Development of attentional networks: An fMRI study with children and adults

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Data on the development of the attentional systems remain scarce. We used structural and event-related functional magnetic resonance imaging to investigate differences in the neural mechanisms associated with alerting, reorienting, and executive control of attention between children (ages 8 to 12 years) and adults, while controlling for effects of performance and brain morphology. Behaviorally, children exhibited a numerically smaller alerting effect and significantly larger invalidity (reorienting) and interference (executive control of attention) effects. Neurally, children showed significantly reduced brain activation in a priori defined regions-of-interest in right-sided frontal–midbrain regions during alerting, in the right-sided temporo-parietal junction during reorienting of attention, and in the dorsolateral prefrontal cortex during executive control of attention. In addition, children activated significantly more brain regions outside the a priori defined regions-of-interest, such as the superior frontal gyrus during reorienting and the superior temporal gyrus during executive control of attention. Functional group differences overlapped with structural group differences in gray matter volume in particular within the frontopolar areas. The data suggest that there is a transition from functional yet immature systems supporting attentional functions in children to the more definitive adult networks and that the differences observed may reflect both developmental changes in cognitive strategies and morphology.
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Introduction

One fundamental objective in basic and clinical neuroscience is to understand the development of the functional organization of the human brain. Such knowledge cannot only inform us about its normal anatomical and functional development but may also help us to understand the consequences of early perturbations to the developing brain or aberrant organizations thereof which are assumed to underlie developmental disorders (Casey, 2000; Schlaggar et al., 2002). Attention plays a critical role in the normal human cognitive, emotional, and social development (Johnson, 2000). Attentional deficits occur in a number of common childhood psychiatric diseases, such as Attention Deficit Hyperactivity Disorder (ADHD), autism, or childhood depression. Developmental studies suggest that some mechanisms of attention are present from early infancy; however, they also provide evidence of a differential development of particular attentional functions (Rueda et al., 2004).

Neural basis of attentional networks

Posner and Petersen (1990) developed an influential model of attentional functions, in which differential neural networks and neuromodulators are assumed to subserve different attentional functions. In this model, alerting is defined as achieving and maintaining an alert state. Orienting and reorienting are required when stimuli occur outside the current focus of attention. Finally, executive control is defined as resolving conflict among responses. While the alerting system has been associated with frontal and parietal regions of the right hemisphere modulated by norepinephrine (Witte and Marrocco, 1997), orienting and reorienting of attention are thought to be mediated by a network which is lateralized to the right temporo-parietal junction and the right inferior frontal gyrus (Corbetta et al., 2000) and which is assumed to be modulated by the cholinergic system (Thiel et al., 2005). The executive attentional control network is supposed to involve the anterior cingulate and lateral prefrontal cortex and to be modulated by dopamine (Marrocco and Davidson, 1998). Several recent neuroimaging studies have investigated these attentional networks in healthy adult subjects and generally support the view that the neural networks subserving as the sources of alerting, reorienting, and conflict effects are anatomically separable, but also stress that

there is substantial functional overlap (Fan et al., 2005). In addition, there are conflicting results concerning the precise anatomical localization of these attentional systems. For example, for the alerting system, some authors point to a right-sided fronto-parieto-thalamic network (Sturm and Willmes, 2001), while others suggest left lateralized parietal and frontal regions (Coull et al., 2001). For the orienting and reorienting system, Corbetta and Shulman (2002) propose two attentional networks: The orienting network which is involved in visual selection and working memory is suggested to depend on bilateral activity in intraparietal sulcus and the human homologue of frontal eyefields. In contrast, reorienting of attention to salient events is achieved by a another network, which is strongly lateralized to the right temporo-parietal junction and inferior frontal gyrus. For the conflict system, previous work with the flanker task show primarily cingulate activity, in addition to prefrontal cortex activation (e.g., Botvinick et al., 2001; Fan et al., 2003; Ullsperger and von Cramon, 2004).

Thus, it can be summarized that the dorsolateral prefrontal cortex and the cingulate gyrus might be involved in either alerting or conflict resolution, while the inferior frontal gyrus and the parietal cortex might be associated with both alerting and reorienting of attention.

Development of attentional networks

Behaviorally, developmental studies of the alertness system suggest that although children and adults encode target relevant information at equivalent rates, children make less use of the warning aspect of the cue (Smothergill and Kraut, 1989). For the orienting system, it has been found that the ability of shifting attention to exogenous cues differs little between children and adults, while the ability to disengage, the speed of shifting attention voluntarily, and the accuracy of its termination seem to improve with age (Brodeur and Enns, 1997; Trick and Enns, 1998). With regard to higher-level forms of attention such as the resolution of conflict among competing stimulus elements, i.e., executive control, the majority of developmental studies has stressed a relative lack of executive control in infants until the age of 12 years (see Ruff and Rothbart, 1996, for a review).

On the neural level, to date, nearly all developmental fMRI studies (i.e., studies that compared children with adults) have focused on aspects of executive control and found evidence for a higher susceptibility to interference in children that was paralleled by maturational differences in underlying frontostriatal circuitry (Bunge et al., 2002; Durston et al., 2002, Casey et al., 2002). Recently, Booth et al. (2003) compared the neural development of selective attention and response inhibition and observed only small developmental changes for the selective attention tasks but large developmental differences in the response inhibition task indicating differential effects for attentional processes in children aged 9 to 12 years. However, no developmental fMRI study has yet investigated all three attentional systems (alerting, orienting/reorienting, and executive control).

Current study

Accordingly, we designed a functional imaging experiment that specifically aimed at investigating developmental differences in the neural mechanisms underlying alertness, reorienting, and executive control in children aged 8 to 12 years relative to adults. This age range was chosen since it has previously been shown that the attentional functions under investigation develop till the end of puberty (Carver et al., 2001; Bedard et al., 2002). Based on previous data, we hypothesized that, behaviorally and neurally, the largest developmental differences between children and adults would occur in the executive control system but that due to the functional overlap between these networks also the alerting and reorienting systems would be affected. More specifically, we assumed that healthy adult subjects would recruit specific and separable neural networks for alerting, reorienting, and executive control of attention. In contrast, for children, we predicted less focal recruitment of the circuitries involved, in particular with regard to fronto-striatal (Giedd, 1999; Casey et al., 2002) and fronto-parietal (Sowell et al., 2002) networks. To test these hypotheses, we measured changes in neural activity in healthy children and healthy adults using event-related fMRI while subjects performed a modified version of the Attention Network Task (ANT; Fan et al., 2002) which measures alerting, orienting, and executive attention.

