Neuropsychological Mechanisms of Visual Motion Processing in Autism Spectrum Disorder

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Abstract

Background: Sensory issues are common in autism spectrum disorder (ASD) and impact multiple developmental abilities, but treatments remain insufficient due, at least in part, to limited understanding of physiological and brain mechanisms of core symptoms. The goal of this study was to develop a more mechanistic understanding of sensory issues as they relate to motor abilities in ASD.

Methods: Fifty-nine individuals with ASD (10-33 years) and 44 typically developing (TD) age-matched controls completed laboratory studies of visuomotor behavior and functional magnetic resonance imaging (fMRI) studies of visual motion perception. During the laboratory study, participants completed a visuomotor task in which they pressed force transducers with their index finger and thumb while receiving visual feedback across different visual gain levels. The gain level was manipulated by changing the visual angle of feedback, or the vertical distance that the force bar moved in response to changes in force output. We examined the variability (coefficient of variation) and complexity (approximate entropy) of the force output. During the fMRI task, we examined brain activation and connectivity in key visual motion regions (V1, V3, and V5) during visual motion processing in contrast to rest.

Results: We found that individuals with ASD showed decreased force complexity relative to TD controls during lower visual gain conditions. There were no differences in brain activation or connectivity in visual motion networks. Individuals with ASD showed increased caudate activation compared to TD controls during visual motion processing. Decreased force complexity was associated with more severe social communication difficulties in ASD. We also found that greater changes in force complexity across gain conditions were associated with more severe sensory sensitivity in ASD.

Conclusions: Our findings of reduced force complexity during lower gain conditions demonstrate that individuals with ASD show an overreliance on visual feedback to carry out precision motor behaviors. Visual motion processing networks functioned similarly in ASD and TD controls, though increased caudate activation in ASD suggests a greater reliance on subcortical networks to inhibit planned motor behaviors during passive viewing of motion. These findings indicate that differences in visually guided motor behaviors reflect dysfunctions of visuomotor brain networks rather than alterations in basic visual processing networks. We also found associations between visuomotor behaviors and core sensory and clinical symptoms implicating shared neural mechanisms underlying visual motor integration impairments and core ASD symptoms.

Keywords: Autism Spectrum Disorder, Sensory Processing, Visual Motion, Visuomotor Behavior, Neuroimaging

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Neuropsychological Mechanisms of Visual Motion Processing in Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a highly heterogeneous neurodevelopmental disorder characterized by social communication difficulties and the presence of restricted and repetitive behaviors, including sensory symptoms (American Psychiatric Association, 2013). Sensory symptoms have long been associated with ASD (Kanner, 1943), though they were not considered to be a core diagnostic component until recently (American Psychiatric Association, 2013). Despite only recent recognition, sensory symptoms are highly prevalent in ASD with up to 95% of autistic individuals reporting some sensory symptoms (Baranek et al., 2006; Ben-Sasson et al., 2019; Tomcheck & Dunn, 2007). Sensory symptoms also vary across individuals; some show no or minor sensory differences, whereas others may show severe sensory sensitivities that disrupt their ability to tolerate even mild exposure to specific stimuli. These issues may include hyper- or hypo-sensitivity to sensory inputs as well as sensory seeking behaviors (e.g., repetitively rubbing their face with a soft object). Sensory abnormalities also impact multiple aspects of development, including social and cognitive abilities (Gliga et al., 2014; Ronconi et al., 2016). For example, atypical sensory sensitivities in ASD are associated with reduced joint attention, language (Baranek et al., 2013), and social play (Hilton et al., 2010; Kuhaneck & Britner, 2013), as well as deficits processing social stimuli in the environment, and switching attention (Gliga et al., 2014). A more mechanistic understanding of the sensory processes disrupted in ASD is necessary to develop better targets for treatments aimed at improving multiple outcomes.

