Developmental Coordination Disorder: Disruption of the Cerebello-Cerebral Network evidenced by SPECT

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Conflict of Interest Notification Page

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Abstract

Little is known about the neurobiological substrate of developmental coordination disorder (DCD), a neuro-developmental syndrome with significant, negative impact on the motor, cognitive and affective level throughout lifespan. This paper reports the clinical, neurocognitive and neuroradiological findings of a 19-year-old patient with typical DCD. As demonstrated by mild ataxia and a close semiological correspondence with the recently acknowledged 'cerebellar cognitive affective syndrome', clinical and neurocognitive investigations unambiguously indicated functional disruption of the cerebellum. Structural MRI of the brain confirmed cerebellar involvement revealing a slight anterior/superior asymmetry of vermal fissures consistent with rostral vermisdysplasia. Although this abnormality of vermal fissuration is generally considered an incidental neuroradiological finding without any clinical relevance a potentially subtle impact on the developmental level has never been formally excluded. In addition to a generally decreased perfusion of the cerebellum, a quantified Tc-99m-ECD SPECT disclosed functional suppression of the anatomoclinically suspected supratentorial regions involved in the execution of planned actions, visuo-spatial processing and affective regulation. Based on these findings it is hypothesized that the cerebellum is crucially implicated in the pathophysiologcial mechanisms of DCD, reflecting disruption of the cerebello-cerebral network involved in the execution of planned actions, visuo-spatial cognition and affective regulation.

Key Words: Cerebellum, developmental coordination disorder, apraxia, executive function, planning, SPECT

Introduction

Developmental coordination disorder (DCD) has an estimated incidence of 5% and can thus be regarded as a common developmental disorder in school-aged children. The condition is typically characterized by difficulties in acquiring motor skills, sensorimotor coordination disturbances, deficient postural control, strategic planning problems, disrupted visuo-spatial information processing and executive dysfunction and has a significant negative impact throughout lifespan [1]. Affective, behavioural and social disturbances often accompany DCD [2].

As this condition constitutes a prominent motor function and visuo-spatial disorder, various studies have advanced the hypothesis that the basal ganglia, the parietal lobe, and also the cerebellum might be crucially implicated in its pathogenesis. Although the bulk of clinical evidence refers to the cerebellum as the main source of neuropathology in patients with DCD, the neurobiological search for its pathophysiological substrate has attracted only limited attention [3,4]. Apart from one study in which two children with DCD were examined with evoked potentials and CT [5] and one study in which nine children with DCD were examined with functional MRI [6], no other studies have been performed to investigate the neural correlates of DCD.

Given the paucity of neurobiological research on DCD, its exact pathophysiological mechanisms remains to be elucidated. To the best of our knowledge, this study is the first in which a semiologically typical patient with DCD was studied with structural and functional neuroimaging in addition to in-depth neurocognitive investigations.

Case Report

A 19-year-old left-handed woman who was diagnosed with DCD at the age of 14, was referred to our department because little progress had been made after 5 years of psychomotor therapy. Besides delayed acquisition of motor milestones, there had been a delayed onset (around age 3) and

subsequent deviant development of speech which had been diagnosed as developmental apraxia of speech (DAS). For several years she had undergone physiotherapy and speech therapy. At the age of 14 years she had also been treated with psychotherapy because of behavioural and affective problems, including avoidance of social contacts, difficulties to establish and maintain peer relationships, significantly decreased self-esteem with strong feelings of worthlessness, anxiety and depressed mood. At the age of 19 years her near relatives and peers still described her to have difficulties in establishing social contacts, as unable to maintain close relationships because of low self-esteem and emotional instability with sporadic outbursts of verbal agression. Medical history was unremarkable. Family history was negative for developmental disorders and learning disabilities. She successfully finished secondary school and was trained as kindergarten teacher.

Detailed clinical neurological examination in which cerebellar functionality was studied with the Brief Ataxia Rating Scale (BARS) revealed very mild ataxia, reflected by a total score of 4/30 [7]. Tandem gait was not possible but normal naturally (BARS score = 1). Lowering of the heel was performed in continuous axis but the movement was decomposed in several phases (BARS score = 1). Oscillating movements of the arm and hand without decomposition of the movement were observed in the finger to nose test (BARS score = 1). Motor speech was mildly disrupted by a few articulation errors, a laboured articulatory setting and oral diadochokinesis (BARS score = 1). No oculomotor abnormalities were found. The EEG was normal but MRI of the brain showed a slight anterior/superior asymmetry of vermal fissures consistent with rostral vermisdysplasia type 1a (Figure 1A-C) [8]. A quantified Tc-99m-ECD SPECT study was additionally performed. Using a previously fixed butterfly needle 740 MBq (20 mCi) Tc-99m-ECD was administered to the patient sitting in a quiet and dimmed room, eyes open and ears unplugged. Acquisition was started 40 min after injection using a three-headed rotating gamma camera system (Triad 88; Trionix Research Laboratory, Twinsburg, Ohio, USA) equipped with lead super-fine fanbeam collimators with a system resolution of 7.3 mm FWHM (rotating radius 13 cm). Projection data were accumulated in a 128 x 64 matrix, pixel size 3.56 mm, 15 seconds

per angle, 120 angles for each detector (3° steps, 360° rotation). Projection images were rebinned to parallel data, smoothed and reconstructed in a 64 x 64 matrix, using a Butterworth filter with a high cut frequency of 0.7 cycles/cm and a roll-off of 5. No attenuation or scatter correction was performed. Trans-axial images with a pixel size of 3.56 mm were anatomically standardized using SPM and compared to a standard normal and SD image obtained from ECD perfusion studies in a group of 15 normally educated healthy adults consisting of 8 men and 7 women with an age ranging from 45 to 70 years. Using a 31 ROI template, Z-scores (SD) were calculated for each region. A regional Z-score of >2.0 was considered significant. In comparison to normal database findings the quantified Tc-99m-ECD SPECT study showed a significant decrease of perfusion in the right cerebellar hemisphere (-2.59 SD) as well as a hypoperfusion in the medial prefrontal left hemisphere (-2.20 SD) and the right occipital region (-2.11 SD). Decreased perfusion in the vermis (-1.83 SD), the left cerebellar hemisphere (-1.96) and the medial prefrontal right hemisphere (-1.68 SD) nearly reached significance (Figure 1D).

[INSERT FIGURE 1 NEAR HERE]

Extensive neuropsychological investigations were carried (Table 1). A strong and consistent left hand preference was formally confirmed by the Edinburgh Handedness Inventory (LQ=-100). Assessment of general intelligence by means of the Wechsler Adult Intelligence Scale-III (WAIS-III) showed a significant discrepancy of 28 IQ-points between the verbal (VIQ=109) and performance level (PIQ=81). A scaled score below -1.5 standard deviations was obtained for the performal subtest “block design” evaluating visuo-constructive skills. As demonstrated by a defective score on copying of the Rey-Osterrieth figure and on the praxis subtests of the Hierarchic Dementia Scale (HDS items 3, 5, 12, 15), drawing, ideomotor, ideational and constructional praxis were disrupted as well (scores below -2SD). Distorted visual-motor integration skills (pct. 1), visual perception (pct. 12) and visual-motor coordination (pct. 4) were reflected by defective scores on the Beery-Buktenica Developmental Test of Visual-Motor Integration. Frontal planning and problem solving were distorted as well (Wisconsin Card

Sorting Test=0 categories). Apart from disrupted visuo-spatial cognition and executive dysfunctions, no evidence was found for any additional cognitive defect. Normal percentile scores on the Stroop Color-Word test indicated that the ability to inhibit a competing and more automatic response set was unaffected. Visual search and sequencing (Trail Making Test) were also normal. Verbal and nonverbal learning, recent memory, biographic memory and working memory as assessed by the Wechsler Memory Scale-Revised (WMS-R) and subtest 17 of the HDS were normal. Visual gnosis (Boston Naming Test and Benton's Facial Recognition Test) as well as orientation (Benton's Right-Left Orientation Test and Judgment of Line Orientation Test) and calculation (arithmetics of the WAIS-III and mental control subtest of the WMS-R) scored within the normal range. Spontaneous speech was characterized by a few inconsistent articulation errors and a somewhat laboured articulatory setting which seems consistent with sequelae of DAS**.** In addition, mildly disturbed diadochokinesis was observed in p-t-k realisation. Apart from this, formal language testing by means of the BNT (visual confrontation naming) and a verbal fluency task (one minute oral production of words belonging to a specific semantic or phonological category) as well as repetition, word reading and writing to dictation (Akense Afasie Test) were normal.

