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Research Report

Dysfunction of the attentional brain network in children with Developmental Coordination Disorder: A fMRI study

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A B S T R A C T

Children with Developmental Coordination Disorder (DCD) present impaired motor skills, frequently associated with impaired attentional and executive functions. The objective of this study was to assess the impact of DCD on effective connectivity applied to a putative model of inhibition. fMRI was performed in 9 children with DCD and 10 control children (8–13 years old) performing a go–nogo task. As previously reported, children with DCD obtained a similar score for correct inhibitions as controls, but responses were slower and more variable than in controls. Compared to controls, Structural Equation Modeling indicated that: (1) path coefficients from both middle frontal cortex (MFC) and anterior cingulate cortex (ACC) to inferior parietal cortex (IPC) increased in children with DCD particularly in the left hemisphere; (2) path coefficients between striatum and parietal cortex decreased in children with DCD in the right hemisphere. Results suggest that DCD could be characterized by abnormal brain hemispheric specialization during development. Furthermore, connectivity in the MFC–ACC–IPC network could indicate that children with DCD are less able than healthy children to easily and/or promptly switch between go and nogo motor responses. However, children with DCD seem to compensate for this poor efficiency by more actively engaging the ACC to prevent commissions allowing maintenance of a good level of inhibition.

Keywords:
DCD, Inhibition, Attention
Go–nogo, Effective connectivity fMRI

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1. Introduction

According to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, American Psychiatric Association, 1994), Developmental Coordination Disorder (DCD) encompasses a diverse spectrum of difficulties that affect a child's ability to learn and carry out coordinated motor skills which cannot be attributed to a mental retardation or general medical condition (e.g. cerebral palsy, hemiplegia, muscular dystrophy and brain lesion identifiable by neuroimaging). Furthermore, the motor difficulties must have a negative impact on academic achievement or daily life activities. DCD affects up to 5% to 6% of school-aged children and many individuals continue to show poor motor skills throughout adolescence and into adulthood (Barnhart et al., 2003; Visser, 2003).

1.1. *Executive functions and attention in DCD*

Most studies conducted in DCD have focused on motor capacities. However, impairments of non-motor functions have also been reported in DCD as well as in prematurely born children who present praxis deficits. In particular, premature children (Dalla Piazza, 1997; Mellier et al., 1999) and children with DCD (for review: Visser, 2003) often present impaired executive and attentional functions. The executive functions constitute a set of cognitive abilities that control and regulate other abilities and behaviors. There is a consensus around several components of executive functions: control, planned actions, inhibition and shifting between cognitive activities. Moreover, attentional functions and working memory are often also included in the executive functions although that this conception is controversial (Miller and Cohen, 2001). Concentration deficits and distractibility to external stimuli have been frequently reported in children with DCD (Dewey et al., 2002; Visser, 2003). Attentional and executive deficits have been demonstrated in children with DCD performing a flanker task (visuospatial conflict) or central cuing task (endogenous orientation of visuospatial attention) (Mandich et al., 2002; Mandich et al., 2003; Wilson et al., 1997; Wilson and Maruff, 1999). Praxis also involves executive functions for planning voluntary gestures. Consequently, clumsiness could partially result from a deficit of executive functions as suggested by impairments reported in children with DCD resulting from early cerebral lesions (Mazeau, 1995). Recent experimental data suggested that deficits in DCD could stem from an impaired coupling between attention and visuo-motor integration. Using the gap paradigm, Wilmut et al. (2007) showed that response time and accuracy deficits in children with DCD could result from interferences between attentional processes and motor system. Wilmut et al. (2007) suggested that children with DCD have deficits in the allocation of attention for action at the level of execution.

Prefrontal cortex plays a crucial role in cognitive control, in the ability to plan action in accordance with goals (Miller and Cohen, 2001) and in attentional functions (Posner and Petersen, 1990) (see also for role of the frontal and prefrontal cortex in executive functions: Koechlin and Summerfield, 2007). Activity of the frontal cortex is integrated in a larger brain network including subcortical structures and posterior cortical areas, especially the parietal cortex (Mesulam, 1999). Posner and Petersen (1990) distinguished the anterior and posterior components of the attentional network. Prefrontal cortex regions send signals to modulate and direct processing to basal ganglia and posterior cortical regions in accordance with current goals and task demands (Ridderinkhof et al., 2004; also see: LaBerge, 1997). The prefrontal cortex is involved in detecting salient events and preparing or inhibiting motor responses, moving the focus of attention, engaging attention at the new target, sustaining attention and maintaining a state of alertness (Corbetta and Shulman, 2002; Gitelman, 2003; Mesulam, 1999; Posner and Petersen, 1990).

Morphologic investigations by magnetic resonance imaging (MRI) performed in children born prematurely have suggested involvement of the right hemispheric parietal regions, basal ganglia or cerebellum when praxis and visuospatial abilities are impaired (Allin et al., 2001; Peterson et al., 2000; Stewart et al., 1999). Many authors have proposed that DCD could be related to a defect of maturation of the right parietal regions (Wilson et al., 1997, 2003), basal ganglia (Ivry, 2003) or cerebellum (Groenewegen, 2003) (for review, also see: Visser, 2003). Attentional processes interfered with motor behavior as shown by Wilmut et al. (2007) suggesting that the anterior cerebral regions could be also involved in DCD. This suggests that relationship between anterior and posterior structures which constitute a large part of the attentional network might not be fully functional in DCD. Precisely, the present work tested the hypothesis that the functional coupling between fronto-striatal and parietal components of the attentional and executive network might be altered in children with DCD.

1.2. *Exploration of the antero/posterior functional coupling*

To date, no functional MRI study has been performed to determine how the attentional brain network is involved during experimental tasks in DCD. Effective connectivity analysis appeared well adapted to study the functional coupling between antero/posterior regions of the attentional network in children with DCD during a go–nogo task.

Effective connectivity resembles the intuitive notion of a connection and can be defined as the influence that one neural system exerts over another, either at a synaptic level (synaptic efficacy) or at a cortical level (Friston, 1994; McIntosh and Gonzalez-Lima, 1994). Electrophysiological studies demonstrated a close relationship between effective connectivity and synaptic efficacy (Aersten and Preissl, 1991). Effective connectivity can be estimated from structural equation modeling (SEM) used to test whether a theoretical model seeking to explain a network of relationships can actually fit the relationships estimated from the observed data. Applied to fMRI, the theoretical model is an anatomical (constrained) model and the data are interregional covariances of activity (Buchel and Friston, 2000). To describe a functional network, network nodes and anatomical connections must be proposed in conjunction with SEM in order to model interregional covariances and determine the intensity of the connections.

1.3. *Predicted model of connectivity for inhibition of response*

The go–nogo task that engages sustained attention and executive network was used to examine this issue. This task, largely used in fMRI studies in children, requires the subject to perform rapid responses on frequent go trials and to inhibit responding to rare nogo trials. Neuroimaging research has converged on a discrete number of regions involved in motor inhibition of a prepotent response which involves both anterior (anterior cingulate cortex (ACC), middle frontal cortex (MFC) and orbito frontal cortex (OFC)), and posterior components (inferior parietal cortex (IPC)) of the attentional network but also the basal ganglia and cerebellum in children (Booth et al., 2003; Bunge et al., 2002; Casey et al., 1997; Durston et al., 2002, 2003, 2006; Simmonds et al., 2007; Smith et al., 2006; Tamm et al., 2002, 2004) fairly similar to those evidenced in adults (Aron and Poldrack, 2006; Garavan et al., 2006; Hester

and Garavan, 2004; Horn et al., 2003; Mathalon et al., 2003; Menon et al., 2001; Watanabe et al., 2002).

Neuroimaging and animal studies suggest that parietal cortex, particularly the IPC, is engaged in sustained activation of competing responses during the period in which the MFC guides selection of the appropriate response and inhibits the erroneous response stored in the IPC (Botvinick et al., 2004; Bunge, 2004; Ridderinkhof et al., 2004). The MFC and IPC are richly interconnected through the superior longitudinal fasciculus, as shown in humans and monkeys by Diffusion Tensor Imaging (Makris et al., 2005; Schmahmann et al., 2007). This direct bidirectional link between MFC and IPC may be completed by two other pathways: one via the ACC and the other via the striatum. The role played by the ACC in detecting potential conflict between stimulus–response and error monitoring has been well documented (for review: Mathalon et al., 2003). The ACC also appears to be more directly involved in inhibition of responses under the influence of the MFC (Dias et al., 2006; Garavan et al., 2002). The ACC may be recruited by the MFC when competition between responses increases and when inhibition of motor response is required (Dreher and Grafman, 2003). In this situation, the ACC is recruited in order to prepare for a nogo motor response representation which is stored in the IPC directly or via the pre-SMA (Picard and Strick, 2001). Strong reciprocal connections between ACC and MFC have been well documented and connections between ACC and IPC have been evidenced in the monkey (Koski and Paus, 2000; Pandya et al., 1981; Petrides and Pandya, 2006; Vogt and Pandya, 1987). The basal ganglia also appear to be involved in the behavioral response via both direct and indirect striatal pathways (Groenewegen, 2003). The indirect striatal pathway could be involved in suppression of unwanted competing movements (Brown et al., 2004; Mink, 1996). Many studies have suggested that the striatum contributes to inhibition of motor responses, but it could also play an important role in automatization of cognitive processes with practice (Brown et al., 2004; Laubach, 2005; Tracy et al., 2001). The involvement of the striatum has been evidenced during learning or practice of memory, motor, and visuospatial tasks (Poldrack et al., 2001; Van Der Graaf et al., 2004). Connections between the striatum and other cortical structures have been evidenced. The striatum receives rich projections from the MFC and is connected bidirectionally with the ACC and IPC (Leh et al., 2007; Nakano, 2000; Weber and Yin, 1984).

