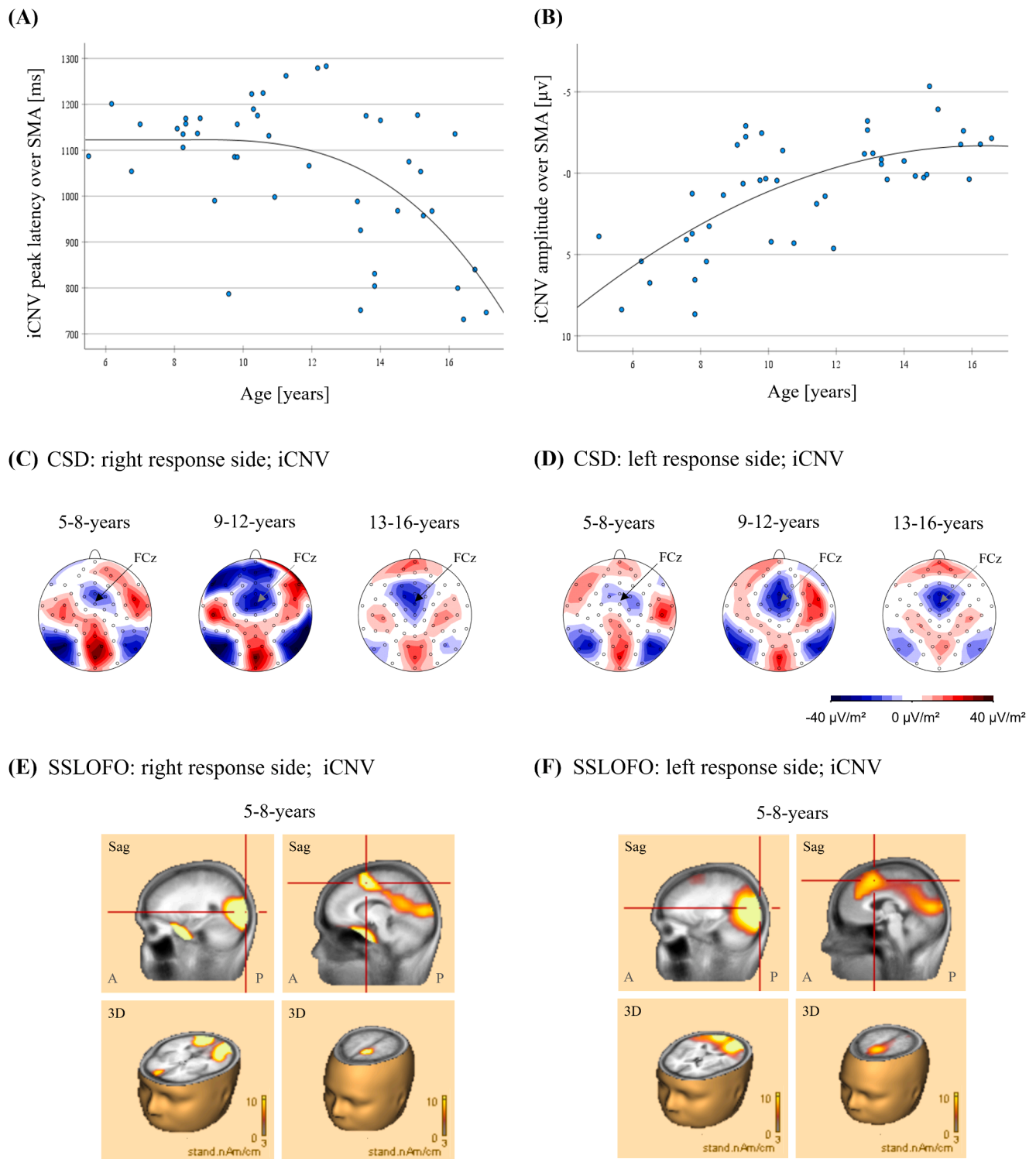


Fig. 3. Developmental characteristics of the early CNV (iCNV) component. **(A)** Scatterplots of iCNV mean peak latencies and **(B)** amplitudes. Data points represent mean amplitudes for both response conditions and each subject over the mid-frontocentral area (Cz, FCz, FC1', FC2'). The grey lines show the corresponding fitting of a curvilinear regression model (age^{-1}), since age-related differences were more pronounced in younger subjects. **(C)** Average current source density (CSD) maps of the iCNV component for 5- to 8-year-old (left), 9- to 12-year-old (middle), and 13- to 16-year-old subjects (right), displayed for the right and **(D)** left response condition. CSD maps are scaled from $-40 \mu\text{V}/\text{cm}^2$ (blue) to $+40 \mu\text{V}/\text{cm}^2$ (red). **(E)** Image of current standardized shrinking LORETA-FOCUSS (SSLOFO) algorithm, calculated for right and **(F)** left response condition during iCNV. Images are displayed for 5- to 8-year-old subjects, to identify especially mid-frontocentral current sources in young subjects. Images showed a pronounced posterior (left images) as well as a mid-frontocentral cortical source (right images), related to the supplementary motor area. A: anterior side of the brain; P: posterior side of the brain; Sag: Sagittal plane.

Table 2

Mean Alpha-ERD amplitude values [%] $\pm$ standard deviation for each CNV component. Significances ($p \leq 0.017$) or trends towards significance ($p < .33$) are indicated for the respective values.

