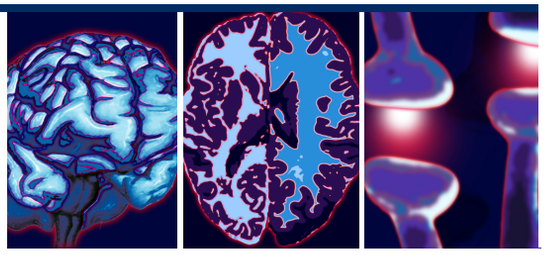
CLINICAL SNAPSHOT



Functional brain connectivity in a child with autism with an enlarged cavum septum pellucidum

Donna L Murdaugh[1], Lawrence W Ver Hoef[2] & Rajesh K Kana*[1]

A 12-year old Caucasian male child with a diagnosis of pervasive developmental disorder not otherwise Specified met criteria for a research protocol that included functional and structural MRI. Additional past medical history was significant for seizures early in childhood, but at the time of his participation in our study he had been seizure free for over 6 years and was not on any anticonvulsant medication. His current medications included Vyvanse® (Company), Intuniv® (Company), oxybutynin and Seroquel® (Company), although he was off the Vyvanse and Intuniv at the time of the scan. The MRI data were collected using a Siemens 3.0 Tesla Allegra head-only Scanner (Siemens Medical Inc., Erlangen, Germany). T1-weighted scans were acquired using a 160-slice 3D MPRAGE (Magnetization Prepared Rapid Gradient Echo) volume scan with TR = 200 ms, TE = 3.34 ms, flip angle = 7, field of view (FOV) = 25.6 cm, 256 × 256 matrix size, and 1-mm slice thickness. This study was approved by the UAB institutional review board. Review of his T1 weighted images revealed mild-to-moderately enlarged ventricles involving the lateral and third ventricles. This was chronic in appearance with no evidence of acute obstruction. Also seen was a prominent anterior cavum septum pellucidum (CSP; **Figure 1**) measuring 33 mm at its widest extent. The CSP is a fluid-filled cavity in the thin midline structure of the septum pellucidum. While the presence of the CSP after birth is not uncommon, enlarged CSP can be considered a neural marker for disruptive brain development, especially midline structures and limbic system [1]. Interestingly, increasing size of the CSP has been correlated with neurodevelopmental disorders, such as Tourette syndrome [2], and neuropsychiatric disorders, specifically, most research has focused on CSP in schizophrenia [3]. However, no studies to date have assessed the correlation between CSP and the prevalence or symptomatology of autism.

As part of the research protocol, the child underwent a functional resting state MRI scan. Specifically, default mode network (DMN) activity has been shown to be highly correlated during rest. Neuroimaging studies in resting state in autism have collectivity found altered connectivity of the DMN in autism, suggestive of deficits in social interactions [4]. Functional MR images were acquired using a single-shot T2*-weighted gradient-echo EPI pulse sequence (TR = 1000 ms, TE = 30ms, flip angle = 60 for 17 oblique axial slices, slice thickness = 5mm, slice gap = 1 mm, FOV = 24 × 24 cm, matrix size = 64 × 64, in-plane resolution = 3.75 × 3.75 × 5 mm^3). Data were preprocessed and analyzed using SPM8 software package (Wellcome Department of Imaging Neuroscience, London, UK). Preprocessing steps included slice timing correction, realignment, motion correction, spatial normalization and smoothing. Owing to the abnormal structure of this child's brain, his averaged T1 weighted image was used to normalize his images to his own brain space. Functional connectivity (synchronization of brain activity across regions) was computed by correlating the average time course of signal intensity of the bilateral

[1]Department of Psychology, University of Alabama at Birmingham, AL, USA
[2]Department of Neurology, University of Alabama at Birmingham, AL, USA
*Author for correspondence: Tel.: +1 205 934 3171; Fax: +1 205 975 6330; rkana@uab.edu

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Figure 1. Functional connectivity analysis showing connectivity between the posterior cingulate cortex and all other voxels in the brain (family wise error = 0.05 corrected). The axial brain view in the bottom panel (extreme right) shows the enlarged anterior cavum septum pellucidum.

posterior cingulate cortex with all other voxels in the brain. Six rigid body head movement parameters were partialled out as regressors of no interest. Correlation coefficients were converted to a normal distribution using the Fisher's r to z transformation. Data were intensity-thresholded at family wise error at 0.05. Results, as shown in **Figure 1**, revealed significant functional connectivity between the posterior cingulate cortex and regions of the DMN, including left dorsolateral prefrontal cortex, left anterior cingulate cortex, and left precuneus. Of note, the majority of functional connectivity was left lateralized, and may be suggestive of abnormal resting state activity, as a bilateral pattern of connectivity is usually seen in neurotypical individuals [5].

This case offers two key points when assessing brain functioning in autism. First, while the CSP appears to be a nonspecific marker for abnormal neurodevelopment, it may be worthwhile to examine the prevalence and effects of CSP in children with autism in future studies. For example, CSP has been found to not only correlate with specific neurodevelopmental and neuropsychological disorders, but is also associated with increased severity of symptoms, lower IQ and verbal memory within the patient population [3]. This is especially relevant considering the findings of macrocephaly in autism in early life. In addition, screening for the presence of enlarged CSP early in childhood (e.g., at a routine pediatrician visit) may be helpful in identifying those children who are at greater risk for a developmental disorder, leading to earlier referral for more specific autism diagnostic testing. Secondly, in neuroimaging research, children with autism who have atypical or abnormal brain structure are most times screened ineligible for the study. This may be introducing a specific sample bias in the population. Our resting state functional connectivity results may reflect the midline cortical structural abnormalities caused by the enlarged CSP in this patient. As such, future studies should assess specific autism populations with similar brain structure abnormalities to determine prevalence and effect on autism symptomology.

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