Brainstem Morphometric Differences

in Children with Autism Spectrum Disorder, Developmental Coordination Disorder and those Typically Developing

Paolo Bosco[1], Laura Harrison[2], Alessandra Retico[3], Christiana Butera[2], Sara Calderoni[4,5], Filippo Muratori[4,5], Lisa Aziz-Zadeh[2] and Jonathan Delafield-Butt[6,*]

(1) Medical Physics and MR Lab, IRCCS Stella Maris Foundation, Pisa, Italy. (2) Brain and Creativity Institute & Chan Division of Occupational Science and Occupational Therapy, University of Southern California, Los Angeles, USA. (3) National Institute for Nuclear Physics, Pisa Division, Pisa, Italy. (4) Department of Developmental Neuroscience, IRCCS Stella Maris Foundation, Pisa, Italy. (5) Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy. (6) Laboratory for Innovation in Autism, University of Strathclyde, Glasgow, UK

1. Introduction

The brainstem is a neglected topic in autism research, despite major lines of evidence indicating its active involvement in sensory, motor, affect, arousal, and social regulation (Dadalko & Travers, 2018). It is the substrate of what affective neuroscience identifies as the 'Core Self' (Alcaro, Carta, & Panksepp, 2017), and disruption to its growth and function appears to disturb core conscious experience in autism (Delafield-Butt, Dunbar & Trevarthen, 2021; Delafield-Butt & Trevarthen, 2017; Trevarthen & Delafield-Butt, 2013).

Although evidence indicates brainstem growth is disrupted in early childhood (Bosco et al., 2019), how these growth differences compare to closely related neurodevelopmental disorders, such a Developmental Coordination Disorder (DCD), is not yet understood.

2. Objectives

To determine brainstem morphometric differences between children with ASD, DCD, and those typically developing (TD).

3. Methods

Study participants were 87 youths ages 8 to 17 assigned to the ASD (n = 30, 7 female), DCD (n =24, 12 female) or TD (n = 33, 12 female) group. Exclusion criteria for all groups included IQ <80. TD were excluded if they had any neuropsychological or psychopathological disorder. DCD eligibility additionally included performance below the 16th percentile on the MABC-2 and no concern about an ASD diagnosis. ASD participants had a previous clinical diagnosis confirmed by ADOS-2 and ADI-R. ASD subjects were permitted any score on the MABC-2. ASD and DCD individuals were excluded if they had another neuropsychological disorder, except attention deficit or anxiety disorder.

T1-weighted MPRAGE (1mm isotropic resolution) MRI data were acquired on a 3T MAGNETOM Prisma (Siemens). Brainstem morphology was analysed using SPHARM-MAT (http://lishenlab.com/spharm/), a 3D Fourier surface representation method. A typical surface was calculated for the TD group, and distances from this norm computed for each vertex. Mean distances at each vertex were computed for each group (ASD, DCD, TD) and compared, taking into account age, gender and supratentorial volume as covariates.

Contact details

* For more information contact,
jonathan.delafield-butt@strath.ac.uk

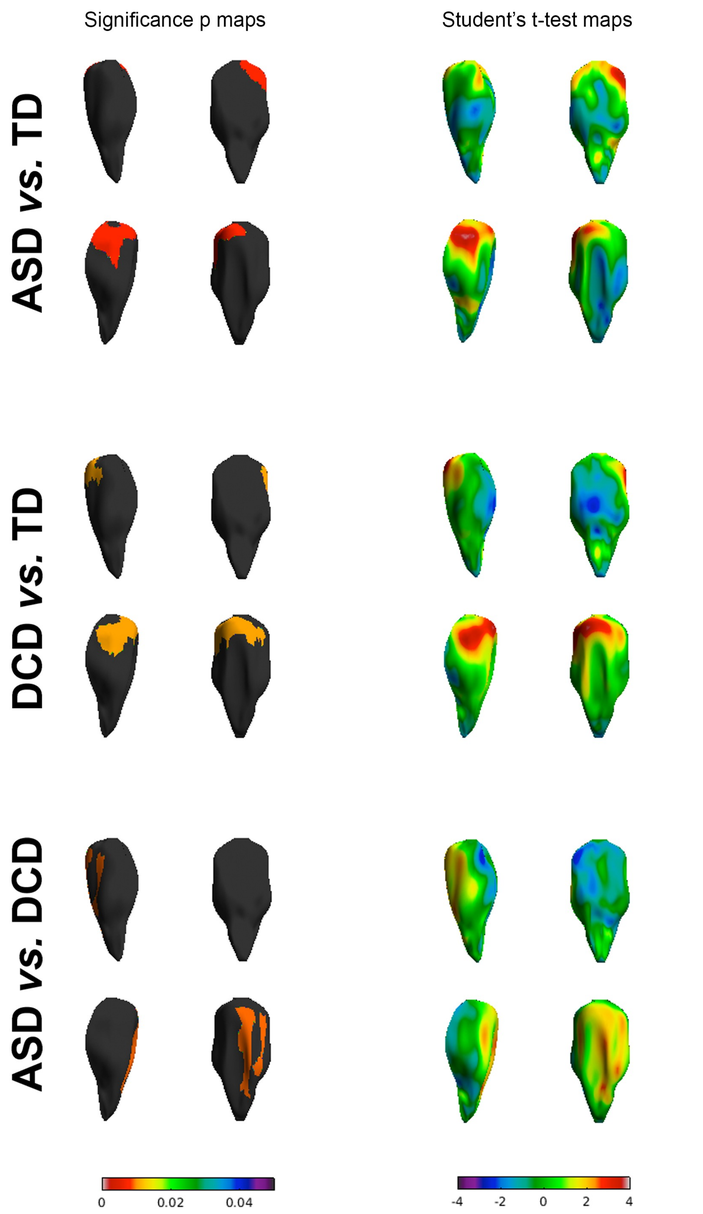

Figure 1. Brainstem morphometric significance p maps and Student t-test maps for group comparisons.

4. Results

Significant brainstem morphological differences were identified between all three groups (TD, ASD and DCD; Figure 1).

1. **Differences between TD and ASD** ($p<0.01$) were identified in a large region of the anterior-most surface, extending caudally along the right posterior surface.
2. **Differences between TD and DCD** groups were similar with reduced significance ($p\sim0.01$), and the pattern diverged with more inclusion of the anterior ventricular surface and less pronouncement at the right anterior border.
3. **Differences between ASD and DCD groups** ($p<0.01$) were found at the anterior midline either side of the ventricular surface, and in two long anteroposterior columns on the left side adjacent and parallel to the fourth ventricle.

5. Conclusions

Surface morphology indicates

- alterations in **local nuclei and/or tract growth**,
- especially at **the anterior surface in ASD and DCD children**,
- and **differentially (ASD *vs.* DCD) at the ventricular surface**.

This may relate to

- growth of the pons and cerebellar peduncle connectivity,
- growth of nuclei such as the hypoglossal, intercalatus, vagus, or inferior olive, and their associated tracts

Disturbance of integrative function of the Core Self is likely, due to tight brainstem structure-function relation.

Higher resolution 7T MRI is required to resolve the underlying differential composition.

More subjects are required to resolve ASD+DCD *vs.* ASD without DCD, and to disentangle sensory, motor, affect, arousal, attention and social regulation elements.

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