2. Results

2.1. *Behavioral results*

No significant difference was demonstrated between DCD and control groups for verbal IQ although this score was lower in children with DCD than in controls (102.1 and 116.0, respectively). The performance IQ was significantly lower in children with DCD (75.6) than in controls (110.5) ($t(2,17)=5.03$, $p=0.00013$).

The difference in the rate of go responses on nogo trials (commissions) was not significantly different between the DCD group and the control group (26.3% and 31.0%, respectively) ($t(2,17)=0.8$, $p=0.43$). Children with DCD made significantly more omissions on go trials than control children (8.4% and 0.7%, respectively) ($t(2,17)=2.87$, $p=0.011$). The rate of anticipations on go trials was weak or null in both groups (0.7% in the DCD group and 0% in the control group, the difference was not significant). Responses on go trials were significantly longer and more variable for children with DCD than for control children in each block (the details of statistical results are shown in Table 1).

2.2. *fMRI analysis*

The statistical parametric maps of group analysis of the brain activated regions within each hemisphere are shown separately for control and DCD children in Figs. 1A and B, respectively.

Each figure presents activated cortical and subcortical regions, Brodmann Areas, standard Talairach coordinates and t corrected values for each significant local maximum within the ROIs in the left hemisphere and right hemisphere. To facilitate the generation of future hypotheses, we also report data for activation clusters that fell outside of the hypothesized ROIs (Tables 2A and 2B). The univariate analysis revealed that similar cerebral regions were activated in children with DCD and in controls: ACC (BA 32), SMA (BA 6), OFC (BA 47), insula (BA 13), MFC (BA 46), IPC (BA 40) and striatum.

We first tested the fit between the predicted model and the empirical data for the two groups using a maximum-likelihood (ML) algorithm. Covariances were estimated by an iterative multiple regression procedure (Glabus et al., 2003)

Table 1 – Mean response time (RT), standard deviation (SD), maximum (Max) and minimum (Min) mean RT and SD in the control and DCD groups

Measure	Block	Control group		DCD group		t	p
		Mean (SD)	[Max–Min]	Mean (SD)	[Max–Min]		
Mean RT	Go(s)	398 (50)	[298–464]	483 (69)	[346–588]	3.12	**
	Go(r)	434 (53)	[360–549]	538 (120)	[386–799]	2.47	*
	Go–Nogo	448 (68)	[341–593]	564 (112)	[396–767]	2.74	*
SD of RT	Go(s)	95 (22)	[70–125]	168 (65)	[79–276]	3.35	***
	Go(r)	94 (34)	[56–152]	173 (54)	[86–259]	3.87	***
	Go–Nogo	107 (30)	[65–154]	172 (66)	[94–287]	2.78	**

The t and p values for differences between groups were indicated for each block (*<0.05, **<0.01, ***<0.005).

using a non-recursive model (i.e. a model including reciprocal connections). We checked the stability of these estimates using the stability indices (Bentler and Freeman, 1983). In both groups, and for both hemispheres, these values were close to zero, indicating good stability of the path coefficients. Residual variances were optimized separately for control and DCD

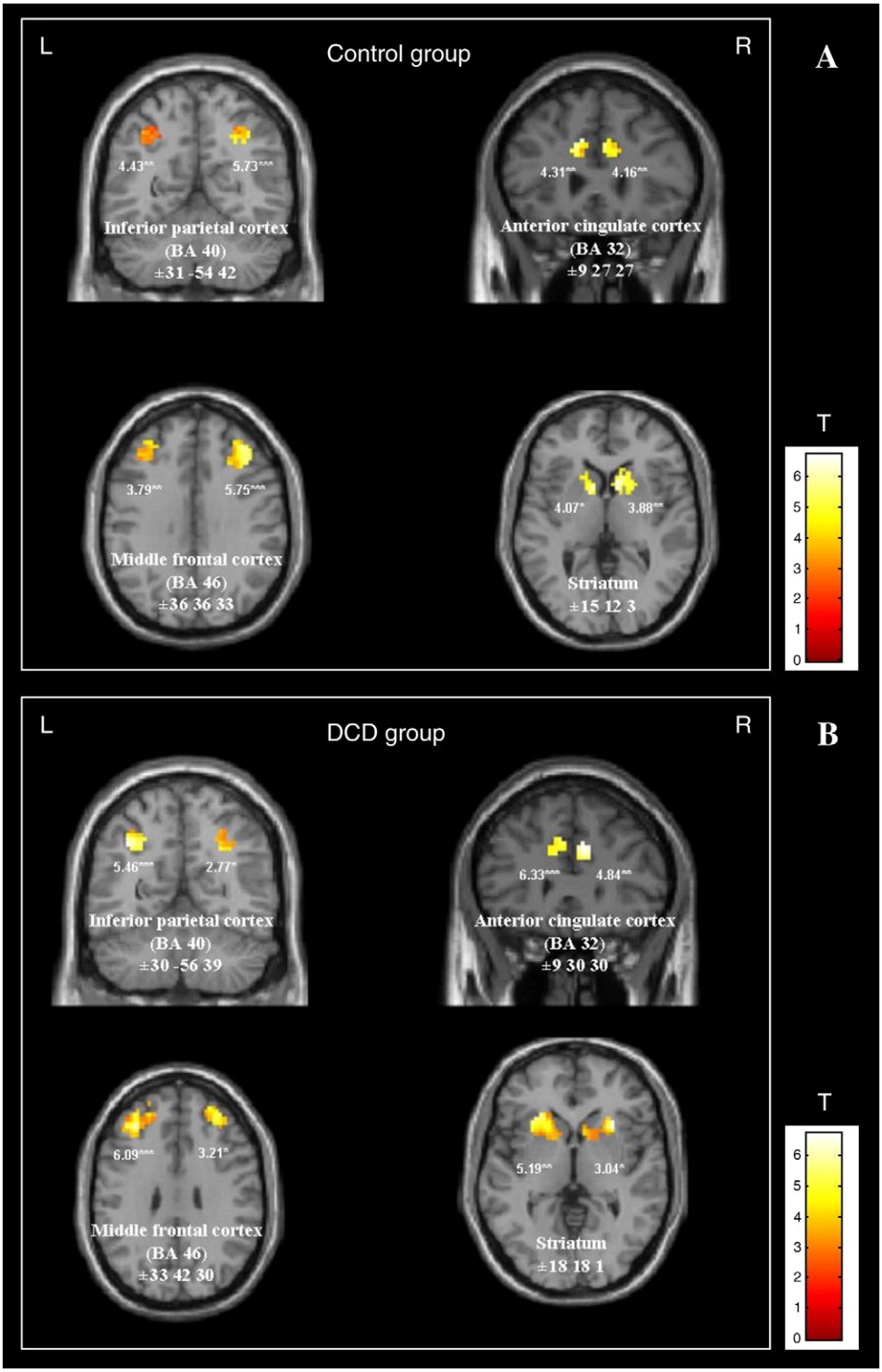

Fig. 1 – (A and B) Activation maps obtained for the contrast Go–Nogo > Go(s) in the middle frontal cortex (MFC), anterior cingulate cortex (ACC), inferior parietal cortex (IPC) and the striatum for the control group (A) and the DCD group (B). Talairach coordinates (±*X*,*Y*,*Z*), *t* values and *p* corrected values for multiple comparisons (*<0.05, **<0.01, *<0.005) are reported for each cerebral region. Left hemisphere = L; right hemisphere = R.**

Table 2A – One-sample t-test of activated regions in the control group is presented

Regions	BA	Stereotaxic coordinates			t^p
		X	Y	Z	
Right hemisphere					
Inferior parietal cortex	40	31	−54	42	5.73***
Middle frontal cortex	46	36	36	33	5.75***
Anterior cingulated cortex	32	9	27	27	4.16**
Striatum	–	15	12	3	3.88**
Orbito frontal cortex	47	39	34	−6	4.06**
Insula	13	39	17	5	3.17*
SMA	6	8	9	57	5.09***
Left hemisphere					
Inferior parietal cortex	40	−31	−54	42	4.43**
Middle frontal cortex	46	−36	36	33	3.79**
Anterior cingulate cortex	32	−9	27	27	4.31**
Striatum	–	−15	12	3	4.07*
Orbito frontal cortex	47	−39	34	−6	3.01*
Insula	13	−39	17	5	3.07*
SMA	6	−8	9	57	4.47**

BA: Brodmann areas; X,Y,Z: Talairach coordinates; t values and p corrected values for multiple comparisons (*<0.05, **<0.01, ***<0.005). Regions included in SEM analysis are shown in bold type.

groups, using a multiple regression model to estimate the values of the parameters (see Table 3).

The path diagram for both the non-constrained and the constrained model was determined. Only path values obtained from the non-constrained model for both groups are retained. Path diagrams are presented separately in the Fig. 2 for the right and left hemispheres in the right and left panel, respectively. In each diagram, estimates of path coefficients between control and DCD children groups are presented. One reciprocal (non-recursive) and five one-way paths (recursive) were found.