Alpha-ERD of CNV Component	Age Group	SMA [%]	M1 right [%]	M1 left [%]
iCNV right response condition	5- to 8-year-old	-6.27 $\pm$ 16.54	-16.24 $\pm$ 23.57 $t(-2.38)$; $p = .03$	-29.32 $\pm$ 22.05 $t(-4.61)$; $p < .001$
		-12.51 $\pm$ 12.79 $t(-4.03)$; $p < .001$	-23.99 $\pm$ 18.08 $t(-5.47)$; $p < .001$	-34.27 $\pm$ 16.6 $t(-8.51)$; $p < .001$
		-33.06 $\pm$ 21.39 $t(-5.78)$; $p < .001$	-35.79 $\pm$ 25.53 $t(-5.25)$; $p < .001$	-51.99 $\pm$ 19.55 $t(-9.95)$; $p < .001$
	9- to 12-year-old	-13.48 $\pm$ 18.88 $t(-2.47)$; $p = .03$	-34.59 $\pm$ 14.83 $t(-8.08)$; $p < .001$	-22.21 $\pm$ 16.84 $t(-4.57)$; $p < .001$
		-17.14 $\pm$ 12.39 $t(-5.71)$; $p < .001$	-37.33 $\pm$ 15.8 $t(-9.74)$; $p < .001$	-28.02 $\pm$ 15.27 $t(-7.57)$; $p < .001$
		-29.34 $\pm$ 19.5 $t(-5.63)$; $p < .001$	-46.64 $\pm$ 22.08 $t(-7.9)$; $p < .001$	-32.74 $\pm$ 21.71 $t(-5.64)$; $p < .001$
	13- to 16-year-old	9.22 $\pm$ 22.49	12.94 $\pm$ 22.65 $t(1.98)$; $p = .05$	-0.88 $\pm$ 20.88
		12.94 $\pm$ 20.23 $t(2.64)$; $p = .02$	24.51 $\pm$ 36.32 $t(2.78)$; $p = .01$	-9.23 $\pm$ 20.49 $t(-1.86)$; $p = .08$
		-4.44 $\pm$ 22.27	11.21 $\pm$ 33.57	-17.94 $\pm$ 23.53 $t(-2.85)$; $p = .01$
iCNV left response condition	5- to 8-year-old	6.91 $\pm$ 20.56	-5.44 $\pm$ 15.65	23.05 $\pm$ 22.12 $t(3.61)$; $p = .004$
		5.39 $\pm$ 17.78	-6.27 $\pm$ 16.57	14.44 $\pm$ 29.22 $t(2.04)$; $p = .06$
		-0.78 $\pm$ 17.74	-16.39 $\pm$ 21.64 $t(-2.84)$; $p = .01$	1.87 $\pm$ 28.42
	9- to 12-year-old	-14.18 $\pm$ 17.43 $t(-2.82)$; $p = .01$	-28.78 $\pm$ 19.72 $t(-5.06)$; $p < .001$	-33.39 $\pm$ 21.89 $t(-5.28)$; $p < .001$
		-24.46 $\pm$ 16.12 $t(-6.25)$; $p < .001$	-35.88 $\pm$ 19.22 $t(-7.7)$; $p < .001$	-42.68 $\pm$ 20.93 $t(-8.41)$; $p < .001$
		-38.86 $\pm$ 25.46 $t(-5.71)$; $p < .001$	-46.71 $\pm$ 25.26 $t(-6.92)$; $p < .001$	-53.19 $\pm$ 23.43 $t(-8.35)$; $p < .001$
	13- to 16-year-old	-18.07 $\pm$ 20.89 $t(-2.98)$; $p = .01$	-37.56 $\pm$ 19.86 $t(-6.55)$; $p < .001$	-23.38 $\pm$ 25.36 $t(-3.19)$; $p = .009$
		-24.37 $\pm$ 18.82 $t(-5.34)$; $p < .001$	-42.45 $\pm$ 20.31 $t(-8.61)$; $p < .001$	-43.86 $\pm$ 19.72 $t(-9.17)$; $p < .001$
		-39.88 $\pm$ 22.26 $t(-6.7)$; $p < .001$	-54.66 $\pm$ 24.5 $t(-8.35)$; $p < .001$	-48.49 $\pm$ 27.31 $t(-6.64)$; $p < .001$
PINV right response condition	5- to 8-year-old	17.43	19.72	21.89
		-24.46 $\pm$ 16.12 $t(-6.25)$; $p < .001$	-35.88 $\pm$ 19.22 $t(-7.7)$; $p < .001$	-42.68 $\pm$ 20.93 $t(-8.41)$; $p < .001$
		-38.86 $\pm$ 25.46 $t(-5.71)$; $p < .001$	-46.71 $\pm$ 25.26 $t(-6.92)$; $p < .001$	-53.19 $\pm$ 23.43 $t(-8.35)$; $p < .001$
	9- to 12-year-old	-18.07 $\pm$ 20.89 $t(-2.98)$; $p = .01$	-37.56 $\pm$ 19.86 $t(-6.55)$; $p < .001$	-23.38 $\pm$ 25.36 $t(-3.19)$; $p = .009$
		-24.37 $\pm$ 18.82 $t(-5.34)$; $p < .001$	-42.45 $\pm$ 20.31 $t(-8.61)$; $p < .001$	-43.86 $\pm$ 19.72 $t(-9.17)$; $p < .001$
		-39.88 $\pm$ 22.26 $t(-6.7)$; $p < .001$	-54.66 $\pm$ 24.5 $t(-8.35)$; $p < .001$	-48.49 $\pm$ 27.31 $t(-6.64)$; $p < .001$
	13- to 16-year-old	17.43	19.72	21.89
		-24.46 $\pm$ 16.12 $t(-6.25)$; $p < .001$	-35.88 $\pm$ 19.22 $t(-7.7)$; $p < .001$	-42.68 $\pm$ 20.93 $t(-8.41)$; $p < .001$
		-38.86 $\pm$ 25.46 $t(-5.71)$; $p < .001$	-46.71 $\pm$ 25.26 $t(-6.92)$; $p < .001$	-53.19 $\pm$ 23.43 $t(-8.35)$; $p < .001$
PINV left response condition	5- to 8-year-old	17.43	19.72	21.89
		-24.46 $\pm$ 16.12 $t(-6.25)$; $p < .001$	-35.88 $\pm$ 19.22 $t(-7.7)$; $p < .001$	-42.68 $\pm$ 20.93 $t(-8.41)$; $p < .001$
		-38.86 $\pm$ 25.46 $t(-5.71)$; $p < .001$	-46.71 $\pm$ 25.26 $t(-6.92)$; $p < .001$	-53.19 $\pm$ 23.43 $t(-8.35)$; $p < .001$
	9- to 12-year-old	-18.07 $\pm$ 20.89 $t(-2.98)$; $p = .01$	-37.56 $\pm$ 19.86 $t(-6.55)$; $p < .001$	-23.38 $\pm$ 25.36 $t(-3.19)$; $p = .009$
		-24.37 $\pm$ 18.82 $t(-5.34)$; $p < .001$	-42.45 $\pm$ 20.31 $t(-8.61)$; $p < .001$	-43.86 $\pm$ 19.72 $t(-9.17)$; $p < .001$
		-39.88 $\pm$ 22.26 $t(-6.7)$; $p < .001$	-54.66 $\pm$ 24.5 $t(-8.35)$; $p < .001$	-48.49 $\pm$ 27.31 $t(-6.64)$; $p < .001$
	13- to 16-year-old	17.43	19.72	21.89
		-24.46 $\pm$ 16.12 $t(-6.25)$; $p < .001$	-35.88 $\pm$ 19.22 $t(-7.7)$; $p < .001$	-42.68 $\pm$ 20.93 $t(-8.41)$; $p < .001$
		-38.86 $\pm$ 25.46 $t(-5.71)$; $p < .001$	-46.71 $\pm$ 25.26 $t(-6.92)$; $p < .001$	-53.19 $\pm$ 23.43 $t(-8.35)$; $p < .001$

more midfronto-central negativity for the oldest age group of 13- to 16-year-olds ($-3.04 \pm 0.64 \mu\text{V}$; $p = .067$) compared to 5- to 8-year-olds. Centro-parietal areas of both the contralateral and ipsilateral hemispheres did not show significant maturational changes.

3.3.2. Alpha-Event-related desynchronization of iCNV component

To investigate oscillatory modulation related to movement preparation and cortical pre-activation before a movement, we analyzed alpha ERD during iCNV.

Repeated measurement ANOVA showed a significant interaction between the movement side and scalp area ($F(2, 76) = 25.59$, $p < 0.001$). A pairwise comparison of the estimated marginal means revealed that alpha ERD over centroparietal areas was highly influenced by the movement side ($p < 0.001$).

Despite pronounced maturational differences of alpha power changes displayed in the related maps and data (Fig. 4A and 4B, Table 2), ANOVA analysis showed a trend towards differences between the age groups ($F(2, 38) = 2.84$, $p = 0.071$). To investigate the data in more detail, we performed a regression analysis over centroparietal motor areas. Regression analysis confirmed a strong trend towards a developmental trajectory with decreasing alpha band synchronization over ipsilateral motor areas and increasing desynchronization over contralateral motor areas (Age; ipsilaterally decreasing synchronization: $R^2 = 0.109$, $F(1, 42) = 5.16$, $p = .028$; contralaterally increasing desynchronization: $R^2 = 0.08$, $F(1, 42) = 3.77$, $p = .059$; significant for $\alpha < 0.025$) (for details see supplementary material, Fig. 1).

