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Original article

Developmental changes in brain activation and functional connectivity during response inhibition in the early childhood brain

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Abstract

Response inhibition is an attention function which develops relatively early during childhood. Behavioral data suggest that by the age of 3, children master the basic task requirements for the assessment of response inhibition but performance improves substantially until the age of 7. The neuronal mechanisms underlying these developmental processes, however, are not well understood. In this study, we examined brain activation patterns and behavioral performance of children aged between 4 and 6 years compared to adults by applying a go/no-go paradigm during near-infrared spectroscopy (NIRS) brain imaging. We furthermore applied task-independent functional connectivity measures to the imaging data to identify maturation of intrinsic neural functional networks. We found a significant group × condition related interaction in terms of inhibition-related reduced right fronto–parietal activation in children compared to adults. In contrast, motor-related activation did not differ between age groups. Functional connectivity analysis revealed that in the children's group, short-range coherence within frontal areas was stronger, and long-range coherence between frontal and parietal areas was weaker, compared to adults. Our findings show that in children aged from 4 to 6 years fronto–parietal brain maturation plays a crucial part in the cognitive development of response inhibition.

Keywords: Optical tomography; NIRS; Response inhibition; Functional connectivity; Development; Early childhood

1. Introduction

The ability to consciously inhibit a pre-potent response is a hallmark of the development of attention. A go/no-go paradigm tests response inhibition by

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requiring the subject to respond to a frequent target stimulus while suppressing the response on the occurrence of a rare non-target stimulus. A number of behavioral studies have employed this paradigm to investigate the development of response inhibition throughout childhood and adolescence [1] suggesting significant maturation changes under age 7 [2]. Developmental psychologists hypothesize that even 3 year old children have the cognitive capacity to master basic functions of response control, as 3-year-olds were able to verbally reproduce the task rules correctly. However, it seems as if developmental constraints prevent them from actually being able to perform the task accurately [3,4]. This has been attributed to the children's immature ability to reflect on the rules required for the tasks [5]. Interestingly, Dowsett and Livesey showed that repeated exposure to the task improved inhibitory control even in 3 year old children, suggesting that neuronal networks underlying response inhibition may develop around this age [1].

Empirical evidence for developmental changes in the neuronal network of response inhibition during early childhood is scarce. Existing studies are mainly focused on event-related potentials (ERP) obtained with electroencephalography (EEG) measurements. For example, the prefrontal N2-ERP component (negative ERP around 200 ms after stimulus onset) for no-go trials is associated with the inhibition of an intended action. Current findings support the assumption of early maturation of response inhibition by showing developmental changes during this period. For example, Rueda and colleagues reported that in a conflict task a prefrontal N2-component could be elicited in 4-year-olds only after training. This ERP-component was similar to that in untrained 6-year-olds, who in turn after training showed a response similar to that of adults. These electrophysiological findings parallel behavioral performance and corroborate the hypothesis that changes of the neuronal network supporting attention undergo plasticity changes depending on brain maturation and training [6].

Functional magnetic resonance imaging (fMRI) in children and adolescents has revealed immature brain activation of response inhibition including deviant responses of fronto–parietal pathways. Task-induced frontal brain activation in children aged from 6 to 12 years was found to be less focalized and more bilaterally extended compared to adults. In addition children showed a stronger recruitment of subcortical structures and a weaker involvement of parietal areas [7,8]. Such evidence of functional plasticity changes from childhood into early adulthood is complemented by anatomical studies, showing maturational processes within frontal and parietal lobes [9], as well as findings from resting-state functional connectivity studies using fMRI. For example, Fair et al. described two complementary mechanisms of network maturation: *integration* and *segregation* [10]. Whereas *integration* describes the organization of brain regions into networks, i.e., the increase of long-range connections, *segregation* refers to the differentiation of sets of regions into separate networks, i.e., a decrease in short-range connections. *Segregation* processes were observed in the fronto–parietal control network; in children (7–9 years) strong (short-range) connections between the right and left frontal cortex, were dominant. At the time of adolescence (10–15 years), both cortical lobes were fully segregated. Network *integration* was supported by the observation of increasing fronto–parietal (long-range) connectivity from childhood through adolescence into adulthood.

In the present study we examined the neuronal underpinnings of response inhibition by investigating children between 4 and 6 years and young adults with (nearly) whole-head near-infrared spectroscopy (NIRS) brain imaging while performing a go/no-go task. Similar to blood oxygenation level dependent (BOLD) fMRI studies, NIRS relies on concentration changes of oxygenated and deoxygenated hemoglobin. Following local neuronal activation there is a blood flow increase causing a transient elevation of oxygenated hemoglobin concentration on a time scale of several seconds. This is accompanied by a washout of deoxygenated hemoglobin, resulting in its relative concentration decrease. The oxygenated hemoglobin response tends to be of larger amplitude compared to deoxygenated hemoglobin change but is less reliable an indicator of neural activation. There are several reasons for this: (a) oxygenated hemoglobin levels are much more prone to inference by extra-cerebral physiological noise such as the heartbeat (~1 Hz), breathing (~0.3 Hz), or blood pressure changes (~0.1 Hz) originating in the skin [11] and (b) HbO is not clearly related to BOLD fMRI signals to which only the deoxygenated hemoglobin contributes [12]. We investigated both task-induced brain activation patterns and functional connectivity using partial coherence analysis. Our key questions were (i) whether the task would lead to differential activation within fronto–parietal pathways between adults and children during response inhibition. We hypothesized a more diffuse frontal activation pattern with less parietal activation in the children's group during the no-go condition. Furthermore, we assumed to find differences in functional connectivity between age groups. (ii) Based on the introduced findings of significant improvement of response inhibition from 4 and 6 years of age, we furthermore hypothesized that within the children's group activation patterns and network architecture might develop with increasing age towards adult-like findings. On the other hand we expected similar activations in the motor cortex during the go condition for both groups.