Since developmental studies of brain morphometry indicate long-lasting maturation processes during childhood and adolescence (Giedd, 1999; Sowell et al., 2002, 2004), in particular within the fronto-parietal networks and the cerebellum, we also obtained anatomical MR images on all subjects, allowing for the assessment of possible structural differences between the two groups, using voxel-based morphometry (VBM) (Ashburner and Friston, 2000).

Materials and methods

Subjects

16 right-handed male volunteers (age range: 20–34 years, mean: 26.6 years) and 16 right-handed boys (age range: 8–12 years, mean: 10.1 years) with no history of neurological or psychiatric disease were included in the study. Mean IQ in the children's group was 105 (range: 97 to 133), measured by the WISC-III (Wechsler, 1991). In addition, exclusion criteria were controlled by a standardized semi-structured interview for the diagnosis of mental disorders (K-SADS) in the children's group, in particular to ensure that no child with Attention Deficit Hyperactivity Disorder was included. The study was approved by the Medical Ethics Committee of the University Hospital of Aachen, and all volunteers and all the boys' parents gave informed consent.

Task

Stimuli and experimental paradigm

We used a modified version of the Attention Network Task (ANT), originally developed by Fan et al. (2002). The ANT is a combination of the cued reaction time task (Posner and Petersen, 1990) and the flanker task (Eriksen and Eriksen, 1974). The ANT requires the participant to determine whether the middle arrow of 5 vertically arranged arrows points left or right. The efficiency of the different attentional networks is assessed by measuring how response times are influenced by alerting cues, spatial valid and invalid cues, and congruent or incongruent flankers.

In order to make the task more comparable with other cueing paradigms and to include a condition that requires attentional reorienting, we modified the task by having the targets appear peripherally (instead of centrally) and by including invalid cues in 20% of all spatially cued trials.

Participants were asked to determine whether the middle arrow (i.e., the target) of five vertically arranged arrows points left or right. The efficiency of the different attentional networks is assessed behaviorally by measuring how reaction times (RTs) are influenced by non-spatial warning cues (double cue), spatial valid and invalid cues, and congruent versus incongruent flankers.

A set of cognitive subtractions is then used to deduct behaviorally the efficiency of the three different attentional networks postulated (Posner and Petersen, 1990): the alerting effect is calculated by subtracting the mean RT of the double cue trials from the mean RT of the no cue trials (i.e., no spatial information is provided in both trial types). The invalidity (reorienting) effect is assessed by calculating the mean RT of validly cued trials from the mean RT of invalidly cued trials. The conflict effect (executive control) is obtained by subtracting the mean RT of all congruent flanker trials, summed across cue types, from the mean RT of incongruent flanker trials. The time course of the different trial types is pictured in Fig. 1.

Stimuli were projected onto a screen in front of the participant in the MRI scanner. Responses in the scanner were collected via two button presses with the right hand using a keyboard which rested in the subject's lap. Viewing distance was approximately 29 cm. Each stimulus consisted of a vertical row of five black visually presented arrows, pointing to the left or to the right, against a white background. The target was the middle arrow which was flanked by two arrows above and two arrows below pointing in the same direction (congruent condition) or in the opposite direction (incongruent condition). The stimuli (one central arrow plus four flankers) consisted of a total visual angle of 4.34° vertically and 14.5° horizontally. Each participant was required to indicate the direction of the middle arrow by pressing the left key for the target pointing to the left direction or the other key for the target pointing to the right direction. Each trial consisted of five events. First, there was a 400-ms fixation period. Then, a warning cue was presented for 150 ms. This was either a non-spatially informative double cue, a spatial cue (either valid or invalid), or alternatively, no cue was presented. Then, there was another 400-ms fixation period after the cue and then the target and flankers appeared simultaneously. The target and flankers were presented for 1550 ms. Trials were presented every 2500 ms. In total, 96 trials included congruent targets and 96 trials included incongruent targets. Additionally, in 24% of all trials, blank trials were included (Josephs and Henson, 1999), leading effectively to variable SOAs, which also helped to avoid an "attention to time" effect. The order of trial types was randomized. Subjects were instructed to maintain fixation throughout the experiment and to covertly detect the peripheral target as fast as possible. Prior to scanning, subjects were informed about the different trial types. They were told that spatial cues were highly informative and encouraged to use these cues to improve performance. A 5-min training session was performed before scanning.

Since a systematical assessment of eye movements in the scanner would have taken too long for children, a decision was made against an eyetracking procedure to ensure good compliance and hence little overall head movements in the MR scanner. However, prior to scanning, all subjects were trained to maintain fixation throughout all trials.

Data acquisition

For each subject, 218 functional whole-brain images were acquired, with a Siemens Sonata scanner (1.5 T) and echo planar
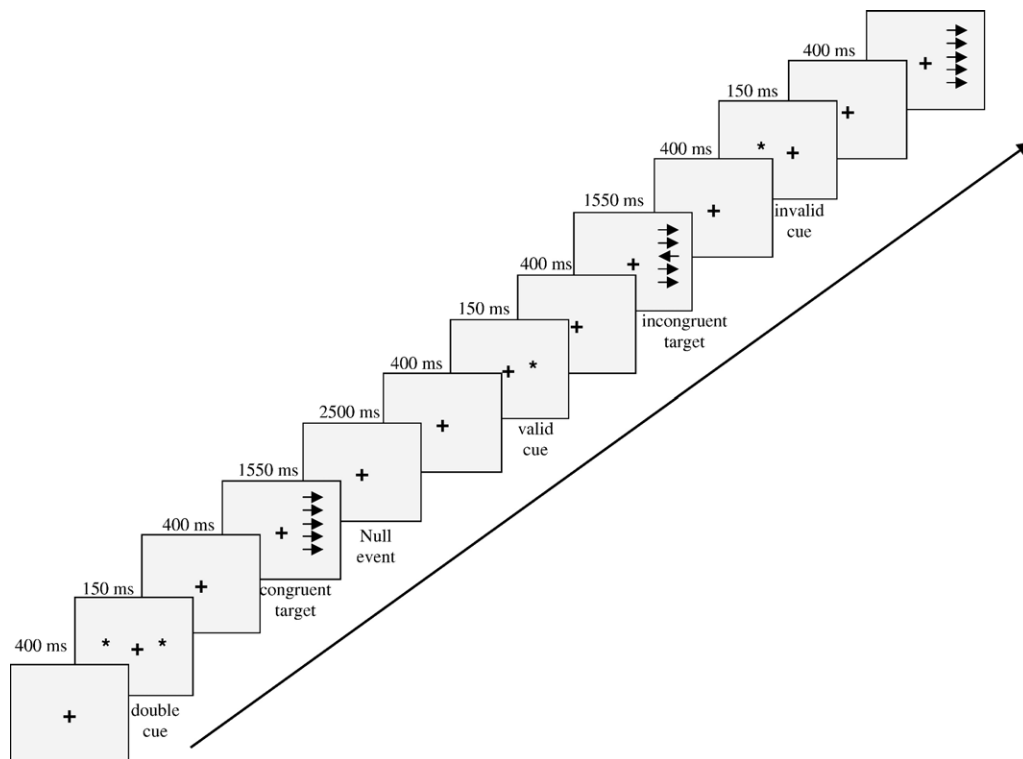

