Title: Familial Deficits in Sensorimotor and Cognitive Control in Autism Spectrum Disorder

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Introduction: Sensorimotor and cognitive control deficits have been repeatedly documented in ASD, are associated with core diagnostic features, and are present in unaffected first-degree relatives of individuals with ASD (Schmitt et al., 2014; Schmitt et al., 2017; Mosconi et al., 2009; Mosconi et al., 2010; D’Cruz et al., 2013; Thakkar et al., 2008; Lopez et al., 2005). These findings suggest sensorimotor and cognitive control deficits may be candidate intermediate phenotypes in ASD, or biologically-based traits that are intermediate between underlying genetic mechanisms and the clinical manifestations of the disorder. Family studies (including the individual with ASD, biological mother, and biological father) may be leveraged to determine the extent to which sensorimotor and cognitive control deficits inter-correlate among family members, and are differentially sensitive to identifying familial risk for ASD and its (sub)-clinical manifestations.

Method: Sixty-two individuals with ASD (probands), 135 unaffected biological parents, and 76 matched controls completed a visually-guided saccade task (VGS; Schmitt et al., 2014) to assess reflexive oculomotor function, a probabilistic reversal learning task (PRL; D’Cruz et al., 2013) to assess behavioral flexibility, and a manual motor stop-signal task (SST; Schmitt et al., 2017) to assess inhibitory control. For VGS, we examined saccade error, trial-wise saccade error variability, and peak saccade velocity. For PRL and SST, we examined error rates. The relationships between sensorimotor and cognitive control deficits amongst ASD family members were assessed, as were relationships with social-communication impairments and restricted, repetitive behaviors (RRBs).

Results: Probands showed increased saccade error and saccade error variability as well as reduced peak saccade velocity relative to controls. Probands also demonstrated increased errors during tasks of behavioral flexibility and inhibitory control. Unaffected parents demonstrated a profile of saccade and cognitive deficits similar to probands, including increased saccade error, reduced peak saccade velocity, and increased behavioral flexibility errors and inhibitory control errors. Peak saccade velocity and inhibition errors each inter-correlated among family members. Behavioral inflexibility was more prominent in parents showing subclinical features of ASD and their affected offspring compared to those parents who did not show any subclinical ASD features and their offspring. More severe behavioral flexibility and inhibitory control deficits were associated with more severe communication issues and RRBs in probands, respectively.

Discussion: Three key findings provide evidence for impairments in saccade dynamics, behavioral flexibility, and inhibitory control tracking different vulnerabilities to ASD in different families. First, unaffected biological parents of individuals with ASD demonstrate a similar, but attenuated, profile of sensorimotor and cognitive control deficits to individuals with ASD. Second, impairments in saccadic eye movements, behavioral flexibility, and inhibitory control were not related to each other and associated with different core features. Third, inhibitory control and saccade deficits each co-segregated among family members and deficits in behavioral flexibility appear to familial in pedigrees showing subclinical features of ASD. Thus, these findings suggest distinct pathophysiological processes may contribute to unique aspects of ASD, and that these different mechanisms of risk may track in different families. This study may have broader implications providing insight into more targeted gene discovery useful for identifying specific pathophysiological mechanisms and more individualized treatments in ASD.
References/Citations:


