Title: Manual Motor Control in Individuals with Autism Spectrum Disorder and Their Unaffected Biological Parents

Authors: Erin Bojanek[1,2], Shannon Kelly[1,2], Lauren Schmitt[3], Stormi White[4], John Sweeney[5], Matthew Mosconi[1,2]

Introduction: Sensorimotor impairments, including feedforward and feedback deficits of skeletomotor and oculomotor behaviors, are prevalent in individuals with autism spectrum disorder (ASD; 1). Multiple oculomotor issues identified in individuals with ASD also have been documented in unaffected relatives of individuals with ASD (2). Fine motor control is necessary to complete everyday tasks and is often significantly impaired in ASD. However, the extent to which fine motor control is disrupted in unaffected parents of individuals with ASD has not yet been determined. To examine the familiality of manual motor behaviors in ASD, we conducted a family trio study of precision manual motor behaviors in individuals with ASD and their unaffected biological parents.

Method: Fifty-four children with ASD (probands; ages 5-17 years) and 100 parents of children with ASD (ASD parents; ages 29-54 years) were studied. Thirty-five typically developing (TD) controls were matched at the group level to probands on age and nonverbal IQ. Forty-five separate controls were matched with ASD parents on age, sex, handedness, and nonverbal IQ. Participants completed two tests of precision grip force. During both tests, participants pressed opposing load cells with their thumb and index finger. They viewed a static red/green target bar and were instructed to press the load cells as quickly as possible when the red target bar turned green and keep pressing so that the white force bar stayed at the level of the green target bar. To assess feedforward control processes, we administered a “rapid” precision grip test consisting of two second trials. We measured the accuracy of the initial force output and the peak rate of initial force increase. To assess sensory feedback control of visuomotor behavior, participants were administered a “sustained” precision grip test in which they maintained a constant level of force during eight second trials. We measured the variability of sustained force and the complexity of the force time series (approximate entropy). Both precision grip tests were completed at 15%, 45%, and 85% of each participant’s maximum voluntary contraction (MVC).

Results: During the rapid precision grip test, probands showed reduced accuracy relative to TD controls including greater overshooting of the target at 15% MVC and greater undershooting of the target at 85% MVC; this was especially true at younger ages (group x age x force level interaction, $p=0.004$). Probands also showed a higher peak rate of force increase than TD controls (group main effect, $p=0.005$). ASD parents and parent controls did not show any differences in rapid force control. During the sustained precision grip test, probands showed greater sustained force variability than TD controls; this group difference scaled with force level and was more severe at younger ages (group x age x force level interaction, $p=0.047$). Similarly, ASD parents showed greater force variability than parent controls at 85% MVC when using their dominant hand and at 45% MVC when using their non-dominant hand (group x force level x hand, $p=0.004$). Probands also showed reduced dominant hand sustained force complexity relative to TD controls, but similar non-dominant hand complexity (group x hand interaction, $p=0.005$); there was no significant difference in force complexity between ASD parents and parent controls.

Discussion: We found that children with ASD show reduced accuracy of initial force output and greater peak rate of force increases compared to TD controls suggesting disruptions in feedforward mechanisms supporting precision motor control. However, feedforward motor control appeared to be intact in ASD parents indicating that initial force output made prior to sensory feedback are selectively disrupted in ASD and not familial. We also found that children with ASD and their unaffected biological parents show increased force variability when attempting to maintain a constant force level suggesting that sensory feedback issues may be familial in ASD. These findings further indicate that reduced ability to precisely adjust motor output in response to sensory feedback may serve as an important intermediate phenotype associated with polygenic risk in ASD. Children with ASD also show reduced dominant hand force complexity relative to controls suggesting that reduced lateralization of precision motor behavior may be characterized by atypical hemispheric specialization in ASD. Overall, these studies implicate cortico-cerebellar circuits involved in sensory feedback control of precision motor behaviors in the pathophysiology of ASD, and highlight new motor physiological targets useful for characterizing genotype-phenotype relationships in family genetic studies.

References: (1) Mosconi, M. W., Mohanty, S., Green, R. K., Cook, E. H., Vaillancourt, D. E., & Sweeney, J. A. (2015). Feedforward and feedback motor control abnormalities implicate cerebellar dysfunctions in autism spectrum disorder. *Journal of Neuroscience, 35,* 2015-2025.

(2) Mosconi, M. W., Kay, M., D'Cruz, A., Guter, S., Kapur, K., Macmillan, C., Stanford, L. D., & Sweeney, J. A. (2010). Neurobehavioral abnormalities in first-degree relatives of individuals with autism. *Archives of General Psychiatry, 67,* 830-840.

[1]Clinical Child Psychology Program & Schiefelbusch Institute for Life Span Studies, University of Kansas, Lawrence, KS, USA

[2]Kansas Center for Autism Research and Training (K-CART), University of Kansas, Lawrence, KS, USA

[3]Division of Developmental and Behavioral Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

[4]Department of Pediatrics, Marcus Autism Center, Emory University, Atlanta, GA

[5]Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, Cincinnati, OH