Fig. 1. Experimental paradigm: Modified version of the Attention Network Task (Fan et al., 2002). This figure illustrates the time course of the four different cue and the two target conditions.

imaging (EPI) with the following parameters: TR (repetition time) = 3020 ms, TE (echo time) = 66 ms, thirty 4-mm-thick axial slices with a 0.4-mm gap, matrix size = 64 × 64, voxel size = 3.125 × 3.125 × 4.0 mm³, field of view (FOV) = 200 mm, flip angle = 90°. The first 5 volumes were discarded to allow for T1 equilibration effects. Images were spatially realigned to the sixth volume to correct for interscan movement, synchronized to the middle slice to correct for differences in slice acquisition time, and normalized to a standard EPI template volume (resampled to 3 × 3 × 3 mm³ voxel). The data were then smoothed with a Gaussian kernel of 10 mm full-width-half-maximum to accommodate intersubject anatomical variability.

Structural images were acquired using an isotrop T1-weighted MP-Rage (magnetization-prepared rapid acquisition gradient echo) sequence with the following parameters: TR = 2200 ms, TE = 3.93 ms, flip angle = 15°; FOV = 256 mm; matrix = 180 × 256; 160 slices, slice thickness 1 mm, inter-slice gap = 0.5 mm.

Data analyses

Data were analyzed with Statistical Parametric Mapping software (SPM2, Wellcome Department of Imaging Neuroscience, London; Friston et al., 1995) employing a random-effects model. At the first level, 9 event types were defined. These consisted of eight effects of interest (double cue congruent/incongruent targets, no cue congruent/incongruent targets, valid cue congruent/incongruent targets, invalid cue congruent/incongruent targets) and one effect of no interest (missed responses/errors). Errors were excluded since it has been demonstrated previously that even a small number of errors might alter activation maps (Murphy and Garavan, 2004). The event types were time-locked to the onset of the cue by a canonical synthetic hemodynamic response function (HRF) and its first-order temporal derivative. The 6 head movement parameters were included as confounds. Estimated motion parameters were examined on a subject-by-subject basis to ensure that the amount of absolute motion did not exceed 3 mm. All subjects exhibited less than 1 mm of absolute motion over the course of the experiment. Both groups did not differ in terms of estimated motion parameters [average movement in adults = 0.20 mm, in children = 0.21 mm; $t(31) = 0.02$, n.s.].

Data were globally scaled to 100 across scans and highpass-filtered at 1/60 Hz. The parameter estimates for the canonical HRF and linear contrasts of these estimates comprised the data for the second stage of analyses. At the second stage, three planned t tests were conducted to identify neuronal correlates of (i) alerting [double−no cue trials], (ii) reorienting of attention [invalid−valid cue trials], and (iii) conflict [incongruent−congruent trials]. Two-sample t tests were performed on contrast images to investigate group differences in activation between children and adults.

Region-of-interest (ROI)-based analyses were performed for each of the three contrasts. Appropriate a priori hypotheses derived from previous work allowed limitation of the search volume in the dorsolateral prefrontal cortex, brainstem, thalamus, and extrastriate cortex for the alerting system (Coull et al., 2001; Sturm and Willmes, 2001; Thiel et al., 2004); the frontal eyefields, right-sided inferior frontal gyrus, temporo-parietal junction, and parietal cortex for reorienting (Corbetta and Shulman, 2002; Downar et al., 2002); and the lateral prefrontal cortex and the anterior cingulate for the executive control system

(Botvinick et al., 2001; Fan et al., 2003). The small volume was a sphere with a diameter of 20 mm centered on the positions defined by the respective a priori hypotheses. In addition, exploratory whole-brain analyses were performed in order to assess the data for less focal activations in particular within the children's group. Activations are reported either for ROI-based analyses at a level of significance set at $P_{svc} < 0.05$ (svc = small volume corrected) and a cluster threshold of greater than 5 voxels or for whole-brain analyses at $P < 0.1$ corrected for multiple comparisons on cluster level.

The local maxima were anatomically localized by reference to a standard stereotactic atlas (Talairach and Tournoux, 1988). For validation of this method of localization, SPM$_{\{z\}}$ statistics were superimposed on the averaged group T1 image which was calculated following stereotactic transformation of each individual's 3D MRI image into the same standard stereotactic space of the Montreal Neurological Institute average brain (Friston et al., 1995) employed as a template by SPM2.

Volumetric analyses

For volumetric analyses, the recently suggested optimized protocol for voxel-based morphometric (VBM) studies as implemented in SPM2 (Ashburner and Friston, 2000, 2001; Good et al., 2001a,b; Specht et al., 2003; Wilke et al., 2001) was applied. This protocol aims at minimizing the contribution of non-brain and non-gray-matter tissue to spatial normalization and segmentation and allows for the investigation of true gray-matter volume. The processing protocol contains, first, a segmentation of the original T1 image into gray-matter, white-matter, and cerebrospinal fluid (CSF) probability maps. This procedure includes also a bias correction, correcting the image inhomogeneities to increase the contrast between the gray-matter and white-matter voxel-value distribution, to improve the quality of the segmentation. Further, all non-brain voxels are removed by rendering the lateral surface of the brain. Only the gray-matter probability maps were normalized into the standard reference space by the use of a standardized gray-matter template. The therefore obtained transformation matrix was applied to the original T1 image to create normalized T1 images, which were segmented a second time. The resulting gray-matter images were 'modulated' in order to preserve the volume of a particular tissue compartment within each voxel. Modulation is a process in which information from the deformation field generated during spatial normalization is used to render the VBM analysis more comparable to ROI analysis. The modulated images were smoothed with an 8-mm FWHM isotropic Gaussian kernel. The resulting smoothed, modulated, normalized regions contained the average amount of gray matter within a region surrounding a voxel. This enabled the investigation of the absolute volume of gray matter (Ashburner and Friston, 2000; Good et al., 2001a,b).