2. Material and methods

2.1. Subjects

Fifty-one healthy subjects completed the study (21 adults, 30 children). Due to either incomplete data sets or motion artifacts we had to exclude one adult and eight children from statistical analysis, resulting in a group of twenty adults (mean age = 26.3 ± 4.3 years, age range 21–36 years, 9 males) and twenty-two children (mean age = 4.8 ± 0.6 years, age range 4–6 years, 11 males). All children underwent a cognitive screening, using a short version of the K-ABC [13] to ensure normal intelligence ($M_{IQ} = 102.3 \pm 11$). To control for attention deficits we performed a semi-structured clinical interview with the children's' parents (K-SADS-PL, attention/hyperactivity section) [14]. Cognitive performance in the adult group was measured via the vocabulary test (Wortschatztest (WST), [15]), a method to estimate roughly general intelligence. All adult participants were native speakers of German, and all were of normal intelligence ($M_{WST} = 33.66 \pm 4.9$). The clinical screening in the adult group included the medical history of neurological and psychiatric disorder as well as the screening questionnaire of the Structured Clinical Interview of the DSM-IV (SKID, [16]). Prior to each experiment we obtained informed consent either from the children's parents or the adult volunteers. The study protocol was approved by the local ethics committee (Charité, Berlin).

2.2. Paradigm

Volunteers were asked to respond to frequent, visually presented targets by pressing a button with the right hand (*go* condition) and to avoid the response to rare non-targets (*no-go* condition). The subjects were instructed to respond to the targets as fast as possible. We presented cartoon images of 'Bob the builder' and 'Wendy' characters as go and no-go stimuli. Task versions were balanced with respect to the stimulus material (i.e., which of the characters was used as the go or no-go condition) and sex of participants for both subject groups ($N_{men,bob} = 4$, $N_{men,wendy} = 5$, $N_{women,bob} = 5$, $N_{women,wendy} = 6$, $N_{boys,bob} = 5$, $N_{boys,wendy} = 7$, $N_{girls,bob} = 6$, $N_{girls,wendy} = 4$). The task consisted of two runs, each of which lasted 250 s and contained a total of 54 trials with 70% go trials and 30% no-go trials. The order of the presentation was randomized. The experimental paradigm was constructed as an event-related design. The stimulus duration was 800 ms and the average inter-stimulus interval (ISI) was 5500 ms (jittered, ranging from 3750 to 12000 ms). ISI was adapted from earlier studies, which examined BOLD signal changes [e.g. 7,21].

2.3. NIRS data acquisition

Brain imaging data was acquired using NIRS. This technique measures the blood oxygenation level of the superficial layers of the human cortex and can distinguish between concentration changes of oxygenated hemoglobin ([HbO]) and deoxygenated hemoglobin ([HbR]). Thereby, it measures a comparable effect like blood oxygenation level dependent (BOLD) fMRI [11]. While concentration of [HbO] is expected to increase after focal activation of the cortex due to higher blood flow, [HbR] is washed out and decreases [12].

The NIRS system used (DYNOT 232, NIRx Medizintechnik GmbH, Berlin, Germany) provides 32 sequentially switched illumination positions (emitters) and 32 parallel acquired detector channels (detectors). Fiber optic probes serving as sources and receivers were equidistantly arranged on the head areas of interest (inter-fiber distance of 28 ± 3 mm). Each pair of neighboring emitters and detectors form a measurement channel which probes a subsurface tissue volume centered in between them. The 52 probes (32 detectors, 20 emitters) used here result in 80 channels, which covered nearly the whole head of the subjects, including the frontal, parietal, and temporal cortices (Fig. 1). NIRS data were continuously sampled at 2.44 Hz. To guarantee optimal

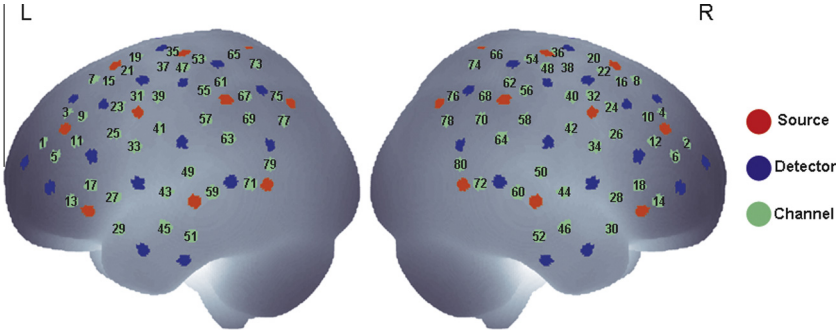

Fig. 1. Optode positions, superimposed onto a brain surface. Red dots: laser emitter positions; blue: detector positions; green: actual NIRS measurement channel positions with channel number. Note the use of even/odd numbers for the right/left hemisphere and small/large numbers for frontal/parietal areas. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

safety and convenience for the subjects, the fiber-optic bundles (emitter: 1 mm and detector: 3 mm in diameter) were integrated into a commercially available EEG-cap (www.easycap.de/easycap/). Optode-positions were defined with reference to the EEG 10–20 system using a 3D digitizing system (Zebris CMS20) and the freeware MATLAB toolbox NFRI (http://brain.job.affrc.go.jp/tools/) described in [17]. We digitized EEG 10–20 positions as spatial reference points for the channel location. All 3D localization measurements were performed on an anatomical head model. Using the NFRI toolbox statistical results for each channel were plotted on the surface of a standardized brain to visualize the topography of brain activation results.