Interestingly, an analysis of the lateralization of alpha-ERD further illustrated that a constant degree of lateralization was maintained during development (Fig. 4C to 4D). Topographic distribution of the lateralized alpha-ERD during iCNV (Fig. 4E and 4F), as well as lateralized alpha-ERD amplitude analysis ($F(2, 38) = 0.014$, $p = .99$), confirmed no significant lateralization differences between the analyzed age groups, despite apparent differences in the contra- and ipsilateral induced alpha power (see Fig. 4A, 4B for the time course and topography of lateralized activation).

3.4. Response postprocessing and evaluation (post imperative negative variation, PINV)

3.4.1. Latency of PINV component

To investigate maturational changes in response evaluation processes, we analyzed cortical activity related to motor post-processing (PINV) within a CNV paradigm. Repeated measurement ANOVA showed a significant interaction between the movement side, the scalp area, and the age group ($F(3.86, 73.3) = 2.75$, $p = .036$).

A pairwise comparison of estimated marginal means indicated that, for the right movement side, negativity over the right ipsilateral hemisphere arose with an increased latency in the oldest age group (1171.18 ± 59.59 ms), compared to the youngest (897.47 ± 67.42 ms, $p = 0.013$) and the middle age group (865.71 ± 58.43 ms, $p = 0.002$). For the left-hand movement, no significant latency differences were observed.

3.4.2. ERP amplitudes of PINV

PINV topography varied strongly between the age groups (see Fig. 2). Younger subjects displayed maximum negativity over centroparietal areas, while in older subjects pronounced negativity was shifted towards more mid-frontocentral areas. The repeated measurement ANOVA indicated a statistically significant interaction between scalp area and age group ($F(4, 76) = 4.12$, $p = 0.004$) and between the movement side and scalp area ($F(2, 76) = 8.9$, $p < 0.001$).

A pairwise comparison of estimated marginal means showed that the movement side had a significant effect on the right ($p = 0.009$) and left centro-parietal scalp area ($p = 0.001$), with more pronounced negativity observed over the contralateral hemisphere.

Maturational influences were found over the left centro-parietal scalp area, with a trend towards amplitude differences between the

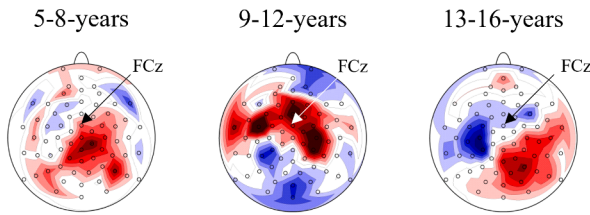
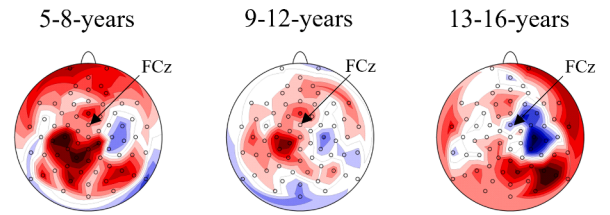
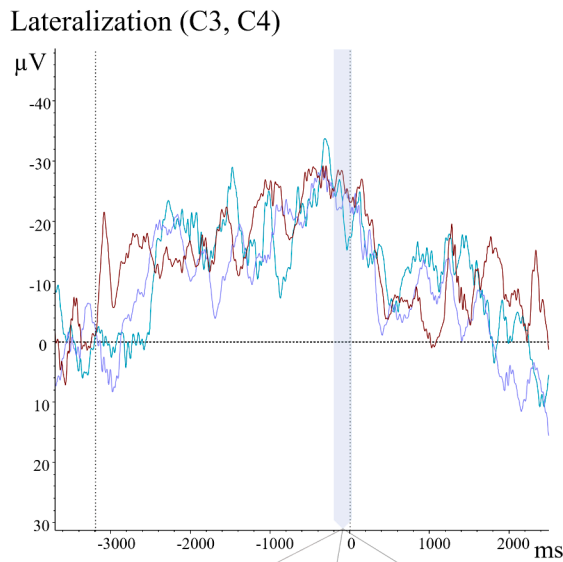
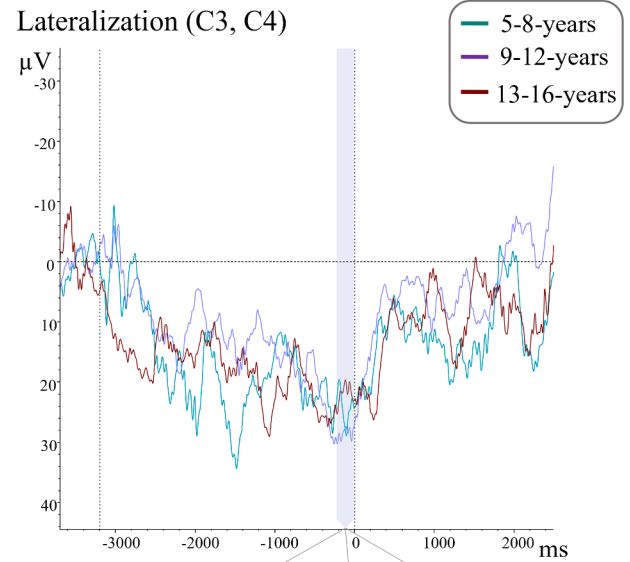
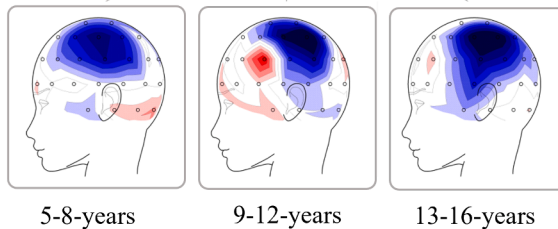
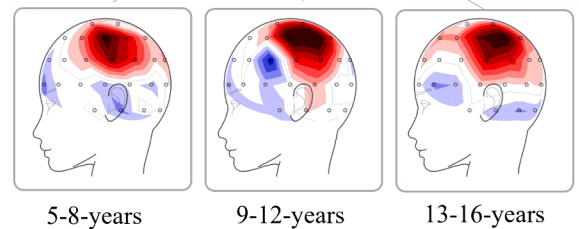
(A) Alpha-ERD: right response side; ICNV**(B)** Alpha-ERD: left response side; ICNV**(C)** Alpha-ERD: right response side**(D)** Alpha-ERD: left response side**(E)****(F)**

Fig. 4. Developmental characteristics of the late CNV (ICNV) component. (A) Isopotential line maps of alpha event-related desynchronization (ERD) during ICNV, shown for right and (B) left response conditions. Maps are displayed separately for the average alpha ERD of 5- to 8-year-old (left), 9- to 12-year-old (middle), and 13- to 16-year-old subjects (right). A decrease in alpha power (ERD) is indicated in blue, increase in alpha power (event-related synchronization; ERS) is indicated in red. Scaling ranges from -30% to $+30\%$ in relation to baseline values. Ipsilateral positivity over centro-parietal areas decreased with age, whereas contralateral negativity increased. (C) Lateralization (LRP) waveforms for the right and (D) left response condition, presented as average for 5- to 8-year-old subjects (green line), 9- to 13-year-old subjects (purple line), and 13- to 16-year-old subjects (red line). (E) LRP voltage maps of the contralateral hemisphere for the right response condition, (F) respectively for the ipsilateral hemisphere of the left response condition for 5- to 8-year-old (left), 9- to 12-year-old (middle) and 13- to 16-year-old subjects (right). Alpha-ERD showed an age-constant strong lateralization to the contralateral movement side during ICNV.

youngest ($-3.56 \pm 0.77 \mu\text{V}$) and the oldest age group ($-1.03 \pm 0.68 \mu\text{V}$; $p = .054$), showing decreasing PINV amplitude over the left-centroparietal area with age. Furthermore, negativity shifted from centro-parietal scalp areas in young subjects to mid-frontocentral areas in older subjects (see supplementary material, Table 1).