Table 2B – One-sample t-test of activated regions in the DCD group is presented

Regions	BA	Stereotaxic coordinates			t^p
		X	Y	Z	
Right hemisphere					
Inferior parietal cortex	40	30	−56	39	2.77*
Middle frontal cortex	46	33	42	30	3.21*
Anterior cingulated cortex	32	9	30	30	4.84**
Striatum	–	18	18	1	3.04*
Orbito frontal cortex	47	41	30	−18	3.45*
Insula	13	36	13	6	4.50*
SMA	6	7	12	63	4.40**
Left hemisphere					
Inferior parietal cortex	40	−30	−56	39	5.46***
Middle frontal cortex	46	−33	42	30	6.09***
Anterior cingulated cortex	32	−9	30	30	6.33***
Striatum	–	−18	18	1	5.19**
Orbito frontal cortex	47	−41	30	−18	3.55*
Insula	13	−36	13	6	4.36**
SMA	6	−7	12	63	4.05**

BA: Brodmann areas; X,Y,Z: Talairach coordinates; t values and p corrected values for multiple comparisons (*<0.05, **<0.01, ***<0.005). Regions included in SEM analysis are shown in bold type.

2.3. *Path analysis, right hemisphere*

The predicted attentional network for the non-constrained model fits the experimental data [$\chi^2_{(6)}=594$, $p=0.424$]. The values of various other indices of fit (RMSEA<0.001, GFI=0.994, SRMR=0.08 and TLI=0.990) were higher than the minimum threshold usually recommended in the literature; in particular the combinatory rules recommended by Hu and Bentler (1999) to indicate that the model adequately fits the data.

In the control group, within the anterior network, the path coefficients indicated "middle" size effects, according to Cohen's norms on size effects (Cohen 1992), between MFC and ACC and between MFC and striatum. The values of reciprocal connections between MFC and IPC indicated a "weak" positive influence of MFC on IPC, and vice versa. In the posterior netwok, the path coefficients indicated "weak" size effects between ACC and IPC and between striatum and IPC. In the DCD group, the connection between MFC and ACC was "weak". "Middle" and "important" connections were observed from ACC to IPC and from IPC to MFC, respectively (Fig. 2, right panel).

Since the non-constrained model cannot be rejected, comparison between the control and DCD groups, using model comparison, was considered possible. The difference between the χ^2 of the non-constrained model and the χ^2 of the constrained model [$\chi^2 diff_{(6)}=20.05$, $p=0.003$] indicated a global statistically significant difference between models, hence between control and DCD groups. Critical ratios for the relevant pairs of path coefficient differences are indicated in Table 4 (top panel).

The results of the pairwise comparisons between the group paths, for the non-constrained model revealed several major differences in strength and directions within the predicted network (Table 5, right panel). Firstly, the anterior network connection between MFC and ACC was significantly higher in the control group than in the DCD group. Secondly, the top-down connection from MFC to IPC was significant and in a positive direction in the control group, while it remained significant, but in the negative direction in

Table 3 – Residual variances in control and DCD groups

Regions	BA	Residual variances	
		Control group	DCD group
R(IPC)	40	0.50	0.86
R(MFC)	46	0.75	0.73
R(ACC)	32	0.45	0.60
R(STRIA)	–	0.66	0.60
L(IPC)	40	0.78	0.86
L(MFC)	46	0.94	0.86
LC(ACC)	32	0.50	0.55
L(STRIA)	–	0.80	0.80

R = right hemisphere; L = left hemisphere; MFC = middle frontal cortex; ACC = anterior cingulate cortex; IPC = inferior parietal cortex; STRIA = Striatum; BA = Brodmann Area.

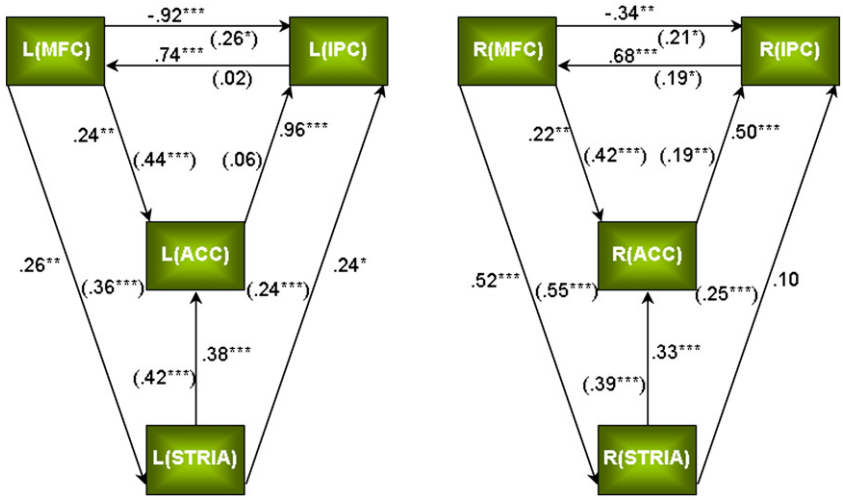

Fig. 2 – Path diagrams from the causal analysis using structural equation modeling involving the right hemisphere (right panel) and the left hemisphere (left panel). Significant reciprocal (non-recursive, double arrow) and one-way (recursive, single arrow) pathways between middle frontal cortex (MFC), anterior cingulate cortex (ACC), inferior parietal cortex (IPC) and striatum are shown. The values of the path coefficients in the DCD group and in the control group (with parenthesis) are indicated. Level of significance for regression weights are: *$p<0.05$, **$p<0.01$, ***$p<0.001$. R = right hemisphere; L = left hemisphere.

DCD group. Thirdly, the posterior network connection between ACC and IPC was significantly higher in the DCD group than in the control group. The posterior network connection between striatum and IPC was close to zero in the DCD group (Table 4).

2.4. *Path analysis, left hemisphere*

The predicted attentional network for the non-constrained model fits the experimental data [$\chi^2_{(6)}=4.66$, $p=0.588$]. The values of various other indices of fit were: RMSEA<0.001, GFI=0.994, SRMR=0.006 and TLI=0.995.

In the control group within the anterior network, the path coefficients indicated "middle" size effects between MFC and ACC and between MFC and striatum. In the DCD group within the anterior network, the connection value from MFC to ACC was significantly decreased. The reciprocal connections between MFC and IPC indicated a "strong" positive influence of IPC on MFC in the DCD group, while this connection was non-existent in the control group. The connection value from MFC to IPC was "strong" and in a negative direction in the DCD group (Fig. 2, left panel).

Since the non-constrained model cannot be rejected, the comparison between control and DCD groups, using model

Table 4 – Estimates of regression weights between control and DCD children groups

Regions	Control group			DCD group		
	Path coefficients	CR	*p*	Path coefficients	CR	*p*
R(IPC)→R(MFC)	0.19	2.26	*	0.68	7.69	***
R(MFC)→R(IPC)	0.21	2.36	*	−0.34	−3.10	**
R(MFC)→R(ACC)	0.42	7.33	***	0.22	2.63	**
R(MFC)→R(STRIA)	0.55	9.10	***	0.52	7.84	***
R(ACC)→R(IPC)	0.19	2.80	**	0.50	4.61	***
R(STRIA)→R(IPC)	0.25	4.00	***	0.10	0.95	NS
R(STRIA)→R(ACC)	0.39	7.32	***	0.33	4.58	***
L(IPC)→L(MFC)	0.02	0.13	NS	0.74	8.48	***
L(MFC)→L(IPC)	0.26	2.04	*	−0.92	−8.19	***
L(MFC)→L(ACC)	0.44	8.25	***	0.24	2.91	**
L(MFC)→L(STRIA)	0.36	5.31	***	0.26	2.80	**
L(ACC)→L(IPC)	0.06	0.76	NS	0.96	7.75	***
L(STRIA)→L(IPC)	0.24	3.20	***	0.24	2.37	*
L(STRIA)→L(ACC)	0.42	7.85	***	0.38	5.00	***

Non-standardized path coefficients and critical ratio (CR) for regression weights are presented. Level of significance for regression weights are: *$p<0.05$, **$p<0.01$, ***$p<0.001$, NS = non-significant. R = right hemisphere; L = left hemisphere; MFC = middle frontal cortex; ACC = anterior cingulate cortex; IPC = inferior parietal cortex; STRIA = striatum.

Table 5 – Pairwise parameter comparisons

Regions	Group comparison			
	Left hemisphere		Right hemisphere	
IPC→MFC	4.81	***	3.94	***
MFC→IPC	−6.94	***	−3.88	***
MFC→ACC	−2.01	*	−1.96	*
MFC→STRIA	−0.88	NS	−0.31	NS
ACC→IPC	5.98	***	2.38	*
STRIA→IPC	0.01	NS	−1.25	NS
STRIA→ACC	−0.85	NS	−0.69	NS

Critical ratios for differences in equivalent paths between the two experimental groups are presented. Levels of significance for critical ratios are: $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$, NS = non-significant. MFC = middle frontal cortex; ACC = anterior cingulate cortex; IPC = inferior parietal cortex; STRIA = striatum.

comparison, was considered possible. The difference between the χ^2 of the non-constrained model and the χ^2 of the constrained model [$\chi^2 diff_{(7)}=39.46$, $p=0.001$] indicated a global statistically significant difference between models, i.e. between control and DCD groups. Critical ratios for the relevant pairs of path coefficient differences are indicated in Table 4 (bottom panel).