[INSERT TABLE 1 NEAR HERE]

Discussion

In this 19-year-old patient the clinical spectrum of developmental, non-progressive motor coordination disturbances associated with cognitive and affective symptoms is consistent with a diagnosis of DCD (DSM-IV). In-depth neuropsychological investigations revealed an asymmetric distribution of cognitive results with depressed non-verbal capacities, impaired visuo-motor cognition and executive dysfunctions affecting frontal problem solving and praxic skills at the ideomotor, ideational, visuo-constructive and speech level. Persisting affective, behavioural and social difficulties were recorded as well. The constellation of cognitive and affective disturbances in this patient strongly suggests that DCD closely relates to the

'cerebellar cognitive affective syndrome' (CCAS) which in addition to executive, visuo-spatial and linguistic inpairments also includes affective dysregulation and which may accompany acquired [9] as well as developmental [10] cerebellar disorders.

In agreement with a bulk of recent evidence demonstrating crucial involvement of the cerebellum in a broad variety of cognitive, linguistic and affective processes [11], including the execution of planned actions [12,13], our findings seem to indicate that the cerebellum might also be involved in the pathophysiology of DCD. Consistent with the pathophysiological substrate of CCAS, anatomoclinical findings in this patient indeed reveal disruption of the cerebello-cerebral network as a possible explanation for DCD. Firstly, structural MRI of the brain showed abnormal fissuration of the anterior vermis consistent with a rostral vermisdysplasia type 1a. Although this type of dysplasia is generally considered to represent an incidental and clinically irrelevant finding [8], we did not find any study in the literature in which in-depth neurocognitive investigations were performed to exclude subtle but clinically relevant neuro-developmental deficits at the cognitive and affective level. Since contemporary data from etiologically heterogeneous patient groups with cerebellar damage have substantiated the view that the vermis is crucially implicated in the modulation of emotional and affective processes [14], future studies are needed to explore more systematically possible cognitive and affective repercussions of abnormal fissuration of the anterior vermal lobe. Secondly, functional neuroimaging with SPECT in this patient disclosed significant perfusion deficits in the anatomoclinically suspected but structurally unaffected supratentorial regions that subserve the execution of skilled motor actions (prefrontal lobe), the regulation of behaviour and affect (prefrontal lobe) and the processing of visual information (occipital lobe). This finding is consistent with recent neuroanatomical evidence disclosing extensive neural circuits connecting the prefrontal, temporal, posterior parietal and limbic cortices with the cerebellum [15]. Within this network, a strong frontocerebellar connectivity has been shown, consisting of closed cortico-cerebellar loops that connect the (dorso)lateral part of the prefrontal cortex (PFC) to the

cerebellum via pontine nuclei while the cerebellum sends projections back to the PFC via the dentate nucleus and thalamus [16,17]. As a result, the anatomoclinical configurations in our patient seem to indicate that similar to CCAS, DCD may also reflect disruption of a close functional interplay between the cerebellum and the supratentorial brain regions crucially involved in the execution of planned motor actions, affective regulation and visuo-motor processing. Insufficient maturation or underdevelopment of the distributed cerebro-cerebellar network that subserves movement, cognition and affect might account for the constellation of motor, cognitive and affective symptoms in DCD. However, future studies of larger cohorts of DCD patients are needed to investigate whether a disrupted maturation or underdevelopment of the neural circuitry connecting the cerebellum with the supratentorial association cortices might possibly account for the motor, cognitive and affective deficits observed in DCD.

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Legends to Figures

Figure 1

Brain MRI axial gradient T1-weighted slices (A-B) and coronal FSE T2-weighted slice (C) reveal a slight anterior/superior asymmetry of vermal fissures consistent with rostral vermisdysplasia type 1a. Quantified Tc-99m-ECD SPECT study (D) shows a significant decrease of perfusion in the right cerebellar hemisphere (lower row) associated with a hypoperfusion in the medial prefrontal left hemisphere and the right occipital region (upper row). Decreased perfusion of >1.5 SD in the vermis, the left cerebellar hemisphere and the medial prefrontal right hemisphere is not indicated as it did not reach a significance level of >2 SD.