3.4.3. Alpha-Event-related desynchronization of PINV component

To study maturational changes of alpha band oscillation related to response evaluation, we analyzed alpha-ERD during PINV.

Desynchronization of alpha power was present for all age groups over mid-frontocentral as well as over centro-parietal areas, and most pronounced in older subjects (Table 2).

ANOVA analysis showed an interaction between the movement side and scalp area ($F(2, 76) = 9.23, p < 0.001$). A pairwise comparison of the estimated marginal means indicated that alpha desynchronization was more pronounced over contralateral centro-parietal scalp areas, especially for the right hemisphere ($p < .001$).

Furthermore, there was a main effect of age group ($F(2, 38) = 5, p =$

0.012) as well as a trend towards an interaction between the scalp area and the age group ($F(4, 76) = 2.23$, $p = 0.074$). In total, alpha desynchronization was less pronounced in younger subjects aged 5- to 8-years ($-24.71 \pm 5.33\%$) than in older subjects aged 13- to 16-years ($-46.61 \pm 4.72\%$; $p = .012$). Regarding maturational differences of the separated scalp areas, negativity over mid-frontocentral areas was more pronounced in the oldest age group ($-39.0 \pm 4.6\%$), compared to the youngest ($-15.05 \pm 5.21\%$; $p = .004$) and the middle age group ($-21.51 \pm 4.51\%$; $p = .03$).

4. Discussion

Brain maturational processes and underlying neuronal mechanisms involved in the transition from an immature child brain to a fully developed adult brain are complex and difficult to identify. Our data provide evidence of pronounced cerebral maturation related to attention allocation, motor preparation, and movement evaluation during childhood and adolescence. The study compared behavioral task performance and cortical activation evoked and induced by a contingent negative variation (CNV) paradigm with a directional warning cue. We collected EEG data of subjects aged 5- to 16-years using a 64-equidistant electrode array.

Our data showed that enhanced SMA activity plays a critical role in increasing the efficiency of motor behavior during cortical maturation. Besides poorer task performance, young subjects displayed qualitatively different cortical activation patterns compared to older subjects. Previous CNV studies in children and adolescents have yielded inconsistent findings, potentially due to limitations in methodology. By employing a visual task paradigm and advanced analysis techniques, we were able to investigate CNV components more precisely and reveal a maturational increase in mid-frontocentral activity attributed to the SMA during different stages of motor control.

Our findings suggest a developmental shift towards proactive motor control. Alpha power exhibited a trend toward transitioning from ipsilateral synchronization (inhibition; deactivation) to contralateral desynchronization (disinhibition; pre-activation) within motor areas during late motor preparation (iCNV). In contrast to other studies (Bender et al., 2005; Flores et al., 2009), our findings demonstrate that motor development extends beyond adolescence. Compared to adults, adolescents still showed distinct cortical activation patterns, lacking the expected contralateral motor area activation during preparation. This suggests a more gradual maturation process.

Age-related reductions in PINV negativity over contralateral motor areas, coupled with increased SMA negativity, suggest reduced movement uncertainty with development (Thiemann, 2010; Bender et al., 2006).

4.1. Behavioral performance

Reaction times as well as performed errors improved with age, as typically observed in other studies (Bender et al., 2005; Bucsuházy and Semela, 2017; Kiselev et al., 2009). Motor improvement was characterized by shorter reaction times and reduced false alarms or wrong responses in older subjects. These results suggest that younger subjects exhibited more premature response reactions compared to older subjects. The observed developmental differences had an influence on the processing speed as well as on the ability to restrain motor behavior. Improved action control developed curvilinearly in the age range of 5 to 16 years, with the most pronounced maturation in the youngest age group of 5- to 8-year-old children.

4.2. Maturation of orienting response (early contingent negative variation)

The early or initial CNV component (iCNV) is associated with orienting processes as a response to a warning stimulus in a CNV paradigm

(Weerts and Lang, 1973). According to Birbaumer et al. (1990), the iCNV reflects prefrontal activation that regulates the activation of more posterior motor areas necessary for movement execution.

The early component was investigated to study the impact of cerebral maturation on the orienting response to an informative external stimulus, including attentional processes and motor program selection. ERP analysis revealed immature iCNV topographies until late childhood and early adolescence. Electrophysiological data showed a pronounced maturation characterized by increasing early mid-frontocentral negativity through the investigated age range (see Figs. 2 and 3B–3D). In agreement with other studies using data from a reduced number of electrodes, young children showed only minor frontal negativity during orienting response (Jonkman et al., 2003; Segalowitz and Davies, 2004), i.e., activation of cortical areas related to the supplementary motor area (SMA) and anterior cingulate cortex (ACC) (Flores et al., 2009; Jonkman et al., 2003). The early frontal negativity stabilized during post-pubertal adolescence, reaching a strength of activation comparable to adult subjects (Tian et al., 2019; Weisz et al., 2002). Furthermore, we observed a consistent shift in iCNV latencies, with mid-frontocentral areas being recruited earlier in older subjects, suggesting faster processing of the warning stimulus (see Fig. 3A).

Besides small frontal negativity, young children showed enhanced processing of the directional warning cue over posterior-temporal and occipital areas related to visual cortices (Bender et al., 2010; Hecht et al., 2016) that caused partial masking of small SMA activity in the ERP analysis. Van Leeuwen et al. (1998) observed similar early topographies and found posterior sources for this so-called CNV/P3 complex. It is likely that other studies reporting contradictory decreasing mid-frontocentral negativity during iCNV with age (Bender et al., 2004), as well as reduced iCNV latencies in younger children (Flores et al., 2009), observed rather frontocentral negativity that was dependent on extended stimulus processing related to a posterior source than true frontal iCNV negativity associated with SMA activity. Enhanced activity reflected in a more pronounced CNV/P3 complex could be explained by an increased effort to process relevant task information. The orienting reaction is thus dominated by sensory post-processing and resource allocation in young children, while more frontal activation with decreasing latencies becomes a dominant part in adolescent subjects.

Since young children reacted with more spontaneous motor responses and showed an increased error rate, posterior networks recruited during movement preparation seem less efficient in attention regulation and action control. Precipitated movements might be caused by inefficient motor inhibition or by reduced efficiency of attention allocation due to an increased effort in target selection processes. The observed maturational shift is consistent with described strategy changes from a posterior, stimulus-driven orienting network in young children to an anterior, top-down attention network in adolescent subjects (Padilla et al., 2014; Smith et al., 2011).