2.4. NIRS data pre-processing

In a first step we identified channels showing excessive noise level or other interferences caused by imperfect optical coupling of the probes to the head, possible light blockage (e.g. hair) or extra-cranial cross-talk. As a criterion, we excluded all channels whose mean signal was either below or above the known interval of acceptable detector operation (i.e., between 0.3 V and 4.0 V photovoltaic output). A value below the lower bound signifies low signal-to-noise ratio, while a value exceeding the upper bound risks detector saturation and hence signal distortion.

For the retained channels we converted attenuation changes measured at 760 nm and 830 nm into [HbO] and [HbR] concentration changes employing the modified Beer–Lambert law [18]. Movement artifacts, a major source of noise in children, were smoothed by a semi-automated procedure which replaces contaminated data segments by linear interpolation [19]. This procedure has proven to be capable of attenuating motion artifacts sufficiently so that data sets, or parts thereof, may be salvaged rather than completely rejected from the analysis. The amount of interpolated data in the children group is 17% percent in average, in the adult group 11% percent in average. There were no significant differences between groups (comparing groups by a two-sided T-test).

2.4.1. General linear model analysis

Following data pre-processing a low-pass filter (0.4 Hz, 3rd order Butterworth) was applied to attenuate high frequency noise and the cardiac signal. In addition, a high pass filter of 1/120 Hz was used to reject signal drifts. We removed trials of incorrect responses (i.e., non-responses to go-stimuli and responses to no-go-stimuli) from the data set and excluded these from further statistical analyses. We used the general linear model to estimates the statistical fit of a predicted hemodynamic model curve to the measured signals. GLM analysis was originally developed for statistical parametric mapping (SPM) of fMRI data and has also been shown to be a robust and reliable analysis method for optical [20]. GLM has been applied in NIRS imaging frequently in recent optical developmental studies [19].

We applied GLM analysis separately to both hemoglobin chromophores ([HbO] and [HbR]), for each condition, and for each subject. The so obtained statistical fitting parameter β is a measure of the stimulus-related relative change of tissue hemoglobin concentration and the basis of all our further statistical analysis. We generated the hemodynamic model functions, or regressors, by convolving the temporal stimulus profile with a canonical hemodynamic response function (HRF). We used a HRF shape proposed by [21], with a peak time of 5 s. Generating the regressors this way accounts for the idiosyncrasy of the sluggish hemodynamic response, which does not reach baseline for some 20 s after stimulus cessation.

2.4.2. Partial coherence analysis

In addition to the GLM analysis of NIRS-data we performed a functional connectivity analysis using partial coherence coefficients (pCC) [22], which performs the correlation analysis in the frequency domain. In contrast to conventional correlation analysis, this partials out influences of neighboring effects and global physiological artifacts which otherwise are likely to overwhelm any true physiological connectivity effects. Functional connectivity analysis on task-induced brain activation data (in contrast to resting-state data) has been performed before in fMRI and NIRS [23]. In general, functional connectivity has so far mainly been investigated on a network-level using independent component analysis and identifying intrinsic and/or resting-state brain networks. However, the approach of partial coherence coefficients has been suggested as a more adequate approach [e.g. 24]. We suppressed task-related effects from the connectivity analysis by regressing out the task-related HRF model function described above in Section 2.4.1.

To evaluate the degree of functional connectivity within the fronto–temporo–parietal network, we generated a coherence matrix with $n^2 = (\text{number of channels})^2 = 80^2 = 6{,}400$ entries, each of which contains the bi-regional coherence coefficients for a specific pair of channels, which were then compared between children and adults.

For coherence analysis the full time courses of the oxygenation changes were used after removing the pauses between the two runs. For each subject, we removed these entries in the coherence matrix that did not pass the signal quality criteria as describe in Section 2.4. Following the approach by [25] we rejected global effects such as caused by cardiac or respiratory pulsation by regressing out the normalized global average of the [HbR] or [HbO] signal For each channel we

computed the first eigenvector by singular value decomposition (SCD), yielding the dominant component of the NIRS signal. A Fisher's Z-transformation was applied to produce a normal distribution. The bandwidth of the signals spectra ranged from 0.01 to 0.122 Hz. Referring to [26], we combined the frequencies into the bins <0.03 Hz; <0.08 Hz, and <0.12 Hz.

2.5. Statistical analysis

2.5.1. Behavioral data

For each subject, the mean reaction time (RT) and accuracy (AC) were calculated. AC was obtained from the number of correct denials of no-go trials (correct rejections, see table 1) and did not consider misses of go trials. The RT was estimated from all correct responses to go trials and did not include incorrect responses to no-go trials. To exclude effects of no interest such as the subject's sex (males vs. females) and stimulus material ('Bob the builder' vs. 'Wendy') we performed a multivariate $2 \times 2 \times 2$ ANOVA (*group* × *sex* × *stimulus material*) using RT and AC as dependent variables.