One sensory domain commonly impaired in ASD is visual processing. Atypical visual processing can result in diverse impairments ranging from motor control deficits to difficulties processing social information. Motion perception, in particular, is related to many higher level abilities (Crookes & McKone, 2009; Mondloch et al., 2002) and is shown to be disrupted in ASD

(Koldewyn et al., 2010; Milne et al., 2002; Spencer et al., 2000; Tsermentseli, et al., 2008). Accurate perception of visual motion is necessary to guide movement, and poor visual perceptual abilities can lead to worse motor execution and disruptions in multiple aspects of behavior (Braddick et al., 2003; Mosconi et al., 2015). Neurophysiological processes underlying visual motion deficits and their impact on motor behavior in ASD as well as their relationship to core symptoms remain unclear. This study addressed multiple gaps in the literature by examining the impact of visual feedback on motor behavior and the neural underpinnings of visual motion perception in ASD to understand key neurodevelopmental mechanisms relating to sensory issues.

Visual Processing in Health

Visual motion perception is the ability to accurately interpret and process motion through the integration of information over both space and time (Hadad et al., 2015). Motion perception is a basic perceptual ability that is essential to both cognition and action (Braddick et al., 2003) and impacts how an individual perceives and interacts with the world (Kaiser & Shiffrar, 2009). It is necessary to guide numerous behaviors ranging from sensorimotor abilities, such as tracking and reaching for an object, to social-communication abilities, such as following nonverbal gestures of others (e.g., shifts in eye gaze communicating attention to an object). Additionally, visual motion perception is related to the development of other visual abilities including sensitivity to facial feature spacing (Crookes & McKone, 2009; Mondloch et al., 2002), processing of higher level patterns (Burack et al., 2000; Kimchi et al., 2005; Mondloch et al., 2003), and the ability to integrate visual depth cues (Nardini et al., 2010). These findings suggest that disruptions in the basic processing and integration of motion information could be related to a range of higher-level perceptual and sensorimotor difficulties in ASD.

Motion perception abilities also are directly linked to the development of motor functions beginning in early childhood (Chakraborty et al., 2017; Thompson et al., 2017). The importance of accurate visual motion perception on motor functioning has been demonstrated through studies of children with visual impairments early in development (Sanchez-Gonzalez et al., 2022). For example, children with infantile strabismus show more significant motor coordination impairments relative to typically developing children suggesting that difficulties integrating visual information during a key developmental window is associated with impairments in motor functioning later in childhood (Vagge et al., 2021). Visual feedback is the primary sensory input used to guide movement and behavior. Improvement in motor behaviors when visual feedback is present has been shown in individuals as demonstrated by increased complexity of motor output during precision motor behavior (Vaillancourt et al., 2006). The ability to integrate visual feedback to refine motor output matures throughout childhood and into adolescence (Deutsch & Newell, 2001; Deutsch & Newell, 2002) and varies according to multiple features of the visual information. One method to manipulate visual information during motor behavior is through alterations in the spatial amplitude of feedback (Archer et al., 2018). For example, visual gain can be manipulated during a precision grip task by changing the vertical distance that a feedback cue moves in response to changes in motor output measured. Adults show decreases in force variability and increases in force complexity with increases in visual angle up to one degree, after which, both measures appear to plateau (Vaillancourt et al., 2006). These findings demonstrate the importance of accurate perception of dynamic visual feedback to control motor behaviors and the impact that altered visual feedback can have on motor precision.

Visual Processing in ASD

Individuals with ASD experience a range of visual processing issues, including atypical binocular integration implicating alterations of cortical inhibition (Robertson et al., 2016), reduced abilities processing social information (Kirchner et al., 2011; Klin et al., 2002), biological motion (e.g., point light displays depicting volitional movement; Kaiser & Pelphrey, 2012), and disruptions in spatial attention systems (Haist et al., 2005). These findings indicate that individuals with ASD show deficits processing both social and non-social information suggesting that basic perceptual processes may interfere with the ability to interpret new information and interact with the environment.