Cortical source analysis of iCNV data using sSLOFO confirmed that the mid-frontocentral negativity is likely to originate from the supplementary motor area (SMA; see Figs. 3E and 3F). It was suggested that the SMA recruits and sustains networks activated during subsequent preparatory processes related to the iCNV (Gomez et al., 2003). In other studies, it was shown that the iCNV arises from the SMA and ACC and that the cortical areas were simultaneously coactivated (Gomez et al., 2003; Lee et al., 1999). Lee et al. (1999) observed that subregions of the SMA were recruited with different temporal profiles and that early stages of motor processing were associated with the activation of anterior SMA parts related to the pre-SMA. The pre-SMA is characterized by extensive pre-frontal connectivity (Luppino et al., 1993) and thought to be involved, inter alia, in maintaining working memory (Pollmann and Yves von Cramon, 2000) as well as motor program selection and movement intention (Lau et al., 2004). Nachev et al. (2007) performed a movement study on a patient with a rare lesion involving the pre-SMA and reported increased reaction times as well as inhibitory deficits. Other studies confirmed that the SMA mediates motor inhibition (Chen

et al., 2010; Toma et al., 1999). These results suggest that pre-SMA exhibits a critical role in action control and indicate that pre-SMA immaturity might be a primary cause for less efficient movement performances in young children. However, it is not possible to exclude an indirect correlation between task performance and SMA activation due to parallel age effects. Therefore, the direct functional relevance of the increased SMA activation in improving movement performance cannot be investigated based on the observed data.

Brain oscillatory activity was analyzed to gain insight into maturational changes of movement-related power modulation. Mu-rhythm desynchronization is observed for cortical areas involved in processes of movement preparation, planning, and execution (Leocani et al., 1997; Pfurtscheller and Lopes da Silva, 1999). During cognitive processing or attention allocation processes, alpha power is reduced and facilitates resources to be allocated to task-relevant processing. Cortical regions that are related to task-irrelevant and potentially disruptive processes exhibit mu-rhythm synchronization, i.e. inhibition of underlying areas (Klimesch et al., 2007). The results showed lateralized mu-rhythm desynchronization over contralateral centro-parietal areas during iCNV for all age groups (see Table 2). This suggests that contralateral motor areas were activated during early processes of movement side selection shortly after the presentation of the informative warning cue. Given that the early motor preparation in young children was already characterized by a lateralized activation of contralateral motor regions, it suggests that also young children exhibit motor-related preparatory processes. Moreover, the results confirm that motor program selection corresponds to the early stages of motor preparation, as reflected by contralateral motor area activation.

Compared to evoked cortical potentials, mu-rhythm desynchronization reflects more general sensorimotor network pre-activation (C. Babiloni et al., 1999; Defebvre et al., 1994). In contrast to evoked potentials, differences in early mu rhythm desynchronization over mid-frontocentral areas were most pronounced between the middle (9- to 12-year-olds) and the oldest age group (13- to 16-year-olds), which suggests a delayed development of preparatory alpha band power in relation to evoked cortical activity.

4.3. Maturation of motor cortical pre-activation (late contingent negative variation)

The late component of a CNV has been suggested to represent sensory and motor pre-activation of resources needed for effective task-specific performance (Gaillard, 1978). Midfronto-central negativity increased with age during response preparation (ICNV; see Fig. 2). Previous results confirm the continuous development of preparatory movement networks and maturation of the motor system into young adulthood (Bender et al., 2002; Jonkman, 2006; Killikelly and Szucs, 2013; Thillay et al., 2015). Significant ICNV activity indicates that adolescent subjects used proactive control strategies to perform more efficient task-related movements.

The late CNV component typically exhibits prominent negativity over the contralateral hemispheres, as reported in various studies (Dirnberger et al., 2003; van der Lubbe et al., 2000; Wauschkuhn et al., 1997). However, our findings deviate from developmental research using simpler CNV paradigms (Bender et al., 2005). In our study, adolescent subjects showed only transient contralateral negativity during early motor preparation, potentially reflecting early motor program selection. Notably, the late contralateral activity over premotor and primary motor areas, commonly observed in adolescents and young adults (Bender et al., 2005; Flores et al., 2009), was absent in our adolescent group. This qualitative difference in activation patterns between our adolescent subjects (up to 16 years old) and those typically observed in adults (Gomez et al., 2003) suggests an ongoing developmental process in cortical areas related to preparatory activity.

The characteristic and complexity of a CNV paradigm significantly influences the resulting waveforms, topographies, and amplitudes. Our

paradigm presented a warning cue specifying the required movement side, unlike simpler paradigms that lack such informative cues or varying movement sides. This additional complexity likely demanded higher levels of executive motor control during preparatory processes. Consequently, the development of sustained lateralized negativity over contralateral central areas might be delayed compared to studies using simpler paradigms. These findings suggest that effective motor preparation for complex movements and pronounced pre-activation of effector-specific motor areas (Dirnberger et al., 2003) matures later, potentially extending into late adolescence or young adulthood.

Consistent with previous research (Nagai et al., 2004), our topographic analysis in adolescents showed that the SMA is also involved in late movement preparation. Notably, the data showed a shift in activation from frontal to more central negativity during preparatory CNV stages, as shown in Fig. 2. This suggests a dynamic engagement of SMA across different phases of motor preparation. Early pre-processing (iCNV) might rely more on the pre-SMA, given its established role in motor program planning (Lee et al., 1999). Conversely, the observed shift towards central negativity during late motor pre-activation (ICNV) potentially reflects increased involvement of the more caudal SMA (SMAC) and premotor areas, which have direct connections to the primary motor cortex (Luppino et al., 1993; Wang et al., 2005). This aligns with the notion that SMAC is crucial for movement initiation and execution (Lee et al., 1999).

Time-frequency analysis revealed that alpha-ERD (excitation) of the contralateral hemisphere linearly increased with age during late movement preparation and planning (ICNV), whereas alpha-ERS (inhibition) of the ipsilateral side decreased (see Fig. 4A and 4B). However, lateralization analysis of the alpha power band showed no differences in lateralization strength between young children and adolescent subjects, as shown in Fig. 4C to 4F. Since synchronized activity is related to deactivation of corresponding brain areas (Lopes da Silva, 2006; Pfurtscheller, 2001), the results suggest that processes related to alpha band oscillation of motor networks were shifted from inhibition of ipsilateral motor-related brain areas to pre-activation of contralateral motor-related areas. These findings sustain the hypothesis of a maturational shift from reactive to proactive motor control (Chevalier et al., 2014). Furthermore, age-consistent alpha-band lateralization showed that small SMA activity observed for young subjects was not evoked due to low motor preparation or a lack of motivation but due to qualitatively different preparatory processes.

4.4. Maturation of movement processing (post imperative negative variation)

The PINV is associated with movement evaluation processes and is suggested to represent uncertainty in task performance (Bender et al., 2006; Klein et al., 1996). Reliance of the PINV on response execution was confirmed due to its correlation with response execution timing rather than the timing of external stimuli (Bender et al., 2004). EEG studies showed enhanced PINV amplitudes in children and adult subjects when they had to perform non-controllable tasks (Kathmann et al., 1990; Yordanova et al., 1997).

ERP data showed a developmental shift from pronounced negativity over contralateral central areas to negativity over more frontocentral areas during performance evaluation (see Fig. 2). The PINV did not depend on preparatory CNV components since topographical distribution differed significantly, as shown in previous studies (Bender et al., 2004; 2005). Since the performance of younger subjects was associated with a lack of control, high PINV amplitudes might reflect the controllability of task-related movements. Moreover, the results suggest that young children were more likely to be uncertain about their response performance, reflected in an increased compensatory effort and enhanced evaluation processes. Future studies should address the question of whether increased motor post-processing supports motor learning in children.

As observed for evoked potentials, alpha band desynchronization increased with age over mid-frontocentral areas during response evaluation (see Table 2). These results indicate that mid-frontocentral areas associated with SMA activity are increasingly recruited with age during movement post-processing and motor maturation. ERP data, similar to observations of preparatory mu rhythm desynchronization, reveal the most prominent maturational shifts in PINV topographies for younger and middle-aged groups, whereas alpha-ERD was characterized by pronounced developmental differences between the middle and the oldest age groups. This pattern strengthens the suggestion of a protracted maturation of alpha-band oscillations, extending into late adolescence or early adulthood.