To estimate the main effect of *group* on response inhibition, we calculated 2×2 ANOVA models using *group* (children vs. adults) and *condition* (no-go vs. go) as independent factors and RT as well as AC as dependent variables. We applied Bonferroni correction for multiple comparisons to our significance levels and regarded effects with $p < .05$ as significant. Age regression analyses were performed within the children group only, using behavioral parameters AC and RT as dependent variables.

2.5.2. Task-induced brain activation and functional connectivity

To analyze differences in brain activation between children and adults we applied a repeated measures ANOVA model with *group* (children vs. adults) as a between-subject factor and *condition* (go vs. no-go) as within-subject factor. We performed the analysis on NIRS data ([HbO] and [HbR]). The group differences in functional connectivity were analyzed using two sample *t*-tests.

Effects of NIRS signal and partial coherence were considered as significant when passing a threshold of $p < .05$, corrected for multiple testing using the Benjamini Hochberg False Discovery Rate (FDR) for 80 tests [27]. In the case of significant group differences in behavioral performance, significantly differing parameters were used as covariates of no interest in the described ANOVA models.

To address the development of response inhibition from age 4 to 6 years, we conducted multiple regression models using the beta values derived from GLM analysis as well as pCC as dependent variables and age as independent variable in the children group only. As AC and RT turned out to be significantly correlated with age, we used them as further independent variables.

Table 1
Condition-specific behavioral performance (accuracy), $n_{children} = 22$, $n_{adults} = 20$.

		Children [M ± SD]	Adults [M ± SD]	Age × AC [*F*]
Go trials	Hits	95.7 ± 4.2	99.9 ± 0.2	1.3, n.s.
Nogo trials	Correct rejections	94.8 ± 2.6	98.4 ± 1.1	
Go trials	Misses	4.3 ± 4.2	0.1 ± 0.2	
Nogo trials	False alarms	5.2 ± 2.6	1.56 ± 1.1	

Note. n.s.: not significant, AC: accuracy, M: mean, SD: standard deviation.

3. Results

3.1. Behavior

An omnibus $2 \times 2 \times 2$ ANOVA (*age* × *sex* × *stimulus material*) revealed an overall effect for both AC and RT ($F_{AC(2,40)} = 9.8$, $p < .01$; $F_{RT(2,40)} = 11.4$, $p < .01$). Significant differences, however, were only found between *age* groups ($F_{AC(2,40)} = 59.4$, $F_{RT(2,40)} = 77.8$, $p < .01$); neither *sex* groups nor *stimulus material* groups differed significantly. Adults responded faster and more accurately in the task than did children (466 vs. 897 ms, $T = 9.7$, $p < .01$; 98.3% vs. 90.8%, $T = 7.4$, $p < .01$, for detailed behavior information see table 1). Absolute values of variances differed between children and adults, however, Levene's test did not reveal significant differences between variances ($F = 2.4$, n.s.). Children-specific correlation analyses revealed a significant relation between age and task performance in the children's group ($r_{age*AC} = .63$, $p < .05$, $r_{age*RT} = -.61$, $p < .05$).

3.2. Task-induced brain activation in childhood compared to adulthood

When using the [HbR] and [HbO] beta values as dependent variable and controlling for AC and RT, the 2×2 (*group* × *condition*) ANOVAs revealed significant interactions in the channels over the right frontal and right parietal cortices (see also Fig. 2 and Table 2). In the frontal channels ([HbR]: channels 4, 14, 24, and 28; [HbO]: channel 6), *group* by *condition* interaction was defined by significantly differing activation patterns: whereas in adults activation increased during no-go trials compared with go trials (reflected by a decrease in the beta values of [HbR]/increase in [HbO]), in children frontal activation was already high during go trials (in