The overall pattern of changes in connectivity between control and DCD groups showed significant differences between the same directional and bidirectional connections as in right hemisphere. The results of the pairwise comparisons between the group paths, for the non-constrained model revealed several major differences in strength and directions within the predicted network (Table 5, left panel). Firstly, the top-down network connection from MFC to IPC was negative and significantly higher (in absolute values) in the DCD group than in control group. Secondly, within the posterior network, the value of the path coefficient between ACC and IPC was close to one in the DCD group, indicating a very "strong" and significant connection between these two regions, while this connection was non-existent in the control group (Table 4). Thirdly, no path coefficient difference was observed between striatum and IPC in either group.

3. Discussion

Children with DCD obtained a quite similar score for correct inhibitions as controls. These results concur with previous observations that children (de Castelnau et al., 2007; Piek et al., 2004) and adults (Cousins and Smyth, 2003) with poor coordination motor skills inhibited prepotent motor responses as effectively as healthy controls. Children with DCD made more omissions than controls as shown previously with go–nogo task (de Castelnau et al., 2007) and flanker task (Mandich et al., 2002). Go responses were slower and more variable in children with DCD than in control children. Slowness and high variability in DCD have been reported previously with the go–nogo task (Cousins and Smyth, 2003; Piek et al., 2004) and with other experimental tasks as in attentional spatial orientation paradigms (Mandich et al., 2003; Wilson et al., 1997; Wilson and Maruff, 1999), or flanker task (Mandich et al., 2002). Two main hypotheses, not mutually exclusive, have been proposed to explain slowness and variability in DCD. A deficit in sensory–motor integration or a weakness of the central control implying attentional and executive functions may contribute to the slowness and variability in DCD (Smits-Engelsman et al., 2003; Wilmut et al., 2007).

Children with DCD activated the same cerebral regions as healthy children performing the go–nogo task. Activation of these cerebral regions have been evidenced in previous fMRI studies in healthy children and adults performing the go–nogo task: ACC (BA 32), SMA (BA 6), OFC (BA 47), insula (BA 13), MFC (BA 46), IPC (BA 39/40) and striatum (Aron and Poldrack, 2006; Booth et al., 2003; Bunge et al., 2002; Casey et al., 1997; Durston et al., 2002, 2003, 2006; Garavan et al., 2006; Hester and Garavan, 2004; Horn et al., 2003; Simmonds et al. 2007; Mathalon et al., 2003; Menon et al., 2001; Smith et al., 2006; Tamm et al., 2002, 2004; Watanabe et al., 2002). Those regions are usually involved when attentional or executive functions are solicited (Corbetta and Shulman, 2002; Mesulam, 1999; Posner and Petersen, 1990; Ridderinkhof et al., 2004).

3.1. *Connectivity in control children*

Results of the SEM analysis seem compatible with our predicted model. A mutual bidirectional direct pathway between MFC and IPC was found and the influence of MFC on IPC seems also implicate two indirect pathways involving the ACC and striatum. The strengths of the connections were higher in both hemispheres in the frontobasal component of the network (MFC–ACC–striatum) than in the posterior component of the network (afferent and efferent connections of the IPC). This result suggested that the fronto-cingulo-basal circuits play a crucial role in inhibition of prepotent motor responses. Using dynamic causal modeling, Stevens et al. (2007) previously reported a similar result by showing that the MFC/striatum and the ACC (associated with other frontal regions) exerted influences on the IPC in adolescents and adults performing a go–nogo task.

Connectivity in control children differed between the hemispheres along the pathways from ACC to IPC and from IPC to MFC, as these two path coefficients were positive in the right hemisphere, but close to zero in the left hemisphere. Recently, Lütcke and Frahm (2008) reported that correct inhibitions activated the ACC only in the right hemisphere, whereas the left ACC was more actively involved in error processing in a letter-based go–nogo task. The involvement of the right ACC via its connection to IPC supported the proposal that ACC, especially in the right hemisphere, could play a direct role in inhibition of motor responses in healthy individuals, as previously suggested (Dreher and Grafman, 2003; Lütcke and Frahm, 2008) and not only in error monitoring. The present results suggesting that execution of the go–nogo task may more actively involve the right brain network in control children are concordant with results obtained previously in many fMRI studies. Activations evidenced during go–nogo tasks and inhibitory tasks in general were predominantly observed in the right hemisphere in adults and

children (Buchsbaum et al., 2005; Durston et al., 2002; Tamm et al., 2002, 2004). Patients with frontal or basal lesions of the right hemisphere present an impaired response during the stop signal task, a variant of the go–nogo task (Rieger et al., 2003). Better capability of the right hemisphere compared to the left hemisphere to inhibit prepotent responses has been evidenced in split-brain patients (Funnell et al., 2004, reported by: Garavan et al., 2006).

3.2. *Connectivity differed in children with DCD and controls*

Globally, the involvement of each intrahemispheric network differed very clearly between children with DCD and healthy children. Firstly, differences in connectivity between groups affected direct and indirect pathways between MFC and IPC. Secondly, compared to the effective connectivity demonstrated in controls, children with DCD showed stronger path coefficients in the left hemispheric network than in the right hemispheric network, indicating that inhibition of a prepotent motor response predominantly involved the left hemispheric network in DCD. This result suggests an abnormal hemispheric lateralization for attentional and inhibitory functions in DCD. Atwood and Cermak (1986) or Flouris et al. (2005) had proposed that DCD could be characterized by an abnormal brain hemispheric specialization during development. It has been suggested in other developmental disorders such as epilepsy or dyslexia that abnormal functional lateralization may be due to persistence of abnormal synaptic connections which are normally lost during development (Chang and Walsh, 2003; Porter et al., 2002; Saugstad, 1998, 1999).

More finely, three major differences were found in the predicted attention/inhibition network between children with DCD and healthy children Firstly, the functional connection between the striatum and IPC was very low in the right hemispheric network in children with DCD, when it was positive in controls. Secondly, the influence exerted by the ACC on IPC was dramatically reinforced in children with DCD compared to controls, especially in the left hemispheric network. Thirdly, the positive path coefficient from IPC to MFC was clearly higher in children with DCD than in controls, whereas the path coefficient from MFC to IPC was strongly negative in children with DCD. These modifications of the coupling between MFC and IPC observed in DCD seem to be more pronounced in the left hemispheric network than in the right network.

Positive and negative path coefficients do not imply excitatory and inhibitory influences in the physiological sense (Schlösser et al., 2006). Indeed, a positive or a negative coefficient is interpreted as the degree to which increase in BOLD activity in the source region predicts increase or decrease, respectively, in the target region. BOLD response is generally thought to be a combination of both excitatory and inhibitory input to a neuronal region that cannot be independently estimated using fMRI (Arthurs and Boniface, 2002, Logothetis et al., 2001), although some studies have shown neural excitatory input to be more representative of the BOLD signal (Waldvogel et al., 2000) and decreases in BOLD signal correlate to a suppression of neural activity (Shmuel et al., 2006).

3.3. *How is inhibition of motor responses exerted in children with DCD?*

These results suggest that the two indirect pathways, via ACC and striatum, by which the MFC may contribute to selection of the response stored in the IPC, appeared to be activated in different ways in the DCD group and control group. In the right hemisphere, the positive influence exerted by the striatum on the IPC in healthy children appeared to be not fully functional in the DCD group. The hypothesis that the basal ganglia could be involved in the pathophysiology of DCD has been proposed previously by Groenewegen (2003), and defects of maturation of the white matter affecting intrahemispheric and basocortical connections have been reported in children born prematurely who presented praxis and attentional deficits (Fujii et al., 1993; Skranes et al., 1993). Many studies have suggested that the striatum contributes to inhibition of motor responses (Brown et al., 2004; Mink, 1996), but could also play an important role in automatization of cognitive and motor processes with practice (Brown et al., 2004; Laubach, 2005). Visser (2003) proposed that children with DCD could have impaired capacities to automatize motor behavior with practice and consequently continue to exert top-down control processes during behavior or tasks which are normally automatized with practice in healthy children.

In each intrahemispheric network, positive path coefficients from IPC to MFC were dramatically higher in children with DCD than in controls, whereas path coefficients from MFC to IPC were strongly negative in children with DCD compared to controls. Two interpretations can be proposed. The negative connection between MFC and IPC in children with DCD could reflect that the MFC inhibited go motor response representation stored in the IPC. Alternatively, Wilson et al. showed that children with DCD oriented spatial attention in a reflexive manner like controls, but disengaged spatial attention less easily and more slowly than controls (Wilson et al., 1997; Wilson and Maruff, 1999; also see: Mandich et al., 2003). Results obtained with attentional spatial orientation paradigms, indicate active involvement of the parietal cortex (Corbetta and Shulman, 2002; Mesulam, 1999; Posner and Petersen, 1990). This suggests that the process subtended by parietal regions could persist for a long time in DCD. The present results obtained in children with DCD performing the go–nogo task could suggest that the IPC "over-reacted" to stimuli and then propagated this excessive or prolonged activity via efferent connections to the MFC. In return, the negative path coefficient from MFC to IPC may reflect some inhibitory influence on the IPC activity by the MFC.