4.5. Limitations

Based on the presented results, it is not possible to identify physiological mechanisms that underlie the observed changes in cortical activity and alpha band oscillation. It is likely that the observed maturation depends, inter alia, on developmental changes in functional connectivity that induce altered network dynamics (Brookes et al., 2018). Future studies should include multi-modal comparisons (fMRI) and connectivity analyses to investigate brain development more precisely. Moreover, studies of developmental changes should include an analysis of longitudinal examinations and not be based exclusively on cross-sectional data. The investigation of cortical maturation on an individual, intra-subject level allows the generation of more reliable and accurate information.

5. Conclusion

Our data revealed pronounced maturational differences in cortical movement preparation and post-processing between child and adolescent subjects. Behavioral results indicated less efficient action pre-processing and a lack of inhibitory control, likely attributed to incomplete frontal lobe maturity in children. Activation of mid-frontocentral areas related to the supplementary motor area during movement preparation and evaluation became increasingly prominent with age. Alpha band power indicated developmental progress from inhibiting ipsilateral motor areas in young children to enhanced pre-activation of contralateral motor areas in adolescents. Based on our data, evoked cortical activation is likely to develop earlier than alpha-band oscillatory activity. The reported results support the hypothesis of a developmental shift from a reactive to a proactive control and indicate immaturity in supplementary-, pre-, and primary motor areas until late adolescence or early adulthood.

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Ethics approval statement

This study was conducted in accordance with the local legislation and institutional requirements. The research protocol was reviewed and approved by the Ethics Committee of the University of Cologne and the Ethics Committee of the University of Aachen.

CRediT authorship contribution statement

Julia Schmidgen: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Theresa Heinen:** Writing – review & editing, Conceptualization. **Kerstin Konrad:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization. **Stephan**

Bender: Writing – review & editing, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2024.120735.

References

- Adornetto, C., In-Albon, T., Schneider, S., 2008. Diagnostik im Kindes- und Jugendalter anhand strukturierter Interviews: Anwendung und Durchführung des Kinder-DIPS. *Klin. Diagn. Eval.* 1 (4), 363–377.
- Babiloni, C., Carducci, F., Cincotti, F., Rossini, P.M., Neuper, C., Pfurtscheller, G., Babiloni, F., 1999. Human movement-related potentials vs desynchronization of EEG alpha rhythm: a high-resolution EEG study. *Neuroimage* 10 (6), 658–665.
- Bender, S., Becker, D., Oelkers-Ax, R., Weisbrod, M., 2006. Cortical motor areas are activated early in a characteristic sequence during post-movement processing. *Neuroimage* 32 (1), 333–351. <https://doi.org/10.1016/j.neuroimage.2006.03.009>.
- Bender, S., Behringer, S., Freitag, C.M., Resch, F., Weisbrod, M., 2010. Transmodal comparison of auditory, motor, and visual post-processing with and without intentional short-term memory maintenance. *Clin. Neurophysiol.* 121 (12), 2044–2064.
- Bender, S., Oelkers-Ax, R., Resch, F., Weisbrod, M., 2004. Motor processing after movement execution as revealed by evoked and induced activity. *Cogn. Brain Res.* 21 (1), 49–58.
- Bender, S., Weisbrod, M., Bornfleth, H., Resch, F., Oelkers-Ax, R., 2005. How do children prepare to react? Imaging maturation of motor preparation and stimulus anticipation by late contingent negative variation. *Neuroimage* 27 (4), 737–752. <https://doi.org/10.1016/j.neuroimage.2005.05.020>.
- Bender, S., Weisbrod, M., Just, U., Pfüller, U., Parzer, P., Resch, F., Oelkers-Ax, R., 2002. Lack of age-dependent development of the contingent negative variation (CNV) in migraine children? *Cephalalgia* 22 (2), 132–136. <https://doi.org/10.1046/j.1468-2982.2002.00334.x>.
- Berchicci, M., Zhang, T., Romero, L., Peters, A., Annett, R., Teuscher, U., Bertollo, M., Okada, Y., Stephen, J., Comani, S., 2011. Development of mu rhythm in infants and preschool children. *Dev. Neurosci.* 33 (2), 130–143. <https://doi.org/10.1159/000329095>.
- Birbaumer, N., Elbert, T., Canavan, A.G., Rockstroh, B., 1990. Slow potentials of the cerebral cortex and behavior. *Physiol. Rev.* 70 (1), 1–41.
- Brookes, M.J., Groom, M.J., Liuzzi, L., Hill, R.M., Smith, H.J., Briley, P.M., Hall, E.L., Hunt, B.A., Gascoyne, L.E., Taylor, M.J., 2018. Altered temporal stability in dynamic neural networks underlies connectivity changes in neurodevelopment. *Neuroimage* 174, 563–575.
- Bucsuházy, K., Semela, M., 2017. Case study: reaction time of children according to age. *Procedia Eng.* 187, 408–413.
- Chen, X., Scangos, K.W., Stuphorn, V., 2010. Supplementary motor area exerts proactive and reactive control of arm movements. *J. Neurosci.* 30 (44), 14657–14675.
- Chevalier, N., James, T.D., Wiebe, S.A., Nelson, J.M., Espy, K.A., 2014. Contribution of reactive and proactive control to children's working memory performance: insight from item recall durations in response sequence planning. *Dev. Psychol.* 50 (7), 1999–2008. <https://doi.org/10.1037/a0036644>.
- Cochin, S., Barthelemy, C., Roux, S., Martineau, J., 2001. Electroencephalographic activity during perception of motion in childhood. *Eur. J. Neurosci.* 13 (9), 1791–1796. <https://doi.org/10.1046/j.0953-816x.2001.01544.x>.
- Côté, S.L., Elgbeili, G., Quessy, S., Dancause, N., 2020. Modulatory effects of the supplementary motor area on primary motor cortex outputs. *J. Neurophysiol.* 123 (1), 407–419.
- Cui, R., Egkher, A., Huter, D., Lang, W., Lindinger, G., Deecke, L., 2000. High resolution spatiotemporal analysis of the contingent negative variation in simple or complex motor tasks and a non-motor task. *Clin. Neurophysiol.* 111 (10), 1847–1859.

