

A DNAS

Reply to Brock: Renewed focus on the voice and social reward in children with autism

We would like to thank Jon Brock for his letter (1) highlighting the importance of delineating causal links between brain connectivity and cognitive function in children with autism spectrum disorders (ASDs). In particular, Brock discusses the challenge of identifying meaningful links between brain connectivity and cognition given the complexity of brain systems and the heterogeneity of behavioral characteristics associated with ASD. We agree that further studies are required to clarify the nature of these brainbehavior relationships in individuals with ASD using targeted functional MRI task paradigms and behavioral measures to further assess reward attribution to speech. Given that brain connections are built and modified throughout development (2), longitudinal studies of children with ASD will also be necessary to better understand the ontogeny of these neural systems. Our current work sheds new light on these issues.

Despite the heterogeneity of symptom presentation and severity in individuals with ASD, speech-related impairments represent a surprisingly common element within this population (3). A goal of our research is to understand the neurobiological bases of speech perception impairments in children with ASD. Our recent publication shows that voice-selective regions of the superior temporal cortex exhibit weak functional connectivity with the reward circuit and amygdala in children with ASD (4). Importantly, our results demonstrate behavioral and neuroanatomical specificity: connectivity between voice-selective cortex and the reward pathway predicted social communication abilities in children with ASD but failed to predict scores on standardized measures of language abilities in these individuals. Moreover, the brain connectivity analysis that we performed examined functional relationships between the posterior superior temporal sulcus and every other voxel in the brain, and group differences were restricted almost entirely to structures of the reward pathway and amygdala, providing a high level of anatomical specificity.

From one perspective, our results may be surprising: speech is typically considered within the context of auditory and language processes, and scientific evidence supporting its role as a rewarding stimulus is relatively sparse. Nevertheless, there is ample anatomical and physiological evidence supporting structural and functional links between auditory structures of the superior temporal cortex and the dopaminergic reward pathway. Moreover, functional MRI research has shown that pleasurable sounds activate the reward pathway (5), and recently it was shown that these sounds increase functional connectivity between the superior temporal cortex and the nucleus accumbens (6), a key node of the reward pathway. We argue that a renewed focus on brain systems that facilitate attention to the human voice, particularly as they relate to motivational and emotional processes, will provide critical new knowledge regarding the biological bases of pervasive social communication deficits in children

with ASD. The results of our current work represent an important first step toward characterizing intrinsic functional brain organization underlying these core features of autism.

Daniel A. Abrams^{a,1}, Lucina Q. Uddin^a, and Vinod Menon^{a,b,c,d,1}

^aDepartment of Psychiatry and Behavioral Sciences, ^bDepartment of Neurology and Neurological Sciences, ^cProgram in Neuroscience, and ^dStanford Institute for Neuro-Innovation and Translational Neurosciences, Stanford University School of Medicine, Palo Alto, CA 94304

2 Uddin LQ, Supekar K, Menon V (2013) Reconceptualizing functional brain connectivity in autism from a developmental perspective. Front Hum Neurosci, 10.3389/fnhum.2013.00458.
3 Kjelgaard MM, Tager-Flusberg H (2001) An investigation of

language impairment in autism: Implications for genetic subgroups. Lang Cogn Process 16(2-3):287-308.

4 Abrams DA, et al. (2013) Underconnectivity between voiceselective cortex and reward circuitry in children with autism. *Proc Natl Acad Sci USA* 110(29):12060–12065.

5 Menon V, Levitin DJ (2005) The rewards of music listening: Response and physiological connectivity of the mesolimbic system. *Neuroimage* 28(1):175–184.

6 Salimpoor VN, et al. (2013) Interactions between the nucleus accumbens and auditory cortices predict music reward value. *Science* 340(6129):216–219.

Author contributions: D.A.A., L.Q.U., and V.M. wrote the paper.

The authors declare no conflict of interest.

¹To whom correspondence may be addressed. E-mail: daa@ stanford.edu or menon@stanford.edu.

¹ Brock J (2013) Connectivity and cognition in autism spectrum disorders: Where are the links? *Proc Natl Acad Sci USA* 110:E3973.