Activation in the ACC is often related to errors (Casey et al., 1997; Garavan et al., 2003; Mathalon et al., 2003), but the fact that children with DCD obtained a similar score of correct inhibitions to controls suggests that the difference between groups in terms of the strength of connections from ACC to IPC was not related to the error rate on nogo responses. As discussed above, the ACC appears to be involved in preparation of the nogo motor response representation stored in the IPC. Interestingly, while the connection between ACC and IPC was increased in children with DCD compared to controls, the connection between MFC and ACC was decreased in children with DCD compared to controls. Garavan et al. (2002) also

reported opposite patterns of activation between MFC and ACC as function of difficulty for healthy adults to inhibit prepotent motor response. Using fMRI, they showed that the MFC was more intensely activated for easy inhibitions, while the ACC was more intensely activated for difficult inhibitions. They proposed that mechanisms of switching to the appropriate response over the prepotent motor response were engaged by the MFC when inhibition was relatively easy, while the ACC was more solicited when inhibition became more difficult. fMRI results obtained in adults performing dual paradigms support this proposal. As shown by Dreher and Grafman (2003), when individuals switched between two tasks, as compared to performing the two tasks simultaneously, activation was observed in the MFC. In contrast, when performing two tasks simultaneously, rather than in succession, activation was observed in the ACC. Kondo et al. (2004), studying connectivity in adults performing a dual task paradigm, demonstrated a similar dissociation in the strength of MFC–ACC and ACC–IPC connections to those observed between children with DCD and controls. Comparing good and poor performers for a dual task, the path coefficient from MFC to ACC was stronger in good performers than in poor performers, whereas the path coefficient from ACC to parietal cortex was stronger in poor performers than in good performers in the study by Kondo et al. (2004). In the study by Kondo et al., compared with the present study, effective connectivity of MFC–ACC–IPC appeared similar in children with DCD and poor performers, while connectivity was similar in healthy children and good performers for dual-tasks.

The results presented above suggest that connectivity in the MFC–ACC–IPC network could indicate that children with DCD are less able than healthy children to easily and/or promptly switch between go and nogo motor responses. However, children with DCD seem to compensate by more actively engaging the ACC to prevent commissions allowing maintenance of a good level of inhibition.

3.4. *Conclusion*

This first effective connectivity study devoted to DCD suggested that children with DCD engaged the same cerebral regions to perform a go–nogo task but in a different way than healthy children. Although these results must be interpreted cautiously due to the small sample size of children participating in the study, they appear coherent with previous proposals concerning the cerebral basis of DCD.

This effective connectivity study in children with DCD suggests that the inhibition cerebral network is engaged less efficiently than in healthy children. This could be due to abnormal maturation of cerebral lateralization for executive function in DCD, as children with DCD more actively engaged the left lateralized network, whereas controls more actively engaged the right lateralized network as reported in previous fMRI studies with healthy children performing a go–nogo task. This result supports the hypothesis proposed by Atwood and Cermak, (1986) and Flouris et al. (2005) that children with DCD could be characterized by an abnormal brain hemispheric specialization during development. Further investigations using a longitudinal methodology or comparing DCD groups at different ages need to be conducted to define the development of hemispheric specialization in DCD. The good level of inhibition demonstrated in children with DCD appears to be obtained at the cost of more top-down control exerted by the anterior component of the attentional and executive network, especially the ACC, on the posterior component network than in control children.

Other brain regions, such as the orbito frontal cortex, insula or cerebellum, not included in our reduced model, play an important role in attentional and executive functions. Future research may define how these regions are engaged in attention/inhibition in children with DCD. Future research will be conducted in order to reproduce the present results and examine whether effective connectivity in children with DCD differs from that observed in healthy children for cognitive functions other than attention/inhibition, such as spatial orientation of attention or the capacity to resist a distractor.

4. Experimental procedures

4.1. *Participants*

Children between the ages of 8 to 13 years referred to a multidisciplinary team of a paediatric neurology department and meeting the DSM-IV criteria for DCD were included. The evaluation included semistructured interview with the child and his or her parents, neurological examination, neuropsychological assessment including the Wechsler Intelligence Scale for Children (WISC-III), the Kaufman Assessment Battery for Children (K-ABC), the attention and executive functions and sensori-motor functions scales of the NEPSY, the Rey Complex Figure, and the Stroop test. Exclusion criteria were: history of neurological or psychiatric disorders other than DCD (children with Attention Deficit Hyperactivity Disorder Conduct Disorder, Oppositional Defiant Disorder or depressive symptoms have been discarded from the study), cerebral lesion documented by MRI or clinically suspected, pharmacologic medication and mental retardation (WISC-III verbal scale score $\leq$80). Typically, the global IQ of the WISC-III cannot be calculated for many children with DCD in reason of a large difference between performance and verbal scales (for a discussion of this point, see: Henderson and Barnett, 1998). All children demonstrated significant praxis and coordination deficits evaluated by clinic examination and sensory–motor scales of test batteries mentioned above (Criteria A of the DSM-IV). These impacted on their daily lives and/or academic performance, according to parent report (Criteria B). None had other medical, neurological conditions (Criteria C) or intellectual difficulties (Criteria D). Twelve children satisfying the criteria for DCD were initially included in the study but images of MRI scans for three of them were uninterpretable due to excessive movements during scan acquisition. Finally, fMRI analysis was performed in only 9 children with DCD and 10 control children (see Table 6 for demographic data and WISC-III scores and Table 7 for psychometric data of the DCD group).

4.2. *Go–nogo task*

The design of the go–nogo task was similar to the paradigm of Casey et al. (1997). The task required the participants to

Table 6 – Demographic data and WISC-III scores for control and DCD groups (mean value, standard deviation (SD), maximum (Max) and minimum (Min) values)

Demographic data and WISC-III scores							
Group	Gender	Age		Verbal IQ		Performance IQ	
		Mean (S.D.)	Max Min	Mean (S.D.)	Max Min	Mean (S.D.)	Max Min
DCD	2 females	9.9	12.9	102.1	126	75.6	97
	7 males	(1.8)	8.0	(19.1)	83	(13.8)	56
Control	3 females	10.0	11.6	116	135	110.5	130
	7 males	(1.1)	8.2	(24.4)	80	(16.2)	80

press a response key to any sequentially presented letter (go trial) except X (nogo trial). The task was run using SuperLab software (Cedrus Corporation) and responses were recorded by a Lumina LP-400 response pad (Cedrus Corporation). All letters including X subtended a vertical 2° visual angle and were displayed centrally for 500 ms. The task was composed of three conditions: (1) the "Go(s)" block consisted of 30 go trials with an Inter-Stimulus Interval (ISI) of 2000 ms, (2) the "Go–Nogo" block consisted of 15 go trials and 15 nogo trials in pseudo-random order with an ISI of 2000 ms, and (3) the "Go(r)" block consisted of 15 go trials with an ISI of 4000 ms. The Go–Nogo block involved the inhibition of a proponent motor response while Go(s) and Go(r) blocks constituted control tasks for the number of stimuli and for the number of motor responses, respectively. Control blocks were designed to verify that activations were not due to stimulus or motor artefacts. According to Casey et al. (1997), this design allows to isolate the cerebral regions involved in suppressing motor response (Go–Nogo) from those involved in stimulus encoding (Go(s)) or response execution (Go(r)). The duration of each block was 60 s. The total duration of the cognitive task was 6 min and 36 s including 12 s required for stabilization of the NMR signal. Before starting fMRI acquisitions, participants were trained by performing 30 trials of the Go–Nogo block (15 go trials and 15 nogo trials in pseudo-random order).

4.3. *Behavioral performance*

Response times less than 100 ms after presentation of the letter on go trials were considered to be anticipatory false responses and were excluded from the analysis. Student *t*-

Table 7 – Mean performance, standard deviation (S.D.), maximum (Max) and minimum (Min) scores obtained by the DCD group for the following cognitive abilities: [Left panel-A] Intelligence scores evaluated by the Verbal and Performance scales of the WISC-III, and the Sequential and Simultaneous scales of the K-ABC; [Middle panel-A] Visuospatial scores evaluated by the Visuospatial Processes scale of the NEPSY; [Right panel-A] Executive function and attentional scores evaluated by the Executive Function and Attentional scale of the NEPSY, and the Interference scale of the Stroop; [Panel-B] Sensori-motor score evaluated by the Copy scale of the Rey figure, the Sensory–motor scale of the NEPSY, the Dominant-Hand and Non-Dominant-Hand scale of the GROOVED PEGBOARD test, and the Dominant-Hand, Non-Dominant-Hand scale, Coordination and Assembly scales of the Purdue pegboard test

A	Intelligence score				Visuospatial score		Executive function attentional score
	WISC-III		K-ABC		NEPSY		Stroop
	Verbal	Performance	Sequential	Simultaneous	Visuospatial processing	Executive function attention	Interface
Mean (S.D.)	102.1 (19.1)	75.6 (13.8)	83.2 (20.9)	79.1 (14.1)	78.8 (14.7)	88.6 (10.7)	0.18 (0.79)
Max	126	97	106	109	97	110	1.19
Min	83	56	52	62	57	77	−0.95

B	Sensori-motor score							
	Rey figure	NEPSY	Grooved pegboard		Purdue pegboard			
	Copy	Sensori-Motor	Dominant hand	Nondominant hand	Dominant hand	Nondominant hand	Coordination	Assembly
Mean (S.D.)	−3.29 (2.50)	80.0 (12.2)	−1.01 (1.36)	−0.61 (1.16)	−1.94 (0.94)	−1.67 (0.41)	−2.32 (0.97)	−2.59 (1.01)
Max	−0.53	100	0.22	0.68	−1.00	−1.18	−0.90	−0.65
Min	−6.52	65	−4.04	−2.61	−3.88	−2.45	−3.74	−4.28

(Standard mean score was 100 and standard S.D. was 15 for the WISC-III, K-ABC and NEPSY tests; Standard mean score was 0 and standard S.D. was 1 for the Stroop, Rey figure, Grooved pegboard and Purdue pegboard tests).

tests were performed on Anticipations, Omissions (no response to a go trial), mean RT variability of RT (intra-individual standard deviation of RTs) for go trials on the mean of Go(s), Go–Nogo and Go(r) blocks. Student *t*-tests on Commissions, defined as go response to nogo trials, were performed for block Go–Nogo. *T*-tests were performed with group (DCD/Control) as a between factor.