- de Jong, R., Wierda, M., Mulder, G., Mulder, L.J., 1988. Use of partial stimulus information in response processing. *J. Exp. Psychol.* 14 (4), 682. : Human perception and performance.
- Deecke, L., Scheid, P., Kornhuber, H.H., 1969. Distribution of readiness potential, pre-motor positivity, and motor potential of the human cerebral cortex preceding voluntary finger movements. *Exp. Brain Res.* 7 (2), 158–168. <https://doi.org/10.1007/BF00235441>.
- Defebvre, L., Bourriez, J.L., Dujardin, K., Derambure, P., Destee, A., Guieu, J.D., 1994. Spatiotemporal study of Bereitschaftspotential and event-related desynchronization during voluntary movement in Parkinson's disease. *Brain Topogr.* 6 (3), 237–244. <https://doi.org/10.1007/BF01187715>.
- Dirnberger, G., Greiner, K., Duregger, C., Endl, W., Lindinger, G., Lang, W., 2003. The effects of alteration of effector and side of movement on the contingent negative variation. *Clin. Neurophysiol.* 114 (11), 2018–2028. [https://doi.org/10.1016/s1388-2457\(03\)00197-4](https://doi.org/10.1016/s1388-2457(03)00197-4).
- Eom, T.H., 2023. Electroencephalography source localization. *Clin. Exp. Pediatr.* 66 (5), 201.
- Fietzek, U., Heinen, F., Berweck, S., Maute, S., Hufschmidt, A., Schulte-Mönting, J., Lücking, C., Korinthenberg, R., 2000. Development of the corticospinal system and hand motor function: central conduction times and motor performance tests. *Dev. Med. Child Neurol.* 42 (4), 220–227.
- Flores, A.B., Digiacomo, M.R., Meneres, S., Trigo, E., Gomez, C.M., 2009. Development of preparatory activity indexed by the contingent negative variation in children. *Brain Cogn.* 71 (2), 129–140. <https://doi.org/10.1016/j.bandc.2009.04.011>.
- Gaillard, A.W.K., 1978. Slow Brain Potentials Preceding Task Performance TU Delft. Delft University of Technology.
- Gerloff, C., Uenishi, N., Hallett, M., 1998. Cortical activation during fast repetitive finger movements in humans: dipole sources of steady-state movement-related cortical potentials. *J. Clin. Neurophysiol.* 15 (6), 502–513. <https://doi.org/10.1097/00004691-199811000-00009>.
- Gomez, C.M., Delinte, A., Vaquero, E., Cardoso, M.J., Vazquez, M., Crommelinck, M., Roucoux, A., 2001. Current source density analysis of CNV during temporal gap paradigm. *Brain Topogr.* 13 (3), 149–159. <https://doi.org/10.1023/a:1007816201345>.
- Gomez, C.M., Marco, J., Grau, C., 2003. Preparatory visuo-motor cortical network of the contingent negative variation estimated by current density. *Neuroimage* 20 (1), 216–224. [https://doi.org/10.1016/s1053-8119\(03\)00295-7](https://doi.org/10.1016/s1053-8119(03)00295-7).
- Gramfort, A., Luessi, M., Larson, E., Engemann, D., Strohmeier, D., Brodbeck, C., Goj, R., Jas, M., Brooks, T., Parkkonen, L., 2013. MEG and EEG data analysis with MNE-Python. *Front. Neurosci.* 7, 267. *Frontiers*.
- Hecht, M., Thiemann, U., Freitag, C.M., Bender, S., 2016. Time-resolved neuroimaging of visual short term memory consolidation by post-perceptual attention shifts. *Neuroimage* 125, 964–977.
- Huttenlocher, P.R., 1979. Synaptic density in human frontal cortex-developmental changes and effects of aging. *Brain Res.* 163 (2), 195–205.
- Jensen, O., Mazaheri, A., 2010. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. *Front. Hum. Neurosci.* 4, 186.
- Jonkman, L.M., 2006. The development of preparation, conflict monitoring and inhibition from early childhood to young adulthood: a Go/Nogo ERP study. *Brain Res.* 1097 (1), 181–193. <https://doi.org/10.1016/j.brainres.2006.04.064>.
- Jonkman, L.M., Lansbergen, M., Stauder, J.E., 2003. Developmental differences in behavioral and event-related brain responses associated with response preparation and inhibition in a go/nogo task. *Psychophysiology* 40 (5), 752–761. <https://doi.org/10.1111/1469-8986.00075>.
- Kathmann, N., Jonitz, L., Engel, R.R., 1990. Cognitive determinants of the postimperative negative variation. *Psychophysiology* 27 (3), 256–263. <https://doi.org/10.1111/j.1469-8986.1990.tb00380.x>.
- Killikelly, C., Szucs, D., 2013. Delayed development of proactive response preparation in adolescents: ERP and EMG evidence. *Dev. Cogn. Neurosci.* 3, 33–43. <https://doi.org/10.1016/j.dcn.2012.08.002>.
- Kiselev, S., Espy, K.A., Sheffield, T., 2009. Age-related differences in reaction time task performance in young children. *J. Exp. Child Psychol.* 102 (2), 150–166.
- Klein, C., 2001. Developmental functions for saccadic eye movement parameters derived from pro- and antisaccade tasks. *Exp. Brain Res.* 139, 1–17.
- Klein, C., Rockstroh, B., Cohen, R., Berg, P., Dressel, M., 1996. The impact of performance uncertainty on the postimperative negative variation. *Psychophysiology* 33 (4), 426–433. <https://doi.org/10.1111/j.1469-8986.1996.tb01068.x>.
- Klimesch, W., Sauseng, P., Hanslmayr, S., 2007. EEG alpha oscillations: the inhibition–timing hypothesis. *Brain Res. Rev.* 53 (1), 63–88.
- Lau, H.C., Rogers, R.D., Haggard, P., Passingham, R.E., 2004. Attention to intention. *Science* 303 (5661), 1208–1210 (1979).
- Lee, K.M., Chang, K.H., Roh, J.K., 1999. Subregions within the supplementary motor area activated at different stages of movement preparation and execution. *Neuroimage* 9 (1), 117–123.
- Leocani, L., Toro, C., Manganotti, P., Zhuang, P., Hallett, M., 1997. Event-related coherence and event-related desynchronization/synchronization in the 10 Hz and 20 Hz EEG during self-paced movements. *Electroencephalogr. Clin. Neurophysiol.* 104 (3), 199–206. [https://doi.org/10.1016/s0168-5597\(96\)96051-7](https://doi.org/10.1016/s0168-5597(96)96051-7).
- Liu, H., Schimpf, P.H., Dong, G., Gao, X., Yang, F., Gao, S., 2005. Standardized shrinking LORETA-FOCUS (SSLOFO): a new algorithm for spatio-temporal EEG source reconstruction. *IEEE Trans. Biomed. Eng.* 52 (10), 1681–1691. <https://doi.org/10.1109/TBME.2005.855720>.
- Lopes da Silva, F.H., 2006. Event-related neural activities: what about phase? *Prog. Brain Res.* 159, 3–17. [https://doi.org/10.1016/S0079-6123\(06\)59001-6](https://doi.org/10.1016/S0079-6123(06)59001-6).
- Luppino, G., Matelli, M., Camarda, R., Rizzolatti, G., 1993. Corticocortical connections of area F3 (SMA-proper) and area F6 (pre-SMA) in the macaque monkey. *J. Comp. Neurol.* 338 (1), 114–140.
- Macdonald, J.A., Beauchamp, M.H., Crigan, J.A., Anderson, P.J., 2014. Age-related differences in inhibitory control in the early school years. *Child Neuropsychol.* 20 (5), 509–526.
- Mennes, M., Wouters, H., Vanrumste, B., Lagae, L., Stiers, P., 2010. Validation of ICA as a tool to remove eye movement artifacts from EEG/ERP. *Psychophysiology* 47 (6), 1142–1150.
- Nachev, P., Wydell, H., O'Neill, K., Husain, M., Kennard, C., 2007. The role of the pre-supplementary motor area in the control of action. *Neuroimage* 36 (Suppl 2(3–3)), T155–T163. <https://doi.org/10.1016/j.neuroimage.2007.03.034>.
- Niedermeyer, E., 1997. Alpha rhythms as physiological and abnormal phenomena. *Int. J. Psychophysiol.* 26 (1–3), 31–49.
- Nunez, P.L., Silberstein, R.B., Cadusch, P.J., Wijesinghe, R.S., Westdorp, A.F., Srinivasan, R., 1994. A theoretical and experimental study of high resolution EEG based on surface Laplacians and cortical imaging. *Electroencephalogr. Clin. Neurophysiol.* 90 (1), 40–57.
- Oldfield, R., 1971. Edinburgh handedness inventory. *J. Abnorm. Psychol.*
- Padilla, M.L., Pfefferbaum, A., Sullivan, E.V., Baker, F.C., Colrain, I.M., 2014. Dissociation of preparatory attention and response monitoring maturation during adolescence. *Clin. Neurophysiol.* 125 (5), 962–970. <https://doi.org/10.1016/j.clinph.2013.10.012>.
- Pfurtscheller, G., 2001. Functional brain imaging based on ERD/ERS. *Vision Res.* 41 (10–11), 1257–1260. [https://doi.org/10.1016/s0042-6989\(00\)00235-2](https://doi.org/10.1016/s0042-6989(00)00235-2).
- Pfurtscheller, G., Da Silva, F.L., 1999. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin. Neurophysiol.* 110 (11), 1842–1857.
- Pfurtscheller, G., Lopes da Silva, F.H., 1999. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin. Neurophysiol.* 110 (11), 1842–1857. [https://doi.org/10.1016/s1388-2457\(99\)00141-8](https://doi.org/10.1016/s1388-2457(99)00141-8).
- Pfurtscheller, G., Woertz, M., Supp, G., Da Silva, F.L., 2003. Early onset of post-movement beta electroencephalogram synchronization in the supplementary motor area during self-paced finger movement in man. *Neurosci. Lett.* 339 (2), 111–114.
- Pollmann, S., Yves von Cramon, D., 2000. Object working memory and visuospatial processing: functional neuroanatomy analyzed by event-related fMRI. *Exp. Brain Res.* 133, 12–22.
- Rockstroh, B. (1982). Slow brain potentials and behavior. (*No Title*).
- Rohrbaugh, J.W., Syndulko, K., Lindsley, D.B., 1976. Brain wave components of the contingent negative variation in humans. *Science* 191 (4231), 1055–1057. <https://doi.org/10.1126/science.1251217> (1979).
- Roland, P.E., Larsen, B., Lassen, N.A., Skinhøj, E., 1980. Supplementary motor area and other cortical areas in organization of voluntary movements in man. *J. Neurophysiol.* 43 (1), 118–136. <https://doi.org/10.1152/jn.1980.43.1.118>.
- Segalowitz, S., Davies, P.L., 2004. Charting the maturation of the frontal lobe: an electrophysiological strategy. *Brain Cogn.* 55 (1), 116–133.
- Shaw, P., Kabani, N.J., Lerch, J.P., Eckstrand, K., Lenroot, R., Gogtay, N., Greenstein, D., Clasen, L., Evans, A., Rapoport, J.L., Giedd, J.N., Wise, S.P., 2008. Neurodevelopmental trajectories of the human cerebral cortex. *J. Neurosci.* 28 (14), 3586–3594. <https://doi.org/10.1523/JNEUROSCI.5309-07.2008>.
- Smith, A.B., Halari, R., Giampetro, V., Brammer, M., Rubia, K., 2011. Developmental effects of reward on sustained attention networks. *Neuroimage* 56 (3), 1693–1704.
- Tanji, J., 2001. Sequential organization of multiple movements: involvement of cortical motor areas. *Annu. Rev. Neurosci.* 24 (1), 631–651.
- Tenke, C.E., Kayser, J., 2005. Reference-free quantification of EEG spectra: combining current source density (CSD) and frequency principal components analysis (fPCA). *Clin. Neurophysiol.* 116 (12), 2826–2846.
- Thatcher, R.W., 1992. Cyclic cortical reorganization during early childhood. *Brain Cogn.* 20 (1), 24–50.
- Thillay, A., Roux, S., Gissot, V., Carteau-Martin, I., Knight, R.T., Bonnet-Brilhault, F., Bidet-Caulet, A., 2015. Sustained attention and prediction: distinct brain maturation trajectories during adolescence. *Front. Hum. Neurosci.* 9, 519. <https://doi.org/10.3389/fnhum.2015.00519>.
- Tian, Q., Xu, S., Guo, Y., Li, J., Han, M., Ma, Y., Hou, X., Chen, J., Luo, D., Hong, Y., Nie, S., Liu, X., 2019. Contingent negative variation for the periodicity of migraine attacks without aura. *JIN* 18 (3), 269–276. <https://doi.org/10.31083/j.jin.2019.03.193>.
- Toma, K., Honda, M., Hanakawa, T., Okada, T., Fukuyama, H., Ikeda, A., Nishizawa, S., Konishi, J., Shibasaki, H., 1999. Activities of the primary and supplementary motor areas increase in preparation and execution of voluntary muscle relaxation: an event-related fMRI study. *J. Neurosci.* 19 (9), 3527–3534.
- van der Lubbe, R.H., Wauschkuhn, B., Wascher, E., Niehoff, T., Kompf, D., Verleger, R., 2000. Lateralized EEG components with direction information for the preparation of saccades versus finger movements. *Exp. Brain Res.* 132 (2), 163–178. <https://doi.org/10.1007/s002219900328>.
- Van Leeuwen, T.H., Steinhausen, H.C., Overtom, C.C., Pascual-Marqui, R.D., Van't Klooster, B., Rothenberger, A., Sergeant, J.A., Brandeis, D., 1998. The continuous performance test revisited with neuroelectric mapping: impaired orienting in children with attention deficits. *Behav. Brain Res.* 94 (1), 97–110.
- Walter, W.G., Cooper, R., Aldridge, V.J., McCallum, W.C., Winter, A.L., 1964. Contingent negative variation : an electric sign of sensori-motor association and expectancy in the human brain. *Nature* 203 (4943), 380–384. <https://doi.org/10.1038/203380a0>.
- Wauschkuhn, B., Wascher, E., Verleger, R., 1997. Lateralised cortical activity due to preparation of saccades and finger movements: a comparative study. *Electroencephalogr. Clin. Neurophysiol.* 102 (2), 114–124. [https://doi.org/10.1016/s0921-884x\(96\)96585-6](https://doi.org/10.1016/s0921-884x(96)96585-6).

