Priority Communication

Biological Psychiatry

Intrinsic Visual-Motor Synchrony Correlates With Social Deficits in Autism

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ABSTRACT

BACKGROUND: Imitation, which is impaired in children with autism spectrum disorder (ASD) and critically depends on the integration of visual input with motor output, likely impacts both motor and social skill acquisition in children with ASD; however, it is unclear what brain mechanisms contribute to this impairment. Children with ASD also exhibit what appears to be an ASD-specific bias against using visual feedback during motor learning. Does the temporal congruity of intrinsic activity, or functional connectivity, between motor and visual brain regions contribute to ASD-associated deficits in imitation, motor, and social skills?

METHODS: We acquired resting-state functional magnetic resonance imaging scans from 100 8- to 12-year-old children (50 ASD). Group independent component analysis was used to estimate functional connectivity between visual and motor systems. Brain-behavior relationships were assessed by regressing functional connectivity measures with social deficit severity, imitation, and gesture performance scores.

RESULTS: We observed increased intrinsic asynchrony between visual and motor systems in children with ASD and replicated this finding in an independent sample from the Autism Brain Imaging Data Exchange. Moreover, children with more out-of-sync intrinsic visual-motor activity displayed more severe autistic traits, while children with greater intrinsic visual-motor synchrony were better imitators.

CONCLUSIONS: Our twice replicated findings confirm that visual-motor functional connectivity is disrupted in ASD. Furthermore, the observed temporal incongruity between visual and motor systems, which may reflect diminished integration of visual consequences with motor output, was predictive of the severity of social deficits and may contribute to impaired social-communicative skill development in children with ASD.

Keywords: Autism, Functional connectivity, Imitation, Independent component analysis, Symptom severity, Visual-motor integration

http://dx.doi.org/10.1016/j.biopsych.2015.08.029

Motor deficits are prevalent in autism spectrum disorder (ASD) (1). Due to the developmental nature of ASD, brain-based mechanisms for mastering motor skills may contribute to the impaired acquisition of skills crucial for normal social and communicative interaction. Imitation, which critically depends on linking visual input with motor output, is vital to the development of motor skills, as well as social skills and social cognition (2). Thus, understanding the brain basis of visual-motor integration deficits may be critical for understanding heterogeneity in the social and communicative deficits at the core of ASD.

Support for the importance of visual-motor integration comes from children with ASD who exhibit a distinctly anomalous pattern of motor learning. When learning novel movements, children with ASD discount visual feedback in favor of proprioceptive feedback (3–5). This bias appears to be specific to ASD (4) and is a robust predictor of motor, imitation, and social skill deficits (3–5). This reduced sensitivity to visual input is consistent with reports that children with ASD perform worse on clinical assessments of visual-motor integration (6) and struggle to incorporate visual input into movement planning (7,8). Children with ASD also display particular difficulty with motor tasks that tax visual-motor coordination (9), including catching, which again appears to be ASD-specific (10,11).

This underreliance on visual feedback and overreliance on proprioceptive feedback may be rooted in the wiring of the brain (5). Temporal congruity in evoked neural activity plays a critical role in integration (12), and accumulating evidence suggests a mechanistic link between the transient changes in brain activity induced by perceptual stimuli and the baseline of ongoing spontaneous fluctuations from which they arise (13). One method for measuring the temporal congruity of spontaneous activity in distributed brain regions is functional magnetic resonance imaging measured at rest (rs-fMRI) (14). rs-fMRI recently revealed increased intrinsic visual-motor synchrony in a chronic spinal cord injury patient, which may reflect cortical reorganization following dorsal column transection and the patient's self-reported overreliance on visual feedback while walking (15). Does intrinsic visual-motor

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ISSN: 0006-3223

synchrony also relate to social skill and imitation ability in children with ASD? Functional connectivity findings in ASD have been mixed depending on the age range of participants and the regions of the brain studied (16). However, there have been consistent reports of an overexpression of localized connectivity in school-age children with ASD (17,18) and a relative underexpression of long-range connectivity (19,20), including connectivity between parietal/occipital and frontal cortices critical for encoding visual feedback (21,22). Given this evidence, we hypothesized long-range visual-motor functional connectivity would be reduced in children with ASD compared with their typically developing (TD) peers.

METHODS AND MATERIALS

Participants

The Johns Hopkins Medical Institutional Review Board approved this experiment. Written assent and written informed consent were obtained from all participants and their legal guardians.