4.4. *Scanning procedure*

Children were scanned through 2 alternating blocks of Go(s), Go(r) and No-Go conditions over a total of 6 periods. The order of conditions was counterbalanced to prevent possible order effect between subjects.

4.5. *fMRI data acquisition and data processing*

Neuroimaging data were acquired with a 1.5 Tesla whole body MRI system equipped with a head volume coil (Signa; General Electric Medical System, Milwaukee, WI). For each participant, a series of echo-planar functional images (EPI) was collected to provide functional images sensitive to Blood Oxygen Level Dependent (BOLD) contrast. Single-shot EPI acquisitions were performed using a typical T2*-weighted gradient-echo sequence. A total of 3472 images were then obtained for each experimental run, using twenty-eight 3.75-mm thick axial slices. One hundred and twenty-four EPI volumes with no gap were acquired (TR/TE = 3000/45 ms, flip angle = 90°, matrix = 64^2, FOV = 240^2 mm^2, isotropic voxel volume = 52.7 mm^3) for each functional imaging session. At the end of each functional run, a series of T1-weighted 3D anatomical images was collected to provide detailed anatomical data. Conventional 3D imaging consisted of SPGR sequence, matrix = 256^2, flip angle = 35°, TR/TE = 22/8 ms, FOV = 240^2 mm^2, 124 partitions — 1.5 mm thick.

Image processing was performed using Statistical Parametric Mapping (SPM5) software (Methodology group, Wellcome Department of Cognitive Neurology, London, UK: http://www.fil.ion.ucl.ac.uk//spm), and Structural Equation Modeling (SEM) analysis was performed using AMOS software (version 5.0.1, Copyright 1994–2003 SmallWaters Corp) (Arbuckle, 2003; Arbuckle and Wothke, 1999). The SPM univariate analysis served as a data reduction step in order to identify significantly activated voxels based on the meaningful single No-Go block versus Go(s) block contrast according to the subtraction method.

4.6. *Individual statistical parametric mapping*

For each subject, the first four scans were discarded; all EPI volumes were corrected to adjust for within-volume time differences and realigned to the last volume to correct for head movements. The functional scans were then spatially normalized into the standard stereotactic space of the Talairach atlas (Talairach and Tournoux, 1998). Spatial smoothing with an eight mm FWHM Gaussian kernel was performed. The hemodynamic responses were modeled as a box-car function convolved with a synthetic hemodynamic response function. A single subject, fixed-effects model analysis was performed for each individual subject in order to perform the based-group random-effect analysis and to prepare for extraction of BOLD signals. In each single subject analysis, a significance level of $p = 0.005$ was applied to detect activated voxels for the meaningful single Go–Nogo versus Go(s) contrast. Because the frequency of the stimuli presentation impacts highly on activations within the attentional brain network (Braver et al., 2001), we choose to present for fMRI results the Go–Nogo versus Go(s) contrast.

4.7. *Group statistical parametric mapping*

While fMRI data were analyzed in a "whole-brain" fashion, we constrained our study to specific hypotheses concerning the inferior parietal cortex (BA 40), middle frontal cortex (BA 46), anterior cingulate cortex (BA 32) and striatum. To facilitate the generation of future hypotheses for connectivity analysis, we also report data for activation clusters that fell outside of the hypothesized ROIs. At the group level, these regions were identified at the second (between-subjects) level using two one-sample *t*-test contrasts testing for activation in both DCD and Control groups with *p* values statistically corrected for multiple comparisons. Local maxima were located within the predefined anatomical regions and then assigned to a Talairach coordinate and a Brodmann area. Anatomical labels for coordinates in SPM5 (MNI brain template) were defined by Talairach Daemon (http://www.ric.uthscsa.edu/projects/talairachdaemon.html) after non-linear transform of MNI brain template to Talairach atlas (http://www.mrc-cbu.cam.ac.uk/Imaging).

4.8. *Region selection for SEM analysis*

Four brain regions in left hemisphere and right hemisphere were selected based on prior knowledge of their interaction in an attentional network and activation or functional connectivity (Stevens et al., 2007; Watanabe et al., 2002). The selected regions were inferior parietal cortex (BA 40), middle frontal cortex (BA 46), anterior cingulate cortex (BA 32) and striatum. Eight millimeters radius spherical masks were placed in each subject at the chosen coordinates, which were guided by two lines of inquiry: (1) previously published locations (Stevens et al., 2007; Watanabe et al., 2002) and (2) coordinates of highest activation in our own population of subjects, as ascertained by the second level random-effect analysis.

Local maxima within the predefined areas and BOLD signals extracted for SEM analysis were identified for each subject and each region of interest (ROI) in left hemisphere and right hemisphere. The weighted mean signal extraction was performed separately in each area. BOLD signals were thereafter normalized and concatenated to allow comparison of BOLD signals across subjects and groups.

4.9. *Path model construction and structural equation modeling*

The path model used in this study is based on a hypothesized network restricted to four topologically distinct brain regions localized in left hemisphere and right hemisphere (Fig. 2): inferior parietal cortex (IPC), middle frontal cortex (MFC), anterior cingulate cortex (ACC) and striatum (STRIA). We used SEM to construct a path model that could account for fMRI data in all regions of interest (ROIs) for the No-Go condition.

Adjusted signals in the four regions of left hemisphere and right hemisphere extracted from the data set were entered as variables. The structural model was assessed by minimizing the difference between observed and predicted covariances of the fMRI data according to the maximum-likelihood algorithm. In this analysis, the variables are considered in terms of the covariance structure.

Typically, in SEM, comparison between groups consists of a comparison of models. Stacked matrices, in which the elements are composed of variances and covariances, are considered for each group. In this approach, constraints, usually equality constraints, are introduced into estimations of the parameters. For example, the estimate of the values of a path coefficient can be constrained to be equal in the various groups. The group comparison therefore amounts to a comparison between a constrained (fixed parameters) and a non-constrained (free parameters) model. In a non-constrained model, there is one value for each path coefficient and each group. In the constrained model used for group comparison, there is only one value for each parameter common to all groups. The model-comparison process is as follows. First, the algorithm estimates the specific parameter values for each group. The fit of the non-constrained model is examined to ensure that the hypothesized causality network can account for the data. The parameters in the constrained model are forced to equality for each of the two groups. If the groups differ in terms of path connectivity, then the non-constrained model is assumed to provide a better fit than the constrained model. In other words, if the fit of the constrained model (using common values for the parameters) is not significantly different from the fit of the unconstrained model (using specific/different values for the parameters in each group), this test allows us to conclude that the differences between groups must be taken into consideration to model the covariance matrix.

Since the constrained model is nested in the non-constrained model, the χ^2 of the difference between the χ^2 of the two models can be used to test the significance of the difference. If this test is statistically significant, then we can conclude that there is a difference between the parameters (i.e. the causal pathways) between the two groups. In order to account for the overall difference found, if any, each pair of parameters can be compared (pairwise comparison). The test used, which follows a Z distribution, is based on the differences between the parameter values divided by the standard error of measurement of these differences (Arbuckle, 2003).

A set of indicators was used to assess the goodness of fit of the model to the data. Each indicator provides different aspects of goodness of fit. This type of approach using several indicators has been largely validated by simulation studies (Hu and Bentler, 1999). The test based on the minimization function χ^2 or test of exact fit was used. The RMSEA (Root Mean Square Error of Approximation) or test of close fit is particularly important because it is relatively independent of the sample size and the number of parameters used in the model (Browne and Cudeck, 1993). SRMR (Standardized Root Mean Square Residual) and GFI (Goodness of Fit Index, (Jöreskog and Sörbom, 2000) were also used to provide an estimation of the part of variance explained by the model. In addition, TLI (Tucker and Lewis Index in Bentler and Bonett, 1980) was used to provide an estimation of the improvement of the data fit provided by the model tested with regard to the independence model.

REFERENCES

Aersten, A., Preissl, H., 1991. Dynamics of activity and connectivity in physiological neuronal networks. In: Schuster, H.G. (Ed.), Non Linear Dynamics and Neuronal Networks. VCH Publishers Inc, New York, pp. 281–302.

Allin, M., Matsumoto, H., Santhouse, A., Nasarti, C., AlAsady, M.H., Stewart, A.L., et al., 2001. Cognitive and motor function and the size of the cerebellum in adolescents born very preterm. Brain 124 (1), 60–66.

American Psychiatric Association, 1994. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, (4th ed.). Author, Washington, DC.

Arbuckle, J.L., 2003. Amos 5.0 Update to the Amos User's Guide. SmallWaters Corporation, Chicago.

Arbuckle, J.L., Wothke, W., 1999. Amos 4.0 User's Guide. SmallWaters Corporation, Chicago.

Aron, A.R., Poldrack, R.A., 2006. Cortical and subcortical contributions to stop signal response inhibition: role of the subthalamic nucleus. J. Neurosci. 26 (9), 2424–2433.

Arthurs, O.J., Boniface, S., 2002. How well do we understand the neural origins of the fMRI BOLD signal. Trends Neurosci. 25, 27–31.

Atwood, R.M., Cermak, S.A., 1986. Crossing the midline as a function of distance from midline. Am. J. Occup. Ther. 40 (10), 685–690.

