Brain Connectomics of Visual-Motor Deficits in Children with Developmental Coordination Disorder

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Objective To extend preliminary findings on associated white matter deficits and structural connectivity in children with developmental coordination disorder (DCD).

Study design Diffusion magnetic resonance imaging-based tractography was used to identify abnormal microstructural properties of specific sensorimotor white matter tracts in 21 children with DCD between 8 and 10 years of age and 20 age- and sex-matched typically developing controls. Graph theoretical analyses were applied to evaluate whole brain connectomics. Associations were also calculated between the tractography/connectome results and visual-motor performance, as measured with the Beery-Buktenica Developmental Test of Visual Motor Integration.

Results Significant positive correlations were obtained between visual-motor trace scores and fractional anisotropy (FA) in the retrolenticular limb of the internal capsule within the group with DCD. Moreover, lower FA in sensorimotor tracts and altered structural connectivity were observed for children with DCD. Compared with controls, subjects with DCD showed decreases in clustering coefficient, and global and local efficiency, suggesting weaker structural network segregation and integration. The degree of decreased global efficiency was significantly associated with poor visual-motor tracing outcomes, above and beyond FA reductions. Specifically, nodal efficiency at the cerebellar lobule VI and right parietal superior gyrus were found significant predictors to discriminate between children with DCD and those with typical development.

Conclusions Specific white matter alterations and network topology features associate with visual-motor deficits and DCD diagnosis indicating the clinical potential of diffusion magnetic resonance imaging-based metrics for diagnosing DCD. *(J Pediatr 2016;169:21-7)*.

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Developmental coordination disorder (DCD) is a neuromotor developmental disorder that significantly interferes with a child's daily activities that require adequate visual-motor skills.[1] DCD affecting quality of life and well-being has a prevalence of approximately 1.8%. Although neuroimaging research on DCD has extended in recent years, the neuropathology of DCD remains poorly understood and is, hence, lacking diagnostic markers.[2]

Brain connectivity has been investigated in DCD, most commonly using functional magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI).[3-9] Functional MRI studies have demonstrated widespread and task-specific activation differences coinciding with DCD-related sensorimotor, as well as cognitive performance difficulties.[2,10] According to recent reviews, data remains lacking on the influence of structural white matter alterations to visual-motor impairment in children with DCD.[10,11] Current evidence suggests altered microstructural development of sensory and motor pathways in children with DCD.[5,9] A pilot study found indications of lower mean diffusivity of the posterior corticospinal tract and posterior thalamic radiation in children with DCD relative to typically developing controls.[9] Alternatively, network-based metrics of structural connectivity can be more sensitive to alterations that are less apparent in gross structure (ie, white matter integrity) because they consider each region's integration into the global unit rather than as an independent entity.

Beery VMI	Beery-Buktenica Developmental Test of Visual Motor Integration
DCD	Developmental coordination disorder
DTI	Diffusion tensor imaging
FA	Fractional anisotropy
MABC-2	Movement Assessment Battery for Children, Second Edition
MRI	Magnetic resonance imaging
PIQ	Performance IQ
RD	Radial diffusivity
TIQ	Total IQ
VIQ	Verbal IQ

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This study aimed to investigate the structural organization of the white matter networks in a group with DCD and typically developing children. Structural connectivity decreases in the group with DCD vs typically developing children were expected to manifest in diffusion MRI metrics of sensorimotor pathways[9] and graph theoretical network metrics assessing overall structural connectivity. Significant decreases in structural connectivity were hypothesized to correlate with deficits of visual-motor performance as well as the DCD diagnosis.

Methods

All 8- to 10-year-old participants were recruited using approved advertisements placed in schools and ambulatory rehabilitation centers. For inclusion, children had to be otherwise healthy, with no history of psychiatric or developmental disorders other than DCD. A pediatrician performed a physical and neurologic examination to rule out other possible causes of motor incoordination. Study permission was obtained from the ethics commission of Ghent University. Written informed consent was acquired from legal guardians and child assent before testing.