The statistical comparison between children and adults was performed as second-level analysis by estimating an ANOVA model, which was adjusted for overall global effects by including the individual brain volume as a covariate of no interest. Group differences in gray-matter (GM) volume were calculated for the same ROIs (sphere = 20 mm; $P_{svc} < 0.05$) as entered in the analyses of functional data and complemented by exploratory whole-brain analyses at $P < 0.01$ corrected for multiple comparisons on cluster level and cluster size of at least 100 voxels.

Results

Behavioral data

An exploratory analysis of the behavioral data across both groups showed no difference between left-pointing and right-pointing targets in any condition, so they were combined [$F(4,28) = 0.6$, $P = 0.5$]. In addition, incompatibility effects in terms of a conflict between arrow direction and side of arrow presentation were analyzed separately for congruent and incongruent targets, but no significant differences appeared [congruent: $F(2,30) = 0.8$, $P = 0.5$; incongruent: $F(2,30) = 1.3$, $P = 0.3$].

Overall, adults were significantly faster and tended to be more accurate than children [RT = 664 ms versus 822 ms, $t(30) = 4.7$, $P < 0.001$; Error rate = 3.2% versus 4.5%; $t(30) = 1.4$, $P = 0.17$]. Error rates were generally low in both groups and did not differ significantly between cueing conditions. However, errors tended to occur more often in incongruent flanker trials [1.8% versus 1.4% in adults, 3.1% versus 1.4% in children, $F(1;30) = 3.0$, $P = 0.09$].

RTs for correct trials were submitted to a $2 \times 4 \times 2$ ANOVA with group (children versus adults) as a between-subject factor and cue (double, no, valid, invalid) and target (congruent versus incongruent) as within-subject factors. Reaction times varied as a function of both cue [$F(3,28) = 24$, $P < 0.001$] and target condition [$F(1,30) = 64$, $P < 0.001$], while no cue by target interaction [$F(3,28) = 0.6$, n.s.] and no cue by target by group [$F(3,28) = 0.9$, n.s.] interaction appeared. In addition, a significant group by cue [$F(3,28) = 4.1$, $P = 0.04$] and a significant group by target interaction [$F(1,30) = 4.4$, $P = 0.03$] was found (see Fig. 2).

Planned contrasts revealed that children (relative to adults) showed a numerically smaller alerting effect [29 ± 16 ms versus 51 ± 16 ms; $M \pm$ SEM; $t(30) = 1.7$, $P = 0.12$] and exhibited a significantly larger invalidity [93 ± 18 ms versus 36 ± 19 ms; $t(30) = -2.5$, $P = 0.01$] and interference effect [80 ± 9 ms versus 56 ± 9 ms; $t(30) = -2.8$, $P = 0.01$].

Correlation analyses with age and IQ in the children's group revealed that only the performance of the conflict network was associated with IQ ($r = -0.56$, $P = 0.03$) and a tendency was found for age ($r = -0.4$, $P = 0.08$). Performance of the reorienting system was found to be only age-dependent ($r = -0.55$, $P = 0.03$). No significant correlation coefficients emerged for the alerting system on the behavioral level.
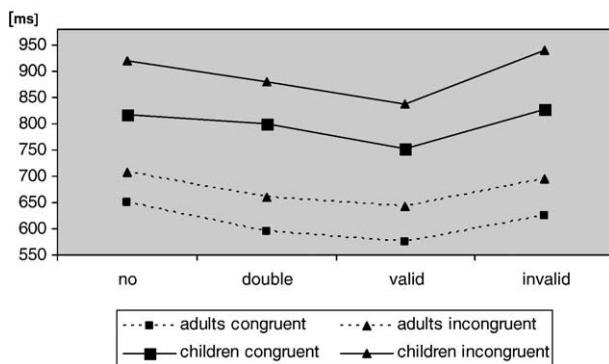

Fig. 2. Behavioral data. Mean reaction times from correct trials as a function of cue and flanker condition, separately for adults (A) and children (B).

Neural mechanisms

In a first step, we identified brain regions that were consistently engaged in children and in adults, respectively, in separate random-effects analyses (see Table 1). Secondly, two-sample t tests were performed on contrast images to assess the significance of any group differences observed in the activation patterns between children and adults (see Table 2 and Figs. 3–5). Third, effects of attentional performance on brain activation were controlled by computing performance-matched subgroups consisting of 8 subjects chosen from each group. This analysis assessed whether differences in brain activation patterns simply reflect performance differences. Because of the large overlap in performance between children and adults, subgroups of 8 matched pairs were chosen for the reorienting and the conflict system, since in both networks significant group differences were found on the behavioral level. Finally, systematic structural group differences might contribute to functional differences (Momenan et al., 2004). Accordingly, a voxel-based morphometric (VBM) analysis was conducted for gray-matter density in order to control for underlying maturational anatomical changes (see Table 3 and Fig. 6).

Alerting

The results of the random-effects analyses separately performed for the children and adults are presented in Table 1.

In adults, neural correlates of alerting, defined as increased activity in double cue trials versus no cue trials, were observed in a priori defined regions-of-interest within the right ventral prefrontal cortex and the left superior parietal gyrus. In addition, a cerebellar activation was found in the posterior lobe.

By contrast, in children, no significant activation was found within the a priori defined regions-of-interest for the alerting system. However, exploratory whole-brain revealed increased neural activity in the right middle occipital cortex extending to the right superior temporal gyrus.

The two-sample t test (adults > children) revealed differential increases in neural activity in the following two ROIs: the midbrain and the right frontal cingulate gyrus (Fig. 3 and Table 2). Fig. 3 also shows the percent MR (BOLD) signal change separately for both groups for the maximally activated voxel as a function of cueing condition (collapsed over congruent and incongruent flanker trials).

The cueing condition differentially modulated neural activity in the cingulate gyrus and in the brainstem in children and adults. Adults exhibited a significantly larger increase in MR signal change in double cue trials in the right frontal cingulate gyrus and in the ponto-mesencephalic junction in the brainstem compared to children. The reverse contrast revealed no significant increases in neural activations for children relative to adults.

Reorienting

Random-effects analyses in adults revealed increased neural activation in the right inferior frontal gyrus, the right temporal–parietal junction and in the superior parietal cortex bilaterally for reorienting of attention (invalidly cued trials > validly cued trials). Whole-brain analyses also revealed increased neural activation in the right insula in adults. In children, neural correlates of reorienting were found in the superior frontal gyrus as well as, bilaterally, in the occipital cortex.

Table 1
Results from the random-effects analyses for the alerting, reorienting, and conflict condition, separately for children and adults

Contrast	Anatomical region	WB/ROI	Side	Talairach coordinates			Volume	Z score
				x	y	z		
Alerting								
Adults	Ventral prefrontal cortex	ROI	R	3	55	−13	16	3.51
	Superior parietal gyrus	ROI	L	−36	−68	45	74	4.16
	Posterior cerebellum	WB	R	30	−65	−19	40	4.32
Children	Middle occipital cortex	WB	R	48	−72	9	12	3.74
	Superior temporal gyrus	WB	R	50	−58	14	18	3.43
Reorienting								
Adults	Inferior frontal gyrus	ROI	R	39	32	−7	21	3.37
	Temporal–parietal junction	ROI	R	59	−40	13	25	3.19
	Superior parietal cortex	ROI	R	36	−43	66	20	3.31
	Superior parietal cortex	ROI	L	−21	−58	58	18	3.25
	Insula	WB	R	48	17	−11	31	3.36
Children	Superior frontal gyrus	ROI	L	−30	30	54	6	3.1
	Occipito-temporal gyrus	WB	R	18	−61	−11	15	3.35
	Occipital gyrus	WB	L	−12	−86	35	18	3.22
Conflict								
Adults	Anterior cingulate gyrus	ROI	R	15	45	12	11	3.4
	Cingulate gyrus	ROI	R	3	−6	33	10	3.6
	Inferior frontal gyrus	ROI	L	−45	12	0	23	3.71
		ROI	R	54	21	9	10	3.18
	Middle frontal gyrus	ROI	L	−30	39	−9	13	3.32
Children	Middle frontal gyrus	ROI	L	−30	39	9	9	3.1
	Superior temporal gyrus	WB	R	50	14	−16	20	4.31
	Occipital gyrus	WB	R	−39	73	4	51	4.07
	Occipital gyrus	WB	L	−15	−96	8	15	3.90

Note. WB = local maxima derived from whole-brain analyses with $P < 0.1$ corrected for multiple comparisons, ROI = local maxima derived from a priori region-of-interest analyses with $P_{svc} < 0.05$, voxel threshold = 5 voxels, R = right, L = left.

The two-sample *t* test (adults > children) showed a small effect of significantly increased activation in the right-sided TPJ (see Fig. 4A) with larger increases in the % signal change during invalid trials in adults. By contrast, children showed significantly increased neural activity (relative to adults) in the posterior aspect of the right-sided putamen extending to the insula and the left superior frontal gyrus (see Figs. 4B,C). The plots of the respective MR signal changes revealed that children showed relatively higher levels of neural activity in the putamen and in the superior frontal gyrus in invalid trials when compared to adults.

Since children showed behaviorally a significantly larger invalidity effect when compared to adults, two-sample *t* tests were

Table 2
Group contrasts between adult and children sample (two-sample *t* tests)

Contrast	Anatomical region	WB/ROI	Side	Talairach coordinates			Volume	Z score
				x	y	z		
Alerting								
Adults > children	Midbrain	ROI	L	−9	−18	−12	29	4.11
	Frontal cingulate gyrus	ROI	R	18	−4	44	27	4.03
Children > adults	No effect							
Reorienting								
Adults > children	Temporo-parietal junction	ROI	R	54	−60	12	9	3.2
Children > adults	Putamen/insula	WB	R	33	−15	−2	27	3.53
	Superior frontal gyrus	WB	L	−30	27	−47	29	3.16
Conflict								
Adults > children	Superior parietal cortex	WB	L	−18	−52	63	34	3.28
	Inferior frontal gyrus	ROI	R	45	38	−4	15	3.15
Children > adults	Superior temporal gyrus	WB	R	53	14	−18	21	3.67
	Superior frontal gyrus	ROI	L	−27	56	17	18	3.37

Note. WB = local maxima derived from whole-brain analyses with $P < 0.1$ corrected for multiple comparisons, ROI = local maxima derived from a priori region-of-interest analyses with $P_{svc} < 0.05$, voxel threshold = 5 voxels, R = right, L = left.
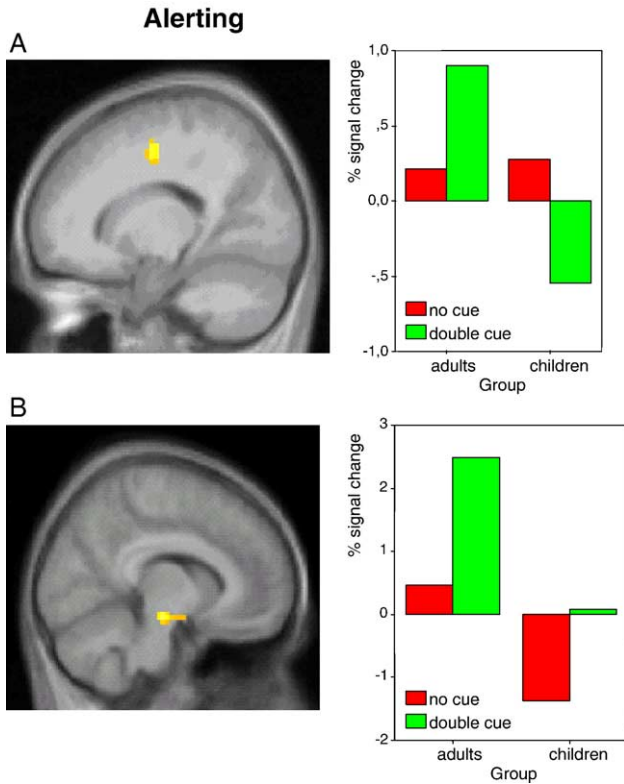
Alerting

significantly larger increase in MR signal in incongruent trials compared to congruent trials, children showed the reverse activation pattern. By contrast, children activated significantly more the right-sided superior temporal gyrus and the left superior frontal gyrus which was due to a significant increase in the MR signal in incongruent trials only in the children's group (see Figs. 5C, D).