Barnhart, R.C., Davenport, M.J., Epps, S.B., Nordquist, V.M., 2003. Developmental coordination disorder. Phys. Ther. 83 (8), 722–731.

Bentler, P.M., Bonett, D.G., 1980. Significance tests and goodness of fit in the analysis of covariance structure. Psychol. Bull. 88 (3), 588–606.

Bentler, P., Freeman, E., 1983. Tests for stability in linear structural equation systems. Psychometrika 48 (1), 143–145.

Booth, J.R., Burman, D.D., Meyer, J.R., Lei, Z., Trommer, B.L., Davenport, N.D., et al., 2003. Neural development of selective attention and response inhibition. Neuroimage 20 (2), 737–751.

Botvinick, M.M., Cohen, J.D., Carter, C.S., 2004. Conflict monitoring and anterior cingulate cortex: an update. Trends Cogn. Sci. 8 (12), 539–546.

Braver, T.S., Barch, D.M., Gray, J.R., Molfese, D.L., Snyder, A., 2001. Anterior cingulate cortex and response conflict: effects of frequency, inhibition and errors. Cereb. Cortex. 11 (9), 825–836.

Brown, J.W., Bullock, D., Grossberg, S., 2004. How laminar frontal cortex and basal ganglia circuits interact to control planned and reactive saccades. Neural Netw. 17 (4), 471–510.

Browne, H.W., Cudeck, R., 1993. Alternative ways of assessing model fit. In: Bollen, K.A., Long, J.S. (Eds.), Testing Structural Equations Models. Sage Publications, Newbury Park, CA , pp. 136–162.

Buchel, C., Friston, K., 2000. Assessing interactions among neuronal systems using functional neuroimaging. Neural Netw. 13 (8–9), 871–882.

Buchsbaum, B.R., Greer, S., Chang, W.L., Berman, K.F., 2005. Meta-analysis of neuroimaging studies of the Wisconsin card-sorting task and component processes. Hum. Brain Mapp. 25 (1), 35–45.

Bunge, S.A., 2004. How we use rules to select actions: a review of evidence from cognitive neuroscience. Cogn. Affect Behav. Neurosci. 4 (4), 564–579.

Bunge, S.A., Hazeltine, E., Scanlon, M.D., Rosen, A.C., Gabrieli, J.D., 2002. Dissociable contributions of prefrontal and parietal cortices to response selection. Neuroimage 17 (3), 1562–1571.
Casey, B.J., Trainor, R.J., Orendi, J.L., Schubert, A.B., Nystrom, L.E., Giedd, J.N., et al., 1997. A developmental functional MRI study of prefrontal activation during performance of a go–no-go task. J. Cogn. Neurosci. 9 (6), 835–847.
Chang, B.S., Walsh, C.A., 2003. Mapping form and function in the human brain: the emerging field of functional neuroimaging in cortical malformations. Epilepsy Behav. 4 (6), 618–625.
Cohen, J., 1992. A power primer. Psychol. Bull. 112 (1), 155–159.
Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. Neurosci. 3 (3), 201–215.
Cousins, M., Smyth, M.M., 2003. Developmental coordination impairments in adulthood. Hum. Mov. Sci. 22 (4–5), 433–459.
Dalla Piazza, S., 1997. L'enfant premature: le point sur la question. De Boeck Université, Bruxelles.
de Castelnau, P., Albaret, J.M., Chaix, Y., Zanone, P.G., 2007. Developmental coordination disorder pertains to a deficit in perceptuo-motor synchronization independent of attentional capacities. Hum. Mov. Sci. 26 (3), 477–490.
Dewey, D., Kaplan, B.J., Crawford, S.G., Wilson, B.N., 2002. Developmental coordination disorder: associated problems in attention, learning, and psychosocial adjustment. Hum. Mov. Sci. 21 (5–6), 905–918.
Dias, E.C., McGinnis, T., Smiley, J.F., Foxe, J.J., Schroeder, C.E., Javitt, D.C., 2006. Changing plans: neural correlates of executive control in monkey and human frontal cortex. Exp. Brain Res. 174 (2), 279–291.
Dreher, J.C., Grafman, J., 2003. Dissociating the roles of the rostral anterior cingulate and the lateral prefrontal cortices in performing two tasks simultaneously or successively. Cereb. Cortex 13 (4), 329–339.
Durston, S., Thomas, K.M., Worden, M.S., Yang, Y., Casey, B.J., 2002. The effect of preceding context on inhibition: an event-related fMRI study. Neuroimage 16 (2), 449–453.
Durston, S., Tottenham, N.T., Thomas, K.M., Davidson, M.C., Eigsti, I.M., Yang, Y., 2003. Differential patterns of striatal activation in young children with and without ADHD. Biol. Psychiatry 53 (10), 871–878.
Durston, S., Mulder, M., Casey, B.J., Ziermans, T., van Engeland, H., 2006. Activation in ventral prefrontal cortex is sensitive to genetic vulnerability for attention-deficit hyperactivity disorder. Biol. Psychiatry 60 (10), 1062–1070.
Flouris, A.D., Faught, B.E., Hay, J., Cairney, J., 2005. Exploring the origins of developmental disorders. Dev. Med. Child Neurol. 47 (7), 436.
Friston, K., 1994. Functional and effective connectivity in neuroimaging: a synthesis. Hum. Brain Mapp. 2 (1–2), 56–78.
Fujii, Y., Konishi, Y., Kuriyama, M., Maeda, M., Saito, M., Ishii, Y., 1993. MRI assessment of myelination patterns in high risk infants. Pediatr. Neurol. 9 (3), 194–197.
Funnell, M., Gazzaniga, M., Garavan, H., 2004. Hemispheric lateralization of inhibitory control and task set in splitbrain patients. Cognitive Neuroscience Society Annual Meeting (April 2004: San Francisco).
Garavan, H., Ross, T.J., Murphy, K., Roche, R.A., Stein, E.A., 2002. Dissociable executive functions in the dynamic control of behavior: inhibition, error detection, and correction Neuroimage 17 (4), 1820–1829.
Garavan, H., Ross, T.J., Kaufman, J., Stein, E.A., 2003. A midline dissociation between error-processing and response-conflict monitoring. Neuroimage 20 (2), 1132–1139.
Garavan, H., Hester, R., Murphy, K., Fassbender, C., Kelly, C., 2006. Individual differences in the functional neuroanatomy of inhibitory control. Brain Res. 1105 (1), 130–142.
Gitelman, D.R., 2003. Attention and its disorders. Br. Med. Bull. 65, 21–34.
Glabus, M.F., Horwitz, B., Holt, J.L., Kohn, P.D., Gerton, B.K., Callicott, J.H., et al., 2003. Interindividual differences in functional interactions among prefrontal, parietal and parahippocampal regions during working memory. Cereb. Cortex 13 (12), 1352–1361.
Groenewegen, H.J., 2003. The basal ganglia and motor control. Neural Plast. 10 (1–2), 107–120.
Henderson, S.E., Barnett, A.L., 1998. The classification of specific motor coordination disorders in children: some problems to be solved. Hum. Mov. Sci. 17 (4), 449–469.
Hester, R., Garavan, H., 2004. Executive dysfunction in cocaine addiction: evidence for discordant frontal, cingulate, and cerebellar activity. J. Neurosci. 24 (49), 11017–11022.
Horn, N.R., Dolan, M., Elliott, R., Deakin, J.F., Woodruff, P.W., 2003. Response inhibition and impulsivity: an fMRI study Neuropsychologia 41 (14), 1959–1966.
Hu, L., Bentler, P.M., 1999. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. Struct. Equ. Modeling 6 (1), 1–55.
Ivry, R.B., 2003. Cerebellar involvement in clumsiness and other developmental disorders. Neural Plast. 10 (1–2), 141–153.
Jöreskog, K.G., Sörbom, D., 2000. LISREL 8.5 User's Reference Guide. Scientific Software International, Chicago, Ill.
Koechlin, E., Summerfield, C., 2007. An information theoretical approach to prefrontal executive function. Trends Cogn. Sci, 11 (6), 229–235.
Kondo, H., Osaka, N., Osaka, M., 2004. Cooperation of the anterior cingulate cortex and dorsolateral prefrontal cortex for attention shifting. Neuroimage 23 (2), 670–679.
Koski, L., Paus, T., 2000. Functional connectivity of the anterior cingulate cortex within the human frontal lobe: a brain-mapping meta-analysis. Exp. Brain Res. 133 (1), 55–65.
LaBerge, D., 1997. Attention, awareness, and the triangular circuit. Conscious Cogn. 6 (2–3), 149–181.
Laubach, M., 2005. Who's on first? What's on second? The time course of learning in corticostriatal systems. Trends Neurosci. 28 (10), 509–511.
Leh, S.E., Ptito, A., Chakravarty, M.M., Strafella, A.P., 2007. Fronto-striatal connections in the human brain: a probabilistic diffusion tractography study. Neurosci. Lett. 419 (2), 113–118.
Logothetis, N.K., Pauls, J., Augath, M., Trinath, T., Oeltermann, A., 2001. Neurophysiological investigation of the basis of the fMRI signal. Nature 412, 150–757.
Lütcke, H., Frahm, J., 2008. Lateralized anterior cingulate function during error processing and conflict monitoring as revealed by high-resolution fMRI. Cereb. Cortex. 18 (3), 508–515.
Makris, N., Kennedy, D.N., McInerney, S., Sorensen, A.G., Wang, R., Caviness, V.S., 2005. Segmentation of subcomponents within the superior longitudinal fascicle in humans: a quantitative, in vivo, DT-MRI study. Cereb Cortex. 15 (6), 854–869.
Mandich, A., Buckolz, E., Polatajko, H., 2002. On the ability of children with developmental coordination disorder (DCD) to inhibit response initiation: the Simon effect. Brain Cogn. 50 (1), 150–162.
Mandich, A., Buckolz, E., Polatajko, H., 2003. Children with developmental coordination disorder (DCD) and their ability to disengage ongoing attentional focus: more on inhibitory function. Brain Cogn. 51 (3), 346–356.
Mathalon, D.H., Whitfield, S.L., Ford, J.M., 2003. Anatomy of an error: ERP and fMRI. Biol. Psychol. 64 (1–2), 119–141.
Mazeau, M., 1995. Déficits visuo-spatiaux et dyspraxies de l'enfant atteint de lésion cérébrales précoces. Masson, Paris.
McIntosh, A., Gonzalez-Lima, F., 1994. Structural equation modeling and its application to network analysis in functional brain imaging. Hum. Brain Mapp. 2, 2–22.
Mellier, D., Fernandez-Berani, L., Fessard, C., 1999. Devenir à 6 ans d'enfants grands prématurés. Enfance 1, 67–78.
Menon, V., Adleman, N.E., White, C.D., Glover, G.H., Reiss, A.L., 2001. Error-related brain activation during a Go/NoGo response inhibition task. Hum. Brain Mapp. 12 (3), 131–143.