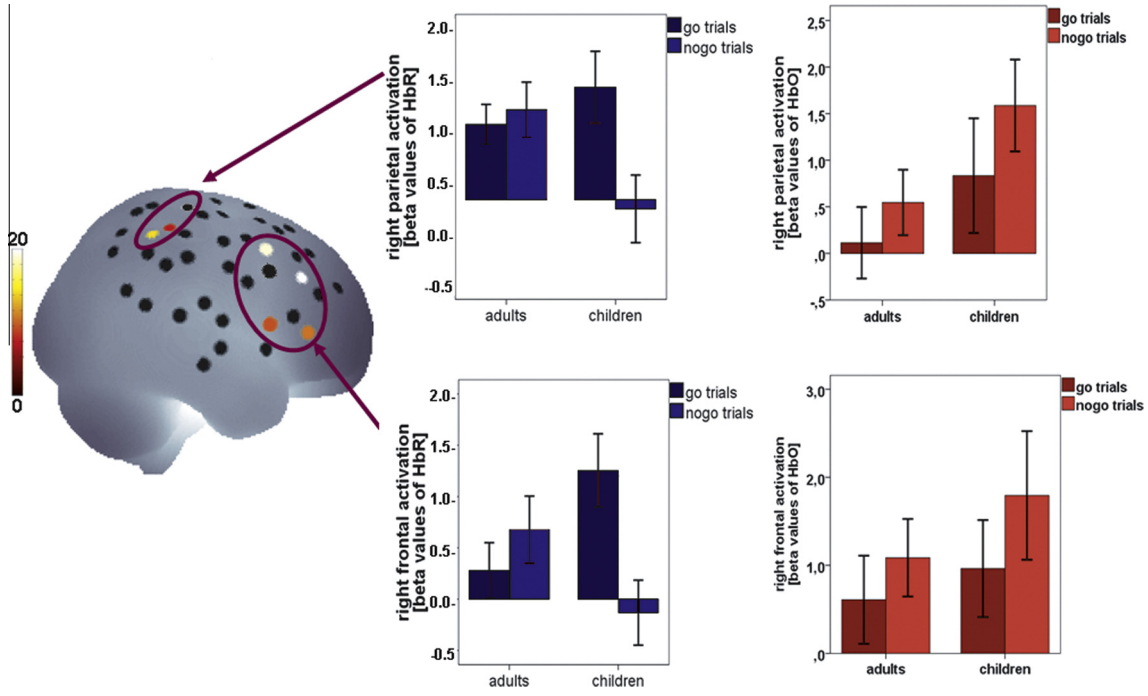

Fig. 2. *Group* × *condition* interaction. *F*-scores of NIRS signal changes are superimposed onto a brain surface. Left bar plots represent group-specific and condition-specific mean beta value of [HbR], right plots of [HbO]. The upper left bar plots is based on the average beta value of the two significant parietal channels of [HbR], and the right plot reflects the significant parietal effect of [HbO]. The lower left bar plot is based the average beta value of the four significant frontal channels, and the right plot reflects the significant parietal effect of [HbO]. Error bars represent ±1 standard error.

Table 2
Significant group × condition interactions in NIRS signal changes, 2 × 2 ANOVA, controlling for ac and rt, $n_{children} = 22$, $n_{adults} = 20$.

Channel	Region	Signal	$Adults_{go}$	$Adults_{nogo}$	$Children_{go}$	$Children_{nogo}$	Stats
Interaction: group × condition							
68	Right parietal	[HbR]	$0.1^{a} \pm 0.5$	$-0.5^{a} \pm 0.6$	$-2.7^{a} \pm 0.5$	$-0.7^{a} \pm 0.7$	$F = 5.6^{a,*}$
68	Right parietal	[HbO]	$0.5^{a} \pm 0.6$	$-0.02^{a} \pm 0.5$	$0.4^{a} \pm 0.7$	$2.3^{a} \pm 0.6$	$F = 5.3^{a,*}$
62	Right parietal	[HbR]	$0.2^{a} \pm 0.5$	$-0.7^{a} \pm 0.6$	$-2.4^{a} \pm 0.5$	$-0.2^{a} \pm 0.6$	$F = 10.1^{a,**}$
28	Right frontal	[HbR]	$0.05^{a} \pm 0.6$	$-0.4^{a} \pm 0.8$	$-1.4^{a} \pm 0.7$	$0.7^{a} \pm 0.9$	$F = 4.6^{a,*}$
24	Right frontal	[HbR]	$0.6^{a} \pm 0.6$	$-0.2^{a} \pm 0.6$	$-2.2^{a} \pm 0.6$	$-0.4^{a} \pm 0.7$	$F = 6.4^{a,*}$
14	Right frontal	[HbR]	$0.8^{a} \pm 0.9$	$0.04^{a} \pm 0.8$	$-2.8^{a} \pm 1.0$	$-0.6^{a} \pm 0.9$	$F = 8.7^{a,*}$
6	Right frontal	[HbO]	$0.8^{a} \pm 0.7$	$0.5^{a} \pm 0.7$	$0.7^{a} \pm 0.7$	$2.4^{a} \pm 0.8$	$F = 4.6^{a,*}$
4	Right frontal	[HbR]	$0.3^{a} \pm 0.7$	$-0.6^{a} \pm 0.6$	$-0.9^{a} \pm 0.8$	$0.3^{a} \pm 0.6$	$F = 4.7^{a,*}$
Condition effect: go > nogo							
41	Left motor	[HbO]	$0.8^{a} \pm 0.6$	$0.4^{a} \pm 0.7$	$2.7^{a} \pm 0.8$	$-0.5^{a} \pm 0.6$	$F = 14.2^{a,**}$
41	Left motor	[HbR]	$-0.5^{a} \pm 0.5$	$0.2^{a} \pm 0.4$	$-2.7^{a} \pm 0.8$	$1.0^{a} \pm 0.6$	$F = 11.9^{a,**}$
39	Left motor	[HbO]	$0.3^{a} \pm 0.6$	$-0.1^{a} \pm 0.6$	$1.8^{a} \pm 0.7$	$-0.7^{a} \pm 0.7$	$F = 9.0^{a,**}$
39	Left motor	[HbR]	$-0.3^{a} \pm 0.5$	$-0.3^{a} \pm 0.4$	$-1.0^{a} \pm 0.5$	$-0.3^{a} \pm 0.5$	$F = 5.6^{a,*}$
37	Left motor	[HbO]	$0.8^{a} \pm 0.5$	$0.8^{a} \pm 0.6$	$0.9^{a} \pm 0.6$	$-0.7^{a} \pm 0.7$	$F = 4.6^{a,*}$
33	Left motor	[HbO]	$0.6^{a} \pm 0.6$	$0.3^{a} \pm 0.6$	$2.0^{a} \pm 0.7$	$-0.1^{a} \pm 0.7$	$F = 5.3^{a,*}$
31	Left motor	[HbO]	$0.5^{a} \pm 0.5$	$0.1^{a} \pm 0.5$	$2.0^{a} \pm 0.5$	$-0.6^{a} \pm 0.6$	$F = 9.5^{a,**}$
25	Left motor	[HbR]	$-0.9^{a} \pm 0.4$	$-0.3^{a} \pm 0.5$	$-1.4^{a} \pm 0.6$	$-0.6^{a} \pm 0.5$	$F = 7.9^{a,*}$
23	Left motor	[HbO]	$0.6^{a} \pm 0.5$	$0.6^{a} \pm 0.6$	$1.3^{a} \pm 0.6$	$-0.5^{a} \pm 0.6$	$F = 6.4^{a,*}$