Motion perception is particularly important for processing dynamic information in naturalistic environments. Reduced skills perceiving visual-spatial information may interfere with individuals' ability to process rapidly changing environmental cues such as social cues (e.g. understanding facial cues or gestures; Van der Hallen et al., 2015). Studies of motion perception in ASD have resulted in inconsistent findings with some studies showing intact visual motion perception skills (Jones et al., 2011; Manning et al., 2015) and other studies demonstrating impaired abilities (Koldewyn et al., 2010; Milne et al., 2002; Spencer et al., 2000; Tsermentseli et al., 2008). A recent meta-analysis found that individuals with ASD showed a small but significant motion perception deficit across both biological and non-biological motion compared to age-matched typically developing (TD) controls (Van der Hallen et al., 2019). It is possible that only a subset of individuals with ASD, such as those with more impairing sensory symptoms, may show deficits in visual motion perception, relative to individuals with ASD with fewer sensory symptoms. Determining how visual motion processing abilities relate to sensory issues in ASD may help determine basic mechanisms of atypical and impairing sensory issues in affected individuals.

To accurately assess visual motion perception, objective readouts of sensory behaviors are needed. One method to assess visual motion perception is through the measurement of change in motor behaviors when visual feedback is manipulated. Examining motor behaviors is beneficial because measurements of motor output are objective, precise, and quantitative. Within ASD, there is evidence of impaired motor performance when viewing dynamic visual information (Lepping et al., 2022; Lidstone et al., 2020; Mosconi et al., 2015). This feedback process involves interpreting sensory information and translating it into new motor commands used to adjust ongoing behaviors (Desmurget & Grafton, 2000; Slifkin et al., 2000; Sosnoff & Newell, 2005). Prior studies have documented increased force variability in ASD when visual information was manipulated both at higher and lower levels of visual gain suggesting a reduced ability to integrate visual feedback to adjust continuous motor behaviors, particularly when the visual feedback is enhanced or degraded (Mosconi et al., 2015). Children with ASD also show reduced accuracy during grip force when they are tracking a moving target but not while viewing static visual feedback in which their force target remains stationary (Lidstone et al., 2020). This impairment was more severe than the issues seen in children with other neurodevelopmental disorders including attention deficit hyperactivity disorder (ADHD) and fetal alcohol spectrum disorder. These results suggest that children with ASD show increased difficulty effectively integrating dynamic rather than static visual feedback to modulate their motor behaviors and that these deficits are more pronounced in ASD relative to other neurodevelopmental disorders (Lidstone et al., 2020).

Neural Correlates of Visual Perception in ASD

One important advantage of studying visual motion processes in ASD is that brain networks associated with impairments may be more clearly defined than for more complex

cognitive and social behaviors. Neural correlates of visual perception have been well delineated in human lesion and non-human primate studies. Visual information is processed along two distinct but interacting cortical pathways, the ventral and dorsal pathways. The ventral, or "what" pathway, is specialized for the processing of object perception and recognition. The dorsal pathway, or "where" pathway, is specialized for the processing of spatial information and the control of sensorimotor behaviors. Initial processing of object information within the dorsal pathway occurs in primary (V1) and secondary (V2) visual "striate" cortices. Neurons within V1 selectively respond to the local orientation of motion (Movshon, 1990; Van der Hallen et al., 2019). Global processing of motion occurs further along the dorsal stream, primarily in middle temporal area (MT) or the human equivalent (V5) as well as the medial superior temporal area (MST). These "extrastriate" cortices are responsible for the integration of local motion into global motion perception (Movshon, 1990; Smith et al., 1994; Van der Hallen et al., 2019). Area MT/V5 also plays a key role in the processing of speed and speed discrimination (Liu & Newsome, 2003; Perrone & Thiele, 2002). MT/V5 activation also scales with increased coherence of motion indicating that V5 is highly direction selective (Rees et al., 2000). Extrastriate circuits also are involved in the integration of signals into global motion perception and guidance of motor commands via intraparietal sulcus (Hadad et al., 2015; Wattam-Bell et al., 2010) as well as posterior parietal cortex (PPC), including both inferior and superior parietal lobules (Robertson et al., 2014).