One hundred 8- to 12-year-old children participated at the Kennedy Krieger Institute (KKI). Fifty had high-functioning autism/Asperger's syndrome and 50 were TD children balanced for age; handedness, using the Edinburgh Handedness Inventory (23); Perceptual Reasoning Index (PRI) from the Wechsler Intelligence Scale for Children, Fourth Edition (24); and socioeconomic status, using the Four-Factor Index of Social Status (25) (Table 1). PRI, which reflects intelligence required to perform the tasks in this study, was used to balance groups because task-specific measures of intelligence are more appropriate than more general measures of intelligence like the full scale IQ for children with ASD (26). If a child's full scale IQ was less than 80 but his/her PRI or Verbal Comprehension Index was at least 80, he or she was still eligible.

Table 1. Demographic and Behavioral Information for KKI Participants by Group

	Typically Developing	Autism
Gender (M/F)	45/5	40/10
Age (Years)	10.44 (1.23)	10.28 (1.44)
Handedness	.69 (.54)	.67 (.51)
PRI	110.0 (14.2)	107.8 (14.7)
SES	52.6 (8.4)	52.5 (10.8)
Mean FD (mm)	.27 (.12)	.32 (.17)
Total Raw SRS	18.9 (9.97)	98.5 (26.8)
Imitation % Correct	69.4 (10.1)	48.6 (16.5)
Total Praxis % Correct	72.1 (9.24)	49.3 (15.4)

The mean is listed for each variable with the standard deviation in parentheses. The SRS questionnaire was scored for all of the typically developing children and most of the children with autism (49 of 50). All typically developing children and 43 out of 50 children with autism completed the praxis exam.

F, female; FD, framewise displacement (a measure of head movement during the resting-state scan); KKI, Kennedy Krieger Institute; M, male; PRI, Perceptual Reasoning Index; SES, socioeconomic status; SRS, Social Responsiveness Scale.

Diagnosis

Children with ASD met DSM-IV criteria for autism or Asperger's syndrome (27) according to the judgment of a clinician with more than 20 years of experience. Diagnoses were confirmed using the Autism Diagnostic Observation Schedule-Generic (28), the Autism Diagnostic Interview-Revised (29), or both. Children with ASD were excluded if they had identifiable causes of autism or known neurological disorders, including epilepsy, based on parent responses during an initial phone screening. Children were excluded from the TD group if they had a first-degree relative with ASD or if parent responses to the Diagnostic Interview for Children and Adolescents-IV (30) revealed a history of a developmental or psychiatric disorder, with the exception of simple phobias.

Social deficits were quantified using the Social Responsiveness Scale (SRS) questionnaire (31). The SRS probes a child's level of motivation to engage in social interactions, his/her ability to recognize emotional and interpersonal cues from other people, to interpret those cues correctly, and to respond to what he/she interprets appropriately. The social deficit severity index generated from the SRS has been shown to be independent of intelligence, continuously distributed in the general population, and consistent across informants (e.g., parents and teachers) (31,32). Raw total scores range from 0 to 195 with higher scores indicating more severe social deficits.

Testing Procedure

Testing was distributed over two onsite study visits (Table 2). On average, the time between visits was 2 weeks and never exceeded 6 months.

Table 2. Testing Outline

Telephone Screening	Day 1	Day 2
The High-Functioning Autism Spectrum Screening Questionnaire (65) (15–20 min)	Consent/Assent	Motor skill testing: PANESS (66) or Praxis (60 min)
Oral Consent	Collect completed parent/teacher rating scales	MRI scan (90 min)
DICA-IV (with parent)	ADOS (ASD only) (45 min)	
ADI-R (with parent)	IQ testing: WISC-IV (60 min)	
	Mock MRI training (45–60 min)	
	Motor skill testing: PANESS or Praxis (60 min)	

Information from the telephone screening was reviewed by SHM. Each eligible child then completed two onsite study visits. On average, the time between visits was 2 weeks and never exceeded 6 months. Within a visit, the order of testing varied based on the availability of MRI facilities and behavioral testing rooms.

ADI-R, Autism Diagnostic Interview-Revised; ADOS, Autism Diagnostic Observation Schedule; ASD, autism spectrum disorder; DICA-IV, Diagnostic Interview for Children and Adolescents-IV; MRI, magnetic resonance imaging; PANESS, Physical and Neurological Examination for Subtle Signs; WISC-IV, Wechsler Intelligence Scale for Children, Fourth Edition.