** $p < .05$, Corrected for 80 comparisons.
* $p < .05$, Uncorrected for multiple comparisons, HbO: oxygenated hemoglobin; HbR: deoxygenated hemoglobin.
[a] Covariates: ac = 94.1, rt = 665.3.

both signals [HbR] and [HbO]). In return, during nogo trials immature activation manifested itself in a strong increase in [HbO] and decrease in [HbR]. We observed the same qualitative behavior in the parietal areas (HbR, HbO: channels 62 and 68): whereas activation increased in [HbO] and [HbR] in adults group in

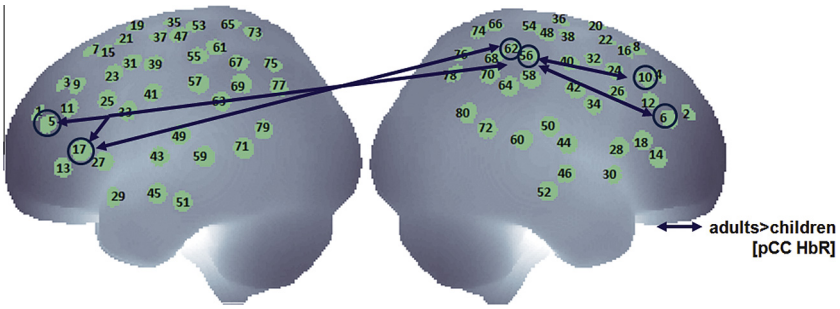

Fig. 3. Sketch of the significant effects in network coherence (*adults* > *children*). Blue arrows mark significantly stronger coherence in adults compared to children, found in the [HbR] signal. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

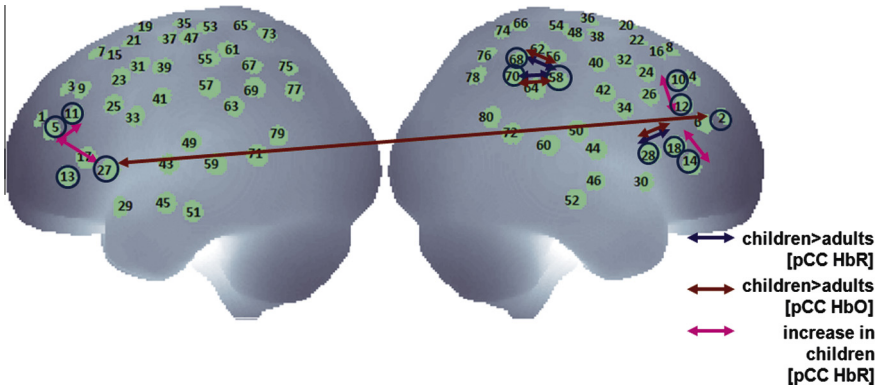

Fig. 4. Sketch of the significant effects in network coherence (*children* > *adults*, $n = 42$). Blue arrows mark significantly stronger coherence in children compared to adults found in the [HbR] signal, red arrows reflect effects in [HbO] signal. Pink arrows mark the increasing coherence with age (*children only*, $n = 22$). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 3
Significant group differences in partial coherence coefficients, two sample *t*-test, $p < .05$, corrected for multiple comparisons.

Signal	Channel 1	Channel 2	f[Hz]	Children	Adults	*T*
Adults > *children*						
[HbR]	5 (Left frontal)	56 (Right parietal)	.08–.12	0.1 ± 0.1	0.3 ± 0.1	3.8*
[HbR]	6 (Right frontal)	56 (Right parietal)	.03–.08	0.1 ± 0.1	0.4 ± 0.1	4.1*
[HbR]	10 (Right frontal)	56 (Right parietal)	.08–.12	0.1 ± 0.1	0.3 ± 0.2	3.8*
[HbR]	17 (Left frontal)	56 (Right parietal)	.08–.12	0.1 ± 0.1	0.3 ± 0.1	3.9*
[HbR]	17 (Left frontal)	62 (Right parietal)	.08–.12	0.04 ± 0.03	0.2 ± 0.1	4.1*
Children > *adults*						
[HbR]	56 (Right parietal)	62 (Right parietal)	03–.08	0.6 ± 0.3	0.1 ± 0.1	5.5*
[HbO]	56 (Right parietal)	62 (Right parietal)	.03–.08	0.4 ± 0.2	0.2 ± 0.1	3.6*
[HbO]	56 (Right parietal)	62 (Right parietal)	.08–.12	0.5 ± 0.2	0.2 ± 0.0	4.3*
[HbR]	56 (Right parietal)	68 (Right parietal)	03–.08	0.3 ± 0.1	0.1 ± 0.1	3.7*
[HbO]	56 (Right parietal)	68 (Right parietal)	.08–.12	0.2 ± 0.1	0.1 ± 0.0	3.7*
[HbR]	18 (Right frontal)	28 (Right frontal)	.08–.12	0.3 ± 0.1	0.1 ± 0.1	3.6*
[HbO]	6 (Right frontal)	13 (Left frontal)	.03–.08	0.1 ± 0.0	0.1 ± 0.0	2.6*

Note. *F*: frequency, measured in Hertz; Hz: Hertz; HbO: oxygenated hemoglobin; HbR: deoxygenated hemoglobin.
* $p < .05$, Uncorrected for multiple comparisons.

nogo trials compared to go trials, children's response during nogo trials was extreme and differed between signals. Considering the absolute beta magnitudes, we found comparable activation magnitudes for the go trials in children and the no-go trials in the adult group.

Table 4
Significant effects of age on functional connectivity [pCC], revealed via multiple regressions with independent regressors age, reaction time and accuracy.

Signal	Channel	f[Hz]	Age	AC	RT
[HbR]	5–11	<.03	$\beta_{adults} = -0.5 \pm 0.1$, n.s. $\beta_{kids} = -0.7 \pm 0.1$, $p < .05$	$\beta_{adults} = -0.4 \pm 0.0$, n.s. $\beta_{kids} = -0.5 \pm 0.0$, n.s.	$\beta_{adults} = -0.4 \pm 0.0$, n.s. $\beta_{kids} = -0.2 \pm 0.0$, n.s.
[HbR]	5–27	<.03	$\beta_{adults} = -0.6 \pm 0.0$, n.s. $\beta_{kids} = -0.8 \pm 0.1$, $p < .05$	$\beta_{adults} = -0.4 \pm 0.0$, n.s. $\beta_{kids} = -0.4 \pm 0.0$, n.s.	$\beta_{adults} = -0.6 \pm 0.0$, n.s. $\beta_{kids} = -0.2 \pm 0.0$, n.s.
[HbR]	10–12	<.03	$\beta_{adults} = -0.5 \pm 0.0$, n.s. $\beta_{kids} = 0.9 \pm 0.0$, $p < .05$	$\beta_{adults} = -0.5 \pm 0.1$, n.s. $\beta_{kids} = -0.3 \pm 0.0$, n.s.	$\beta_{adults} = -0.5 \pm 0.0$, n.s. $\beta_{kids} = -0.4 \pm 0.0$, n.s.
[HbR]	14–18	<.03	$\beta_{adults} = -0.7 \pm 0.0$, n.s. $\beta_{kids} = 0.8 \pm 0.1$, $p < .005$	$\beta_{adults} = -0.7 \pm 0.0$, n.s. $\beta_{kids} = -0.1 \pm 0.0$, n.s.	$\beta_{adults} = -0.0 \pm 0.0$, n.s. $\beta_{kids} = -0.1 \pm 0.0$, n.s.

Note. AC = accuracy, RT = reaction times, pCC = partial coherence coefficient, *F*: frequency, measured in Hertz; Hz: Hertz, n.s.: not significant; HbO: oxygenated hemoglobin; HbR: deoxygenated hemoglobin.

In addition to the interaction effect, we found a significant change in the NIRS signals in the left motor areas when testing the for the condition effect (go > no-go) (see also Table 2), which reflected the motor response with the right hand.

Our partial coherence analysis revealed stronger (short-range) coherence in children compared to adults within the right frontal cortex ([HbR]: 18–28), within the right parietal lobe ([HbO] and [HbR]: 56–62, 56–68) as well as between right and left frontal areas ([HbO]: 6–13). In contrast, adults showed stronger (long-range) coherence between bilateral frontal and parietal areas ([HbR]: 5–56, 6–56, 10–56, 17–56, 17–62) compared to children (see also Figs. 3 and 4 and Table 3).

3.3. Development from age 4 to 6 years

Due to significant correlation between age and both behavioral parameters (RT and AC) we performed multiple regression analyses to reveal developmental effects on brain parameters. Out of 80 channels, only one significant effect of task-induced brain activation with age was found: in the channel 30, located in the right frontal lobe, age correlated significantly with the beta values, revealed by the GLM analysis, of [HbR] ($r = -.82$, $p < .05$). Similarly, age correlated significantly with coherence in two channels within the left frontal and two within the right frontal lobe. The regressors RT and AC did not reach the significance level in any analysis (see Fig. 4 and Table 4).

4. Discussion

In this study, we examined response inhibition in children aged 4 to 6 years in comparison to adults. We analyzed inhibition skills on three different levels; (i) behavioral performance through RT and AC, (ii) task-induced brain activation (NIRS signals of the deoxygenated [HbR] and oxygenated [HbO] hemoglobin concentration changes), and (iii) functional connectivity using partial coherence. In addition to group comparisons, we performed regression analyses to look for developmental processes within the age range from 4 to 6 years.

In line with developmental studies, children showed immature performance in response inhibition in that they responded slower and committed more errors than adults. However, accuracy was about 90% even in the children's group, indicating that they were able to perform the task. Likewise, performance improved linearly with maturation, supporting the findings of a significant improvement of inhibition skills during early childhood.

In task-induced brain activation patterns during the go condition, we found a left-lateralized central activation across both groups, reflecting the motor activation during the go trials. We did not find any significant group difference in the go condition, supporting the behavioral finding of the children being capable of executing the go trials. During the inhibition condition, however, significant group differences were detected. In line with previous imaging studies, adults showed a strong increase in task-induced fronto–parietal activation during the *no-go* condition compared to the *go* condition. In contrast, the immature activation pattern in children was characterized by high frontal activation during go trials in combination with a high increase of [HbO] and decrease in [HbR] during no-go trials. This immature response pattern fits well into the discussion of which cognitive processes are involved in a go no-go task and what improvements are made during development. For example, Cragg and Nation studied response inhibition in a group of young children (5–7 years) and older children (9–11 years). They suggested that the higher AC during the no-go trials of 9 to 11-year-olds might be more likely due to a higher inhibition speed than a weaker motor preparation and initiation. This means that older children were faster to inhibit the motor response and therefore did not complete the motor action whereas motor preparation also took place in older children [28]. Thus, they differentiated between partial inhibition (response initiation) and successful inhibition (no response initiation) and found that in 5