Functional magnetic resonance imaging (fMRI) studies have demonstrated that individuals with ASD show abnormal activation in motion sensitive cortex, including both enhanced (Samson et al., 2012) and reduced (Robertson et al., 2014; Takarae et al., 2014) activation across V1, V5, and PPC. One previous report suggested that individuals with ASD

show a dorsal stream vulnerability impacting motion perception, but that ventral stream function is relatively unaffected supporting intact form perception (Spencer et al., 2000). Subsequent ASD studies have documented abnormal dorsal pathway function, including reduced activation in V1 and V5 during a forced choice motion perception task (Robertson et al., 2014) and increased activation in V5 during passive viewing of visual motion (Brieber et al., 2010; Takarae et al., 2014). When viewing biological motion, reduced activation of V5 (Herrington et al., 2007), posterior superior temporal sulcus (pSTS) and bilateral parietal cortex along the inferior parietal sulcus also have been documented in individuals with ASD compared to controls (Koldewyn et al., 2011). Together, these findings suggest that fundamental motion processing is disrupted in ASD and is associated with atypical function of dorsal pathway circuits including V1 and V5. Further, these visual motion processing dysfunctions may disrupt higher-level processing of more complex biological movement and social information processing in afferent targets of V1 and V5 (e.g., pSTS). Brain activation and connectivity also show differences in ASD relative to typically developing (TD) controls within PPC, premotor, and striatal circuits during visuomotor behavior suggesting visual processing and visuomotor network functions may contribute to sensorimotor impairments (Lepping et al., 2022).

Electrophysiological studies also have documented altered cortical activation in ASD including reduced P1 event related potential latencies when passively viewing visual gratings (Brieber et al., 2010; Shuffrey et al., 2018) and increased spectral power which scaled across increasing stimulus contrasts (Takarae et al., 2016). These findings suggest that individuals with ASD may show increased excitatory or reduced inhibitory modulation of local circuits resulting in visual motion perception deficits (Shuffrey et al., 2018; Takarae et al., 2016). Additionally, these cortical differences were associated with increased sensory sensitivities in ASD (Shuffrey

et al., 2018; Takarae et al., 2016) suggesting that individuals with ASD show atypical cortical processes supporting low level visual processing that may contribute to separate sensory and clinical symptoms of ASD.

Functional Connectivity of Sensory and Sensorimotor Brain Networks in ASD

ASD is increasingly viewed as a disorder involving disrupted connectivity across and between brain networks rather than disruptions in isolated brain regions (Minshew & Williams, 2007; Oldehinkel et al., 2019). FMRI studies during rest have shown atypical structural and functional connectivity in ASD affecting visual, sensory (Cardon et al., 2017; Oldehinkel et al., 2019) and sensorimotor networks (Khan et al., 2015; Oldehinkel et al., 2019). FMRI studies of task-based functional connectivity during motion perception in healthy adults have shown strong connections between V5 and middle occipital gyrus, also referred to as human V3A (Hampson et al., 2004), as well as between V1 and V5 (Brieber et al., 2010). During visuomotor coordination, individuals with ASD show reduced connectivity relative to controls between V1 and inferior frontal cortex suggesting that they may show disruptions in dorsal stream function and visuomotor networks (Villalobos et al., 2005). However, there is also evidence during a task-based fMRI connectivity study that individuals with ASD show similar V1-V5 connectivity as controls (Brieber et al., 2010), yet this study focused on a small sample of adolescents with above average IQs suggesting that individuals with ASD without comorbid intellectual disabilities may show intact motion perception (Brieber et al., 2010). The inconsistent findings within the literature suggest that we need a better understanding of the linkage between neural mechanisms supporting motion perception and quantitative measures of motion perception to understand the functional properties of cortical networks supporting visual motion processing in ASD. The current study will extend previous findings by examining motion perception in

relation to objective and quantitative measures of visually guided motor behavior in a larger sample of individuals across a wide age range.

Based on the current literature, we tested the overarching hypothesis that individuals with ASD show reduced visual motion perception abilities involving atypical V1-V5 functional connectivity that contribute to difficulties in visually guided motor control. We also proposed that atypical processing of visual motion and V1-V5 functional connectivity are associated with reduced sensitivity to sensory stimuli. The following aims were pursued: 1) quantify visual motion perception in ASD during motor performance to determine how these measures vary as a function of changes in visual motion gain; 2) characterize neural systems of visual motion perception in ASD; and 3) clarify the relationships between visuomotor processes and core sensory and clinical issues in ASD. Aim 1 examined visual motion perception by utilizing objective measures of precision gripping (e.g., visuomotor variability and complexity) during varying conditions of visual motion gain. Consistent with the hypothesis that individuals with ASD show impairments integrating visual motion information to carry out precision motor behaviors, we predicted that individuals with ASD would show increased force variability and decreased force complexity compared to TD controls when visual gain is amplified or degraded.