Diagnoses of DCD and typical development were supported by direct interview of the child and parents together using a clinical questionnaire (parent version of the Movement Assessment Battery for Children, Second Edition [MABC-2] checklist), and assessment of the MABC-2.[12] Children with DCD were included only with a MABC-2 performance ≤5th percentile.[1] Typically developing children were excluded from participation in case of an MABC-2 score ≤16th percentile.

DCD symptom presence in activities of daily living was confirmed by the MABC-2 checklist. All children had to obtain an estimated total IQ (TIQ) of ≥85 using the *Wechsler Intelligence Scale for Children, Third Edition* (Dutch version).[13] TIQ was calculated using averaged standardized scores of performance (block design and picture arrangement) and verbal (word similarities and comprehension) intelligence subtests. Performance IQ (PIQ) and verbal IQ (VIQ) resulted from averaging standardized scores on the performance and verbal intelligence subtests.

Visual-Motor Skill Assessments

Visual-motor skills were comprehensively assessed using the Beery-Buktenica Developmental Test of Visual Motor Integration (Beery VMI), which is a valid clinical test battery with age-norm references.[14] The Beery VMI copy and Beery VMI trace test were administered as well as a as a motor-free control test (Beery VMI visual discrimination).

MRI and Diffusion Tensor MRI Data

Standard protocols were used for high-resolution T1, and DTI to assess white matter disruption. MRI examination took place without sedation on a 3T Siemens Magnetom Trio MRI scanner system (Siemens Medical Systems, Erlangen, Germany) with an 8-channel phased-array head coil. A diffusion weighted single shot spin-echo echoplanar imaging run was acquired with data acquisition matrix = 96 × 96; field of view = 190 × 190 mm^2; repetition time = 9900 ms, echo time = 102 ms, and 60 contiguous sagittal slices (slice thickness = 2.0 mm; voxel size = 2.0 × 2.0 × 2.0 mm^3) covering the entire brain.[15] Diffusion gradients were applied along 30 noncollinear directions with a *b*-value of 1400 s/mm. In addition, a set of images with no diffusion weighting $b = 0$ s/mm was acquired. Moreover, for all subjects, high-resolution T1-weighted structural images were collected in the sagittal plane (176 slices with parameters: repetition time = 1550 ms, echo time = 2.39 ms, image acquisition matrix = 256 × 256, field of view = 220 × 220 mm^2, flip angle = 9°, slice thickness = 0.9 mm, distance factor = 50%, voxel size = 0.9 × 0.9 × 0.9 mm^3 [resized to 1 × 1 × 1 mm^3]).

DTI data were analyzed and processed in ExploreDTI,[16] as previously described.[17,18] The DTI processing consisted of subject motion and eddy-current induced geometrical distortions correction[19] and diffusion tensor estimation using a nonlinear regression procedure.[20] Fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity were calculated in a selected set of afferent and efferent pathways, considered important for visual motor integration and eye-hand coordination.[21]

Network Construction and Graph Analyses

Brain networks were reconstructed using identical procedures as in previous studies.[22,23] A deterministic streamline fiber tractography approach was applied on each individual dataset.[24] Seed points were defined at 2 mm isotropic resolution. For defining pathways, the main diffusion direction (as defined by the principal eigenvector) was tracked until entering a voxel with FA <0.20 or high angular turn (angle >45 degrees). The step size was set at 1 mm. The resulting whole-brain fiber tract reconstructions were parcellated using the automated anatomical labeling atlas.[25] Interregional connectivity was examined by determining the percentage of tracts (number of fiber connections normalized for the total number of tracts) between any 2 masks (ie, any 2 of 116 regions of the anatomical labeling atlas template). This value became the edge weight in the connectivity matrix. Besides this weighted matrix, an unweighted binary network was constructed with all nonzero weights set to 1 and to 0 otherwise.[26] For every individual data set, these different kinds of white matter networks ("percentage of tracts" and binary) were constructed, each of which was represented by a symmetric 116 × 116 matrix.

The properties of the structural network were investigated at the global and regional (nodal) levels using the Brain Connectivity Toolbox.[27] Standard global graph theoretical network metrics included characteristic path length, mean clustering coefficient, global efficiency, "small-world network," normalized path length (λ), and normalized clustering coefficient (γ). We also calculated regional efficiency (ie, global efficiency computed for each node) as a standard nodal connectivity measure.[28]