Mesulam, M.M., 1999. Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. Philos. Trans. R Soc. Lond. B Biol. Sci. 354 (1387), 1325–1346.
Miller, E.K., Cohen, J.D., 2001. An integrative theory of prefrontal cortex function. Annu. Rev Neurosci. 24, 167–202.
Mink, J.W., 1996. The basal ganglia: focused selection and inhibition of competing motor programs. Prog. Neurobiol. 50 (4), 381–425.
Nakano, K., 2000. Neural circuits and topographic organization of the basal ganglia and related regions. Brain Dev. 22, S5–S16.
Pandya, D.N., Van Hoesen, G.W., Mesulam, M.M., 1981. Efferent connections of the cingulate gyrus in the rhesus monkey. Exp. Brain Res. 42 (3–4), 319–330.
Peterson, B.S., Vohr, B., Staib, L.H., Cannistraci, C.J., Dolberg, P., Schneider, K.C., et al., 2000. Regional brain volume abnormalities and long-term cognitive outcome in preterm infants. JAMA 284 (15), 1939–1947.
Petrides, M., Pandya, D.N., 2006. Efferent association pathways originating in the caudal prefrontal cortex in the macaque monkey. J. Comp. Neurol. 498 (2), 227–251.
Picard, N., Strick, P.L., 2001. Imaging the premotor areas. Curr. Opin. Neurobiol. 11 (6), 663–672.
Piek, J.P., Dyck, M.J., Nieman, A., Anderson, M., Hay, D., Smith, L.M., et al., 2004. The relationship between motor coordination, executive functioning and attention in school aged children. Arch. Clin. Neuropsychol. 19 (8), 1063–1076.
Poldrack, R.A., Clark, J., Pare-Blagoev, E.J., Shohamy, D., Creso Moyano, J., Myers, C., et al., 2001. Interactive memory systems in the human brain. Nature 414 (6863), 546–550.
Porter, B.E., Brooks-Kayal, A., Golden, J.A., 2002. Disorders of cortical development and epilepsy. Arch. Neurol. 59 (3), 361–365.
Posner, M.I., Petersen, S.E., 1990. The attention system of the human brain. Annu. Rev. Neurosci. 13, 25–42.
Ridderinkhof, K.R., van den Wildenberg, W.P., Segalowitz, S.J., Carter, C.S., 2004. Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. Brain Cogn. 56 (2), 129–140.
Rieger, M., Gauggel, S., Burmeister, K., 2003. Inhibition of ongoing responses following frontal, nonfrontal, and basal ganglia lesions. Neuropsychology 17 (2), 272–282.
Saugstad, L.F., 1998. Cerebral lateralisation and rate of maturation. Int. J. Psychophysiol. 28 (1), 37–62.
Saugstad, L.F., 1999. A lack of cerebral lateralization in schizophrenia is within the normal variation in brain maturation but indicates late, slow maturation. Schizophr. Res. 39 (3), 183–196.
Schlösser, R.G., Wagner, G., Sauer, H., 2006. Assessing the working memory network: studies with functional magnetic resonance imaging and structural equation modeling Neuroscience 139 (1), 91–103.
Schmahmann, J.D., Pandya, D.N., Wang, R., Dai, G., D'Arceuil, H.E., de Crespigny, A.J., et al., 2007. Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. Brain 130 (3), 630–653.
Shmuel, A., Augath, M., Oeltermann, A., Logothetis, N.K., 2006. Negative functional MRI response correlates with decreases in neuronal activity in monkey visual area V1. Nat. Neurosci. 9, 569–577.
Simmonds, D.J., Fotedar, S.G., Suskauer, S.J., Pekar, J.J., Denckla, M.B., Mostofsky, S.H., 2007. Functional brain correlates of response time variability in children. Neuropsychologia 45 (9), 2147–2157.
Skranes, J.S., Vik, T., Nilsen, G., Smevik, O., Andersson, H.W., Rinck, P., et al., 1993. Cerebral magnetic resonance imaging (MRI) and mental and motor function of very low birth weight infants at one year of corrected age. Neuropediatrics 24 (5), 256–262.
Smith, A.B., Taylor, E., Brammer, M., Toone, B., Rubia, K., 2006. Task-specific hypoactivation in prefrontal and temporoparietal brain regions during motor inhibition and task switching in medication-naive children and adolescents with attention deficit hyperactivity disorder. Am. J. Psychiatry 163 (6), 1044–1051.
Smits-Engelsman, B.C., Wilson, P.H., Westenberg, Y., Duysens, J., 2003. Fine motor deficiencies in children with developmental coordination disorder and learning disabilities: an underlying open-loop control deficit. Hum. Mov. Sci. 22 (4–5), 495–513.
Stevens, M.C., Kiehl, K.A., Pearlson, G.D., Calhoun, V.D., 2007. Functional neural networks underlying response inhibition in adolescents and adults. Behav. Brain Res. 181 (1), 12–22.
Stewart, A.L., Rifkin, L., Amess, P.N., Kirkbride, V., Townsend, J.P., Miller, D.H., et al., 1999. Brain structure and neurocognitive and behavioral function in adolescents who where born very preterm. Lancet 353 (9165), 1653–1657.
Talairach, J., Tournoux, P., 1998. Co-Planar Stereotaxic Atlas of the Human Brain: 3-Dimensional Proportional System: An Approach to Cerebral Imaging. Medical Publisher, New-York.
Tamm, L., Menon, V., Reiss, A.L., 2002. Maturation of brain function associated with response inhibition. J. Am. Acad. Child Adolesc. Psyc. 41 (10), 1231–1238.
Tamm, L., Menon, V., Ringel, J., Reiss, A.L., 2004. Event-related fMRI evidence of frontotemporal involvement in aberrant response inhibition and task switching in attention-deficit/hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry 43 (11), 1430–1440.
Tracy, J.I., Faro, S.S., Mohammed, F., Pinus, A., Christensen, H., Burkland, D., 2001. A comparison of 'Early' and 'Late' stage brain activation during brief practice of a simple motor task. Cogn. Brain Res. 10 (3), 303–316.
Van Der Graaf, F.H., De Jong, B.M., Maguire, R.P., Meiners, L.C., Leenders, K.L., 2004. Cerebral activation related to skills practice in a double serial reaction time task: striatal involvement in random-order sequence learning. Brain Res. Cogn. Brain Res. 20 (2), 120–131.
Visser, J., 2003. Developmental coordination disorder: a review of research on subtypes and comorbidities. Hum. Mov. Sci. 22 (4–5), 479–493.
Vogt, B.A., Pandya, D.N., 1987. Cingulate cortex of the rhesus monkey: II. Cortical afferents. J. Comp. Neurol. 262 (2), 271–289.
Waldvogel, D., van Gelderen, P., Muellbacher, W., Ziemann, U., Immisch, I., Hallett, M., 2000. The relative metabolic demand of inhibition and excitation. Nature 406, 995–998.
Watanabe, J., Sugiura, M., Sato, K., Sato, Y., Maeda, Y., Matsue, Y., et al., 2002. The human prefrontal and parietal association cortices are involved in NO-GO performances: an event-related fMRI study. Neuroimage 17 (3), 1207–1216.
Weber, J.T., Yin, T.C.T., 1984. Subcortical projections of the inferior parietal cortex (area 7) in the stump-tailed monkey. J. Comp. Neurol. 224, 206–230.
Wilmut, K., Brown, J.H., Wann, J.P., 2007. Attention disengagement in children with developmental coordination disorder. Disabil. Rehabil. 29 (1), 47–55.
Wilson, P.H., Maruff, P., 1999. Deficits in the endogenous control of covert visuospatial attention in children with developmental coordination disorder. Hum. Mov. Sci. 18, 421–442.
Wilson, P.H., Maruff, P., McKenzie, B.E., 1997. Covert orienting of visuospatial attention in children with developmental coordination disorder. Dev. Med. Child Neurol. 39 (11), 736–745.
Wilson, P.H., Maruff, P., Lum, J., 2003. Procedural learning in children with developmental coordination disorder. Hum. Mov. Sci. 22 (4–5), 515–526.