Aim 2 characterized neural system correlates of visual motion perception in ASD. Aim 2a examined visual motion processing using an fMRI test of visual motion perception. We predicted that individuals with ASD would show abnormal activation in V1, V3, and V5 associated with greater force variability and reduced force complexity during visuomotor behavior. Aim 2b examined task-based functional connectivity during an fMRI test of visual motion perception. We expected that reduced V1-V5 connectivity in ASD versus TD controls would be associated with increased sustained force variability and reduced force complexity at

higher and lower visual gains during precision gripping. These findings would suggest that disruptions in visuomotor brain networks involved in the perception of motion may contribute to deficits in precision motor control in ASD.

Aim 3 clarified the relationships between visuomotor processes and core sensory and clinical issues in ASD. Consistent with our overarching model that atypical processing of visual motion in ASD is associated with developmental disruptions in processing sensory information and social-communication behaviors, we examined the relationships between our measures of visuomotor behavior and visual motion physiology with clinical ratings of sensory and social-communication issues in ASD. We hypothesized that deficits in visuomotor control across higher gain levels relative to lower gain levels and reduced V1-V5 activation and connectivity each would be associated with increased clinical sensory issues in ASD. Specifically, we hypothesized that increased visuomotor variability and reduced complexity across higher relative to lower gain levels and atypical V1-V5 activation and connectivity would be associated with reduced sensitivity to sensory stimuli (i.e., hyposensitivity). Further, based on the hypothesis that difficulties with visuomotor control reflect difficulties processing sensory information and disrupt complex social information processing, we predicted that visuomotor abilities and physiology alterations would be associated with more severe social-communication abnormalities. By determining the relationship between visuomotor abilities, visual motion physiology, and sensory and clinical impairments in ASD, this study aims to develop a more mechanistic understanding of sensory and social-communication differences.

Methods

Participants

Fifty-nine individuals with ASD (ages 10-33 years) and 44 age-matched TD control individuals (ages 8-34 years) completed visuomotor testing involving precision gripping with visual feedback (Tables 1-2). A subset of these participants (38 ASD and 33 TD controls matched on age) also completed an fMRI test of visual motion perception (Table 3).

Participants with ASD were recruited through the Kansas Center for Autism Research and Training (K-CART) and University of Kansas Medical Center (KUMC) Frontiers Patient Registries. To determine participant eligibility, individuals with ASD completed the following procedures. First, caregivers of eligible participants, or eligible participants over the age of 18, completed the Social Communication Questionnaire (SCQ; Rutter et al., 2003). Individuals who scored $\geq$ 15 on the SCQ completed the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2; Lord et al., 2012) and their caregivers completed the Autism Diagnostic Interview-Revised (ADI-R; Lord et al., 1994). Participants who met diagnostic criteria on the ADI-R and ADOS-2 and received a consensus diagnosis of DSM-5 ASD based on expert clinical opinion were eligible to participate. Due to the COVID-19 pandemic and restrictions on in person data collection, 15 participants with ASD were unable to complete the ADOS-2. Therefore, diagnostic criteria were based on the ADI-R, conducted via secure telehealth, and expert clinical opinion.

TD control participants were recruited through the Kansas Intellectual and Developmental Disabilities Research Center (KIDDRC) typically developing registry for infants and children and advertisements in the community. Caregivers of TD control participants less than 18 years of age or participants themselves if 18 years of age or older completed a brief phone interview and the SCQ. Participants with a score of less than eight and no current or past learning, psychiatric, or neurological disorders, family history of ASD in first- or second-degree

relatives, or family history of developmental or learning disorders, psychosis, or obsessive-compulsive disorder in first-degree relatives based on the initial phone interview were eligible to participate.

No ASD or TD control participants were positive for any genetic disorder associated with ASD, took any medication known to interfere with sensory processing or motor control including stimulants, anticonvulsants, or antipsychotics (Reilly et al., 2008), or had a history of non-febrile seizures or head trauma with loss of consciousness. IQ was assessed using the Weschler Abbreviated Scale of Intelligence-Second Edition (WASI-II; Wechsler, 2011) and all participants had a Full-Scale IQ (FSIQ) >70. Seventy-six participants (43 ASD and 33 TD Control) completed the 4-subtest WASI-2. Due to COVID-19 and restrictions on in-person contact, 23 participants (16 ASD and 7 TD Control) completed the two-subtest WASI-2 via secure telehealth. Due to the smaller number of subtests administered during remote testing, VIQ and PIQ were not calculated for these participants. Four TD control participants were unable to complete the WASI-2 due to scheduling difficulties. Participants' handedness was measured using the Annett Hand Preference Questionnaire (Annett, 1970). All participants had corrected visual acuity of >20/40.

Apparatus and Procedures

Behavioral Visuomotor Precision Grip Task

During precision grip testing, stimuli were presented on a 67cm Samsung LCD display monitor (1920x1080 resolution, 120-Hz refresh rate). Participants were seated 52 cm from the monitor in a darkened room. They sat with the elbow of their dominant hand positioned at 90 degrees and their forearm resting in a custom arm brace fixed to the table to provide stability during testing. Participants completed grip testing with a tendon vibrator (VB 115, Techno

Concept, Cereste, France) securely fastened on their wrist using a Velcro strap. Towels were placed underneath the participants' wrist to cushion the tendon vibrator from the surface of the table. This device was turned off during testing for this study. Participants used their thumb and index finger of their dominant hand to press against two opposing force load cells (ELFF-B4-100N; Entran) 1.27 cm in diameter that were secured to a custom grip device attached to the arm brace. A Colbourn (V72-25) resistive bridge strain amplified load cell analog signals. Data were sampled at 100 Hz with a 16-bit analog-to-digital converter (DI-720; DATAQ Instruments) and converted to Newtons.

Prior to testing, each participant's maximum voluntary contraction (MVC) was calculated for their dominant hand using the average of three trials in which they were asked to press as hard as they could for three seconds. During precision grip testing, the target force was set to 45% of the participants' MVC to control for differences in strength across participants. During testing, participants viewed a white horizontal force bar that moved upwards with increased force and a static target bar that was red during rest and turned green at the start to cue the participant to begin pressing. Participants were instructed to press the load cells as quickly as possible when the red target bar turned green and to keep pressing so that the white force bar stayed at the level of the green target bar.

To measure the impact of visual motion on precision gripping behavior, participants completed visuomotor testing across multiple visual gains. As in our previous studies (Mosconi et al., 2015; Shafer et al., 2021), visual gain was manipulated by changing the vertical distance that the force bar moved in response to a unit of change in force output as measured by the visual angle. The three visual gain conditions used in the present student were 0.059 degrees (low gain) 0.623 degrees (medium gain), and 6.575 degrees (high gain). These gain levels were selected

based on findings from Vaillancourt et al., (2006) which showed decreases in force variability and increases regularity as visual angle increased up to one degree, beyond which force variability and regularity were relatively constant.

Participants completed one block of five trials at each gain level using their dominant hand (five trials x three gain levels = 15 trials). Blocks alternated between a 15 second pressing condition and a 15 second rest period. Each block was separated by 30 seconds of rest. The order of the gain levels was randomized across participants.

fMRI Visual Motion Task

MRI testing took place during a second research visit at the KU Medical Center Hoglund Biomedical Imaging Center (HBIC). Prior to the MRI, participants reviewed a "social story" and became familiar with the MRI procedures. Participants were provided the option to complete a practice scan in our MRI scanner to become familiar with the MRI procedures prior to their real scan.

Participants completed an fMRI precision grip task similar to the laboratory task completed prior to the MRI. Prior to the scan, participants' MVC's were estimated using a custom Bragg grating fiber optic force transducer (Neuroimaging Solutions, Gainesville, FL). During the fMRI precision grip task, instructions were the same as the laboratory task. There was an additional vision only condition (i.e., visual motion condition) in which participants observed the white force bar moving to match the target bar, but they were instructed not to press. During this 26 second visual motion condition, participants observed their previous performance on the precision grip task. Participants completed three sequences of 26 second blocks of the following conditions: vision+motor and visual motion. Ten second rest conditions between each task condition also were presented, and the task started and ended with 26 second rest blocks.

