Title: Deficits in feedback and feedforward processes are distinct and vary across age in individuals with autism spectrum disorder

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Introduction: Sensorimotor abnormalities are among the most common comorbid features of autism spectrum disorder (ASD), and are early emerging, related to core social and cognitive impairments, and predictive of worse functional outcomes. Deficits in both rapid, feedforward processes executed prior to availability of sensory feedback, and continuous, feedback guided motor behaviors each have been reported. Owing to their highly translational and quantifiable nature and well-defined brain networks, sensorimotor behaviors offer a powerful target for understanding heterogeneity of behavioral phenotypes and determining underlying pathophysiology. The purpose of this study was to characterize multiple sensorimotor behaviors in ASD across a wide range of development, to determine whether feedback and feedforward processes are differentially affected within individuals, and whether these behaviors differ as a function of important demographic (age, sex) or clinical characteristics (IQ, ASD severity).

Method: Eighty-two Individuals with ASD and 81 typically developing (TD) controls matched on age range (4-28 years) completed two tests of manual motor control (precision grip) and a test of oculomotor control (saccades). During the precision grip tests, participants were instructed to press against opposing load cells using their thumb and index finger to move a horizontal FORCE bar upward toward a parallel TARGET bar and maintain this level of force for the duration of the trial (8 seconds). Target force for grip tasks was calculated separately for each participant based on their maximum voluntary contraction (MVC). Grip tasks were varied across level of force output required (Force test) and quality of visual feedback provided (Gain test). Error [1 – (mean force output/ target force of the trial)], force variability (coefficient of variation; CoV) and regularity (approximate entropy; ApEn) were examined. During the saccade test, participants fixated a central cross-hair and peripheral targets were presented at 12 degrees to the left or right of center. Saccade accuracy and latency were examined. Symptom severity was measured using Autism Diagnostic Interview-Revised (ADI-R) algorithm scores and Repetitive Behavior Scale-Revised (RBS-R) subscale and total scores.

Results: Individuals with ASD demonstrated reduced accuracy, increased CoV, and reduced ApEn relative to controls across both force and gain tests. Deficits in ASD were more severe at higher levels of force and when visual feedback was reduced. Differences between groups in force variability and regularity varied as a function of age; at 15% MVC, younger individuals with ASD showed pronounced increases in CoV compared to age-matched controls, while group differences were less severe at increased age. In contrast, ApEn deficits were more severe during the high force condition in older participants with ASD relative to age-matched controls. While males with ASD demonstrated reduced ApEn relative to male controls across all levels of force, females with ASD differed from female controls only during medium and high force conditions. Saccade latencies were shorter in males with ASD relative to control males, but not in females with ASD relative to control females. Saccade accuracy was impaired in older individuals with ASD relative to age-matched controls, but not in younger individuals. In control participants, increased grip force error and CoV, and reduced ApEn were each associated with reduced saccade latency and increased saccade error; no associations were observed in ASD. Among individuals with ASD, increased CoV and saccade accuracy were associated with more severe communication abnormalities and clinically-rated RRBs.

Discussion: Consistent with previous studies, we demonstrate deficits in feedforward and feedback processes in ASD suggesting dysfunction in internal models that support precise motor control in the absence of sensory information and systems for translating sensory input to guide ongoing motor behavior and reduced stability. Our results indicate that feedforward processes are most impacted at younger ages and may serve as important developmental markers, while feedforward problems may become more severe with age. Unlike TD controls, we find no association between grip and saccade behaviors, suggesting independence of sensorimotor deficits in ASD that reflect separate neurodevelopmental processes giving rise to different sensorimotor behaviors. Finally, we find that grip force performance and saccade accuracy are associated with severity of core

symptoms of ASD implicating the neurodevelopmental processes governing both feedforward and feedback processes may play a central role in the development of core ASD behaviors.

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