Performance-based group comparisons for the conflict system [adults: $M = 59 \pm 16$ ms, children: 61 ± 18, $t(14) = 0.01$, n.s.], did not show any differences between the performance-matched group

Fig. 3. Differential activation of adults and children as identified in a two-sample test for the alerting condition (thresholded at $P_{svc} < 0.05$, extend threshold 5 voxel, shown on averaged group T1 image). (A) Increased activation in the right cingulate gyrus in adults compared to children. (B) Increased brainstem activity in adults compared to children. Plots of the percent BOLD signal change are shown separately for both groups as a function of trial type (pooled over congruent and incongruent targets) for the respective activation maximum.

also calculated with performance-based subgroups in order to account for behavioral differences between adults and children. For the reorienting system [adults: 26 ± 20 ms, children: 28 ± 20 ms, $t(14) = 0.07$, n.s.], this subgroup comparison revealed the same brain activation patterns as reported for the whole groups, the exception being the activation in the putamen in children compared to adults.

Executive control of attention

The conflict condition (incongruent > congruent targets) activated a frontal network including the right-sided anterior cingulate gyrus as well as bilateral inferior frontal gyrus and left-sided middle frontal gyrus in adults.

In children, random-effects analyses revealed a small activation within the left-sided middle frontal gyrus (derived from the ROI analyses). In addition, children activated the right superior temporal gyrus as well as the bilateral occipital cortex during executive control of attention. Two-sample t tests for the executive attentional system revealed increased activation in the left-sided superior posterior parietal cortex and right-sided ventro-lateral prefrontal cortex in adults compared to children (see Figs. 5A, B). Target conditions (i.e., incongruent versus congruent trials) differentially modulated neural activity, resulting in significant group by target interactions for both areas: While adults showed a
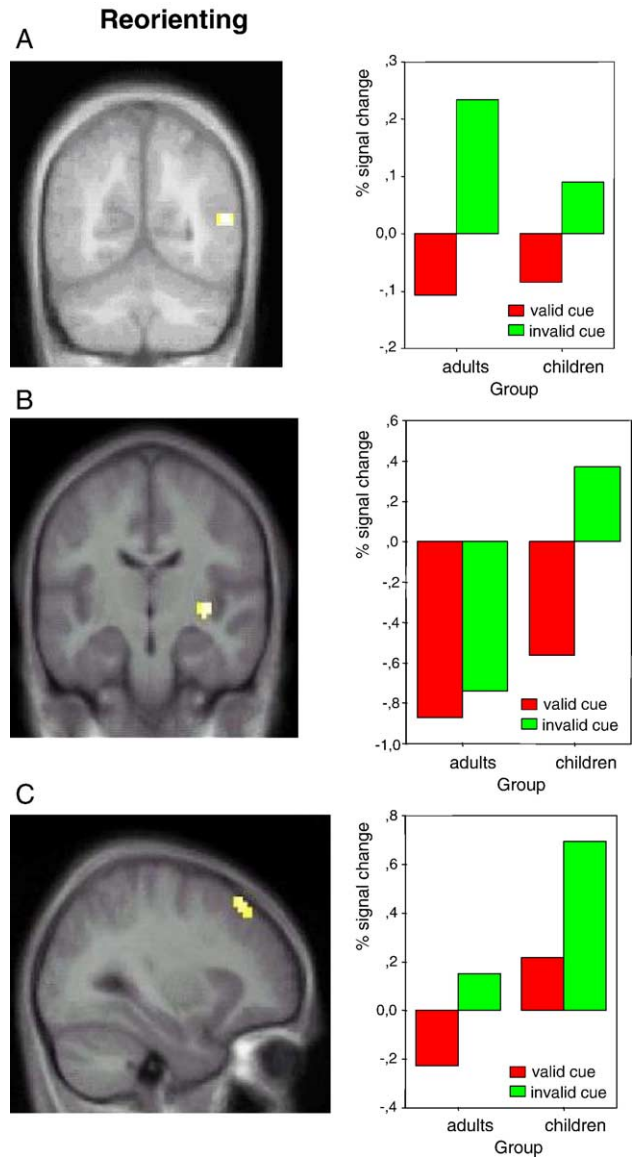
Reorienting

Fig. 4. Differential activation of adults and children as identified in a two-sample test for the reorienting condition (thresholded at $P_{svc} < 0.05$ or $P < 0.1$ corrected for multiple comparisons for whole-brain analyses, extend threshold 5 voxel, shown on averaged group T1 image). (A) Increased activation in the right-sided temporo-parietal junction in adults compared to children. (B) Stronger activation in the putamen and insula in children compared to adults. (C) Increased activation in the superior frontal gyrus in children compared to adults. Plots of the percent BOLD signal change are shown separately for both groups as a function of trial type (pooled over congruent and incongruent targets) for the activation maximum.
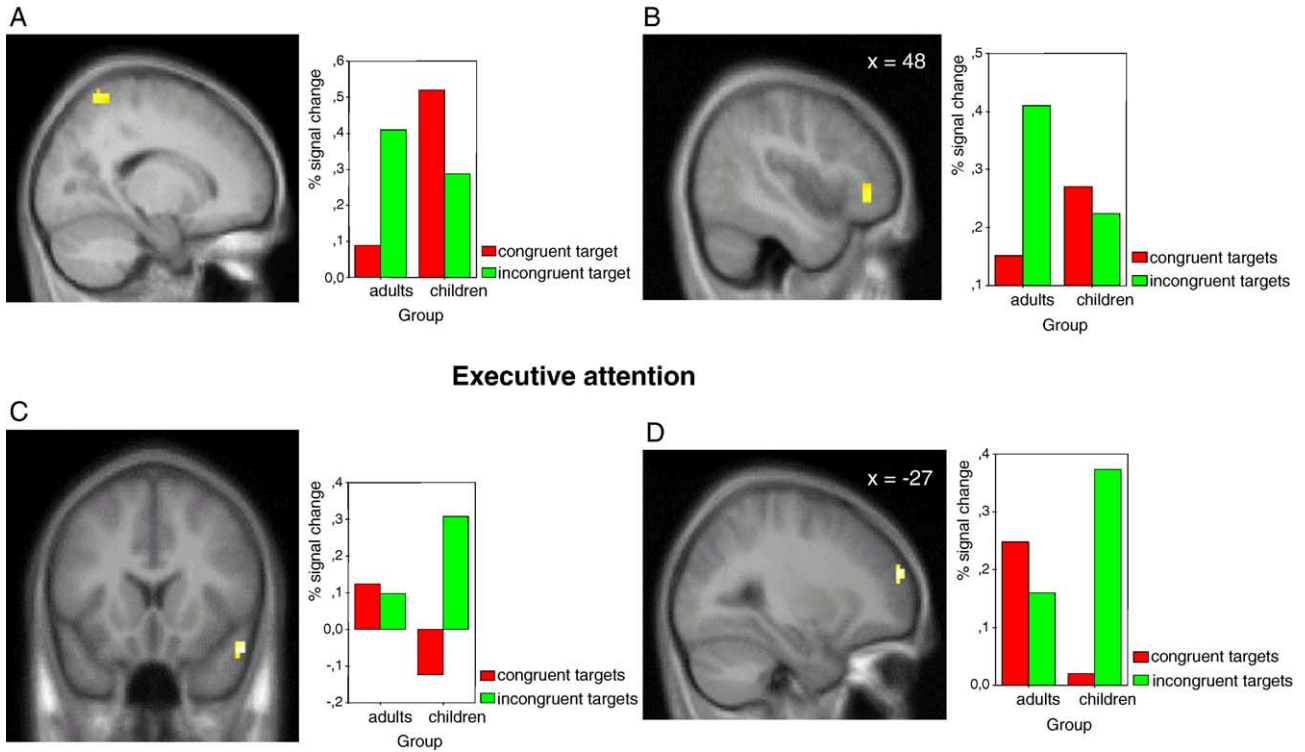
Fig. 5. Differential activation of adults and children as identified in a two-sample test for the executive control condition (thresholded at $P_{svc} < 0.05$ or $P < 0.1$ corrected for multiple comparisons for whole-brain analyses, extend threshold 5 voxel, shown on averaged group T1 image). (A) Increased activation in the superior parietal cortex and (B) inferior frontal gyrus in adults compared to children. (C) Increased activation in the superior temporal gyrus and (D) superior frontal gyrus in children compared adults. Plots of the percent BOLD signal change are shown separately for both groups as a function of target type (pooled over cueing conditions) for the activation maximum.