Participants completed separate runs with their right and left hands. The order of the runs was randomized across participants. We examined blood-oxygen-level-dependent (BOLD) signal activation during the visual motion and rest conditions when participants were completing the task with their right and left hands. We did not examine the vision+motor condition for the current study.

Data Processing and Analysis

Precision Grip Task Data Processing

Force traces for each trial were low-pass filtered using a double-pass fourth-order Butterworth filter at a cutoff of 15 Hz in MATLAB (MathWorks, Inc., Natick, MA). Data were processed using a custom MATLAB scoring program previously developed by our lab (Wang et al., 2015). To measure performance during the laboratory test, we examined participants' force during the 12 seconds prior to the stop cue. Data were excluded if there was less than eight seconds of sustained force output, participants stopped pressing for greater than one second, there were calibration errors with the load cells, participants' mean force exceeded twice the target force, participants' force exceeded their MVC, or participants used fingers other than their index finger or thumb to press.

To measure sustained force variability during the sustained phase, we measured the coefficient of variation (CoV). CoV was calculated as the standard deviation of the force time series divided by mean force. CoV was examined to account for differences in mean force across participants. To examine the time-dependent structure of the force time series, approximate entropy (ApEn) was calculated (Slifkin & Newell, 1999; Vaillancourt et al., 2001). ApEn returns a value between zero and two, reflecting the predictability of future values in a time series based

on previous values. For example, a lower ApEn suggests greater regularity of the sequence while a higher ApEn suggests a less predictable, more complex signal.

fMRI Data Acquisition and Preprocessing.

MRI testing was completed at the KU Medical Center HBIC using a research dedicated three Tesla whole body MRI Siemens Skyra scanner and 20 channel head coil. In addition to the precision grip task, participants completed a high-resolution T1-weighted sequence (MPRAGE). T1 images were acquired while participants viewed a movie of their choice, and these images were used for alignment and standardization. Anatomical images (T1) were acquired in 160 contiguous sagittal slices at one x one x one mm resolution using the following parameters: FOV 256 x 204 x 160 mm, matrix 256 x 204 x 160, TR=8.1 ms, TE=3.7 ms, shot interval=2100 ms, inversion delay to the center k-line 1100 ms, flip angle=12º, bandwidth=192 HZ, duration 3:57. FMRI task data was acquired using a single-shot gradient EPI pulse sequence (TR/TE/flip=200 ms/30ms/60º, parallel imaging factor two, FOV 220 x 220 mm, acquisition matrix 64 x 64; 36 axial slices; three x three x four mm).

Image Processing and Analysis.

All MRI data were processed using the Analysis of Functional Neuroimages (AFNI; https://afni.nimh.nih.gov/) software suite. Anatomical images were first uniformized, skull-stripped, and nonlinearly warped to MNI standard space (MNI152) using the *@SSwarper* program. The first five volumes of each functional run were discarded to allow for magnetization equilibration. Slice-timing correction was applied using standard AFNI procedures, and consecutive volumes with more than 0.5 mm of movement was discarded. Remaining volumes were aligned to the nonlinearly warped, skull-stripped anatomical (T1) image using the minimum outlier volume (i.e., volume with the least movement) as a reference. Volumes were

spatially smoothed to a full-width half-maximum of 5 mm and scaled to the mean voxel timeseries values of 100. Regression analyses (*3dDeconvolve* and *3dREML*) for each subject used a standard block function while regressing out six motion parameters and their first derivative (three rotations, three translations). The dependent variable was the estimated β-coefficient (percent signal change) of the regressed time series comparing activation during visual motion versus rest.