to 7-year-olds only one third of correct inhibition trials were a complete successful inhibition, whereas in the remaining no-go trials a go response was at least initiated [28]. This mechanism might have played a role in our group of children, too. Immature fronto–parietal activation pattern in response to no-go trials in our children sample might reflect a delayed inhibition initiation at the onset of the presentation of the no-go target. Instead, they might have initiated a motor response, which they were able to stop before conducting the motor response as seen in behavioral data. Unfortunately, we did not use a paradigm differentiating between partial and successful inhibition, and therefore can only speculate. However, the brain responses seem to indicate similar processes in our study. The higher frontal activation during the go trials in contrast to adults might reflect higher working memory demand for the children, keeping online on which stimuli they had to react and on which they did not. In the context of the introduced behavioral discussion about the difference between theoretical understanding of a go/nogo task and the actual behavioral performance [1,3–5], our results suggest immature inhibition skills rather than impaired rule reflection: although we measured signal changes of nearly the whole cortex, we found significant developmental differences only within a fronto–parietal network, commonly associated with executive attention and response inhibition. Following the idea of immature rule reflection one might have expected differences in areas such as medial frontal and cingulate regions [e.g. 29].

In functional connectivity patterns, we found stronger partial coherence in short range functional connectivity in the right frontal and right parietal cortex in children compared to adults, combined with significantly weaker long range functional connectivity between right frontal and right parietal regions as well as left frontal and right parietal structures. Weaker fronto–parietal functional connectivity in long range connections in children agree well with Fair et al. [10]. With regard to their findings of frontal maturation (abundance of short range functional connectivity in childhood, differentiation during adolescence) our results might point towards a developmental pattern in the parietal lobe, which is similar to the frontal pattern: We found interparietal (short-range) functional connectivity that was significantly stronger in children compared to adults. Thus, this pattern might be valid not only for the frontal lobe but also for other cortical lobes.

However, in contrast to their findings we did not observe a strong interhemispheric functional connectivity between right and left frontal areas (only one channel in [HbO] signal). One reason for the weak interhemispheric coherence might be the still immature corpus callosum in our subjects. A relation between the splenium size and performance in response inhibition at the age of 4 years has been shown by Stewart and colleagues, reporting that a smaller splenium size was associated with a higher number of errors [30]. From morphometrical studies we know that the corpus callosum is still developing in the age range from 4 to 6 years of age [31]. Although the relation between functional and structural connectivity remains unclear, it seems not unreasonable to assume that the immaturity of the corpus callosum may have an influence on the connectivity pattern.

Referring to the discussion about ‘understanding the rules of the task’ versus ‘being able to perform it correctly’ as mentioned before, the weaker connectivity between cerebral regions might contribute to the inability to perform the task like an adult.

In addition to group differences in partial coherence, we found developmental changes in connectivity between the ages 4 and 6 years. It seemed as if connectivity within the right frontal lobe increased during that time of age, whereas connectivity in the left frontal lobe decreased. These regions of increasing and decreasing partial coherence seem to be similarly located within the frontal lobes to regions of immature brain activation: diffuse, bilateral frontal activation in young children in contrast to a right lateralized fronto–parietal network in the matured brain [7]. Furthermore, changes in connectivity might be rather intrinsically triggered than performance dependent maturation of functional connectivity, as multiple regression showed a significant influence on partial coherence only for age, not for AC or RT. However, based on our data, these interpretations remain somewhat speculative, but are highly interesting for further studies.

As a final note, our results were mostly based on changes in [HbR] and not in [HbO]. Although some articles suggest a higher effect of the hemodynamic response in [HbO], we believe the [HbR] signal to be the more sensitive parameter. Our rational for this is the fact that [HbO], although generally showing higher magnitudes than [HbR], is much more prone to contamination through physiological noise and global effect such caused by the heartbeat, breathing, and systemic blood pressure changes [11,12] Also, a recent combined fMRI-NIRS study with further evaluation of extra-cerebral signals has demonstrated that only oxygenated hemoglobin is significantly influenced by extra-cerebral artifacts [32].

To our knowledge, this study is one of the first brain activation and network coherence reports in early childhood. It revealed neuroplastic changes within a fronto–parietal network, which might deliver further information in the discussion of the development of response inhibition. Due to methodological restraints of the NIRS methodology, however, we could probe only the upper layer of the cortices and therefore were not able to provide the fine spatial resolution or depth

discrimination provided by MRI. Especially the lack of information about subcortical activation is a notable disadvantage because children are known to activate subcortical structures stronger. On the other side, numerous studies showed that NIRS is an adequate methodology to measure functional brain development, as (i) movement artifacts are more tolerable (although still accompanied with the loss of data) compared to e.g. fMRI, and (ii) NIRS is a silent and relatively undemanding method that enables the measurement of children's brain responses in relatively natural surroundings, thus increasing the participant's comfort and compliance as well as ecological validity.

5. Conclusion

In this study we applied the relatively new and promising method of NIRS to the field of neuroimaging of brain development. Beside the methodological constraints and the high data loss in the children's group, we might conclude that we were able to report new findings with regard to the developmental processes of response inhibition in this study based on (i) the multilevel approach (behavioral performance, brain activation, functional connectivity) and (ii) the study of an (at least for imaging studies) early phase of cognitive development.

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