- Weerts, T.C., Lang, P.J., 1973. The effects of eye fixation and stimulus and response location on the contingent negative variation (CNV). *Biol. Psychol.* 1 (1), 1–19. [https://doi.org/10.1016/0301-0511\(73\)90010-0](https://doi.org/10.1016/0301-0511(73)90010-0).
- Weisz, N., Schandry, R., Jacobs, A.M., Mialet, J.P., Duschek, S., 2002. Early contingent negative variation of the EEG and attentional flexibility are reduced in hypotension. *Int. J. Psychophysiol.* 45 (3), 253–260. [https://doi.org/10.1016/s0167-8760\(02\)00032-6](https://doi.org/10.1016/s0167-8760(02)00032-6).
- Werner, J., Weisbrod, M., Resch, F., Roessner, V., Bender, S., 2011. Increased performance uncertainty in children with ADHD?—Elevated post-imperative negative variation (PINV) over the ventrolateral prefrontal cortex. *Behav. Brain Funct.* 7, 1–9.
- Yordanova, J., Dumais-Huber, C., Rothenberger, A., Woerner, W., 1997. Frontocortical activity in children with comorbidity of tic disorder and attention-deficit hyperactivity disorder. *Biol. Psychiatry* 41 (5), 585–594. [https://doi.org/10.1016/s0006-3223\(96\)00096-0](https://doi.org/10.1016/s0006-3223(96)00096-0).