comparisons and the results of the two-sample t tests of the whole groups as reported above.

Morphometrical group differences

Anatomical group differences in gray-matter volume between children and adults were examined within the same ROIs as applied for the functional analyses and complemented by whole-brain analyses. Adults showed an increased gray-matter volume only within the anterior lobe of the cerebellum bilaterally extending to the fusiform gyrus of the temporal lobe, when compared to children. By contrast, children showed larger GM volumes primarily within the frontopolar, superior parietal, and superior temporal lobes bilaterally (see Table 3). Fig. 6 also demonstrates the overlap between functional and structural group differences for the executive control system.

Discussion

In this study, we examined the development of the neural circuitry involved in key aspects of attention (alerting, reorienting, executive control). Children aged 8 to 12 years differed from adults with respect to both their behavior and the associated brain activations. Consistent with previous studies, we found that children were more susceptible to interference (i.e., executive control) and less able to disengage attention after an invalid cue (reorienting system). These behavioral differences between children and adults for the conditions of executive control and reorienting were paralleled by differential brain activation patterns. Children showed significantly reduced neural activity in a priori defined regions-of-interest for all three attentional systems and exhibited significantly more diffuse brain activation outside the a priori defined regions for

Table 3
Differences in gray matter volume between children and adults

Comparison	Anatomical region	WB/ROI	Side	Talairach coordinates			Volume	Z score
				x	y	z		
Adults > children	Cerebellum	WB	L	−20	−38	−48	434	4.86
	Cerebellum/gyrus fusiformis	WB	R	32	−44	−28	272	3.52
Children > adults	Frontopolar	ROI	R	27	66	8	292	4.17
	Frontopolar	ROI	L	−31	58	23	184	3.12
	Superior temporal gyrus	ROI	R	62	−4	−1	395	4.2
	Middle temporal gyrus	ROI	L	−57	−4	−5	440	4.8
	Superior parietal cortex	ROI	R	24	−68	59	507	4.9

Note. WB = local maxima derived from whole-brain analyses with $P < 0.1$ corrected for multiple comparisons, ROI = local maxima derived from a priori region-of-interest analyses with $P_{svc} < 0.05$, voxel threshold = 100 voxels, R = right, L = left.
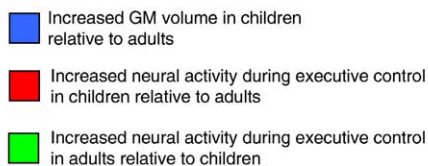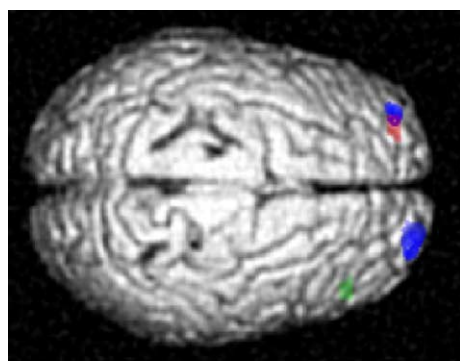
Fig. 6. Anatomical overlay of the functional group differences of the executive control condition and the increased gray-matter volume in the children's group compared to young adults. Increased gray-matter volume in children (relative to adults) is depicted in blue color, increased neural activation for the executive control condition in children (relative to adults) is depicted in red color and increased neural activation for the executive control condition in adults (relative to children) is depicted in green. Group differences in gray-matter volume and neural activations are thresholded at $P_{svc} < 0.05$ and rendered on an individual brain.

reorienting of attention and executive control of attention. This indicates that the development of attentional networks is still in progress in the age range 8 to 12 years and that maturational changes are not limited to the system of executive attentional control.

Although children did not differ significantly from adults in their alerting performance, significant group differences in neural activity were also observed for the alerting system. The latter finding is compatible with recent suggestions that behavioral measures might be less sensitive than brain activation measures under particular circumstances (Wilkinson and Halligan, 2004; Fink et al., 2002; Thiel et al., 2005).

Several aspects of our results deserve particular mention. First, because both children and adults exhibited high accuracy on all trial types, similar numbers of correct trials were submitted to the fMRI analysis for both groups. Furthermore, the event-related design allowed for examination of correct trials only, so that differences between children and adults cannot be attributed to brain activations associated with errors. Finally, and importantly, an analysis of a subgroup of children whose behavioral performance was similar to that of the adults enabled us to confirm that the observed group differences in brain activation patterns cannot be explained by performance differences.

Alerting

In line with previous studies of healthy adult subjects (Coull et al., 2001; Sturm and Willmes, 2001), we found a fronto-parietal network associated with alerting in the group of adult subjects. By contrast, random-effects analyses within the children's group revealed only increased neural activation outside the a priori defined ROIs during alerting. Adults (relative to children) activated significantly more the right cingulate gyrus, but showed a larger

relative decrease of the BOLD signal in the brainstem. It is often assumed that neural activity in subcortical regions is modulated by a "top–down" mechanism (Sturm and Willmes, 2001), facilitating processing of stimuli at attended locations and that parietal and frontal regions, in particular in the right hemisphere, are the source of such a top–down bias (Fink et al., 1996; Kastner et al., 1999). Thus, the results of our group comparison suggest that, on average, in children aged 8 to 12 years, this top–down modulation process may not yet be fully established. This result fits well with recent models of a developmentally still immature top–down modulation process in children (Casey et al., 2004).

Reorienting

Neural correlates of reorienting in adults were found in the right inferior frontal gyrus, the right temporal–parietal junction, and the bilateral superior parietal cortex. This is in good accordance with previous studies showing that the inferior and superior parietal cortex (Yantis et al., 2002), and specifically the temporo-parietal junction (Corbetta and Shulman, 2002), as well as inferior frontal regions are involved in shifting attention. By contrast, children showed increased neural activity only outside the primary areas of interest. The direct comparison of the two groups in the a priori defined ROIs revealed that adults activated the right-sided temporo-parietal junction significantly more than children. According to Downar et al. (2002), TPJ activity emerges with salient, unexpected, or rare stimuli and modulates activity of the orienting network when stimuli occur outside the current focus of attention. The reduced TPJ activation in the children's group thus reflects immature neural responses to invalid cues resulting in longer reaction times to invalidly cued targets. By contrast, children showed higher levels of neural activity in a right-striatal–insula circuitry and the left superior frontal gyrus when compared to adults. Note, however, that no difference in putamen activation was found, when controlled for performance differences between the groups. Thus, for the reorienting system, the data indicate that in the absence of the typical activation patterns observed in adults, children recruit additional brain areas which may reflect compensatory or immature processes. The data also suggest that the increased activation of the ventro-lateral circuitry in children cannot compensate adequately for attentional performance of the reorienting system.

Executive control of attention

In adults, the executive attention task activated a frontal network including the anterior cingulate gyrus as well as the dorsolateral prefrontal cortex bilaterally. Statistical group comparisons revealed that children activated less the right inferior frontal gyrus and the left superior parietal cortex when compared to adults in the conflict condition, suggesting immature fronto-parietal networks in children (Durston et al., 2002; Casey et al., 2002, 2004). There is a controversy whether or not decreased frontal activity in children just mirrors poorer conflict performance (Booth et al., 2004). The latter, however, cannot be the case in our study since this brain activation group difference was still observed after controlling for behavioral between-group differences. The data thus match the results for the alerting system, which also indicated impaired top–down modulation processes in fronto-parietal areas.

By contrast, children activated significantly more the left superior frontal gyrus and the right superior temporal gyrus. Accordingly, our results suggest differences in lateralization

between children and adults in the flanker task conditions. This result is supported by data from a recent study where successful interference suppression was associated with right-sided dorsolateral prefrontal activation in adults, while in children, this brain–behavior correlation was found for the left hemisphere (Bunge et al., 2002). It has been suggested that those group differences in hemispheric laterality may be related to differences in strategy with children solving this task with a somewhat more verbal strategy than adult subjects (Bunge et al., 2002). Changes in frontal lobe hemispheric asymmetry patterns dependent upon age have also been reported for memory processes (HAROLD model, Cabeza, 2002). On a more general level, this suggests that frontal lobe processes might be particularly vulnerable to age effects from childhood to old age.

Brain structure–function relationship

In line with previous morphometric studies (O'Donnell et al., 2005; Sowell et al., 2002; Giedd, 1999), we found significant group differences in GM volume with increased GM volume in frontal, parietal, and temporal lobes in children aged 8 to 12 years compared to young adults. In addition, the results of our VBM analysis support previous reports that the cerebellum is the last brain structure to mature during development (Nguon et al., 2005).

These structural group differences may at least in principle contribute to the observed functional group differences. Generally, we found reduced cortical activity in a priori defined ROIs for all three attentional tasks and additionally, more diffuse neural activations for reorienting and executive control of attention in the children's group. These functional differences were paralleled by an increased GM volume in the frontal, parietal, and temporal lobes of children. Taken together, our findings may indicate that by eliminating inefficient or unnecessary dendritic connections in the cortical ribbon during brain maturation, more effective and accurate synaptic transmission becomes possible (O'Donnell et al., 2005) resulting in more focal and less distributed neural networks supporting specific attentional functions.

However, we only found one area in which structural and functional group differences directly overlapped. For executive control of attention, we found an increased left-sided frontal activity in the children's group which overlapped anatomically with an increased GM density. In this area, interestingly, however, children showed larger GM density in the frontopolar areas bilaterally, while the functional difference only occurred within the left hemisphere. One could speculate that this might indicate a dissociation between structural and functional maturation processes. For example, the dominant hemisphere, although structurally yet immature, might functionally already begin to specialize and take over top–down modulation processes of attention. Such dissociations might also contribute to group differences in task strategies as described above. These issues remain to be further investigated in future studies.

Conclusion

This study constitutes a first step in combining fMRI and morphometric methods to further our understanding of developmental aspects of attention. Using a modified version of the Attention Network Task (ANT; Fan et al., 2002), we observed significant developmental differences in brain activation patterns related to key aspects of attention. While, in general, the neural activations observed in adults fitted well with previous investigations of Posner and Petersen's model of attention, activation patterns in children were found to be less specific. In particular, top–down modulation exerted by fronto-parietal and temporo-parietal areas seemed to be less established. Overall, the data suggest that, during normal development, a transition from functional yet immature systems to the more definitive adult networks occurs which may reflect qualitative differences in cognitive strategies for task performance between children and adults. Furthermore, the morphometric data suggest that differences in brain activity between age groups may also be influenced by differences in neuronal connections/synaptic pruning that occur during development (Bourgeois et al., 1994) which stresses the importance to take into account both functional and structural data in future developmental studies of brain function.

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