For the functional connectivity analyses, a context-dependent correlation analysis (generalized psychophysiological interaction gPPI; Friston et al., 1997; McLaren et al., 2012) was used to compare changes in whole brain-V1, -V3, and -V5 connectivity between groups as a function of task. Separate gPPI analysis were conducted for each task (left- or right-hand condition) and for each of the six seed regions of interest (ROIs), including left and right V1, V3, and V5. Individuals' preprocessed images were analyzed using a generalized linear model (GLM) containing predictors for the visual motion and rest blocks (modelled using a canonical hemodynamic response function (HRF)), the seed timeseries, visual motion*seed and rest*seed PPI regressors, 12 motion regressors (six rotations/translations and their first derivatives), and a second-order orthogonal polynomial. PPI regressors were calculated as the interaction between the estimated neural signal from the seed region (by deconvolving the HRF) and the visual motion or rest timeseries, which was then reconvolved with the HRF. The resulting contrast images were entered into a second-level group analysis with participant as a random effect to compare the β weights of the two PPI regressors.

The AFNI programs *3dttest++* and *3dLME* were used to create separate group statistics maps and a group contrast statistics map. In light of recent concerns regarding false-positive rates in fMRI research (Eklund et al., 2016), best-practice recommendations from AFNI (Cox et

al., 2017) were applied using the auto-correlation function (ACF) function within the *3dClustSim* program to correct for multiple comparisons and false positive clusters. In short, simulated noise-only volumes using ACF blur values were created, thresholded, and clustered, providing recommended cluster-size thresholds (denoted as α) to use for given voxel-wise thresholds (denoted as p). All fMRI analyses used a second nearest-neighbor (NN2) and bi-sided thresholding method. Using these methods, we present results for a family-wise error rate of $p < .01$ and cluster-size threshold of $\alpha < .05$ with a cluster value of > 56 for between group activation contrasts and >248 for between group connectivity contrasts needed to detect significance.

Clinical Ratings

The ADI-R and ADOS-2 were used to examine ASD symptoms to confirm participants' ASD diagnosis. The ADI-R (Lord et al., 1994) is a semi-structured caregiver interview assessing current and past social interaction and communication symptoms of ASD, as well as the presence of restricted and repetitive behaviors. The ADOS-2 (Lord et al., 2012) is a semi-structured play-based assessment that uses developmentally appropriate social and play-based interactions to elicit behaviors typically impaired in ASD, including language and communication, reciprocal social interaction, play, and restricted and repetitive behaviors. The ADOS-2 has five different modules differentiated according to the child's age and language ability. Participants in the present study completed Module 2 (phrase speech), Module 3 (children with fluent speech), or Module 4 (adolescents or adults with fluent speech).

Caregivers of ASD participants completed the Sensory Profile 2 (SP-2), a caregiver report questionnaire of sensory abnormalities for children ages three to 14 years (Dunn, 2014). The Sensory Profile has been normed on a large national sample (Dunn & Westman, 1997) and is a valid and sensitive measure of sensory issues in ASD (Dunn et al., 2002). Individuals with

ASD over the age of 14 years completed the Adolescent/Adult Sensory Profile (Brown & Dunn, 2002), a self-report measure of sensory abnormalities. Both measures include scores across sensory domains (e.g., auditory processing, visual processing, touch processing, movement processing, body position processing, and oral sensory processing) as well as separate "quadrant" scores that reflect the nature of sensory issues across interacting neurological thresholds and behavioral responses (e.g., registration, seeking, sensitivity, and avoiding; Brown & Dunn, 2010). *Registration* is the degree to which a child misses sensory input; *seeking* is the degree to which a child seeks additional sensory input; *sensitivity* is the degree to which a child notices sensory input; and *avoiding* is the degree to which a child is bothered by sensory input. Visual processing and quadrant scores each were examined.

Individuals with ASD also completed the Social Responsiveness Scale, 2nd Edition (SRS-2; Constantino & Gruber, 2012), a caregiver- and self-report questionnaire validated for individuals ages 2.5 years to adulthood. Caregivers of individuals ages 18 years and younger completed the caregiver-report measure and individuals ages 19 and over completed the self-report questionnaire. The SRS-2 is a quantitative assessment of autism traits (Frazier et al., 2014) used to determine the presence and severity of social communication abnormalities associated with ASD. The SRS-2 total and subscale scores (e.g., social awareness, social cognition, social communication, social motivation, and restricted interests and repetitive behaviors) were examined.

Statistical Analyses

For the laboratory task of visuomotor behavior (Aim 1), we examined variability (CoV) and complexity (ApEn) using separate multilevel models (MLM). This approach allowed for the examination of within-subject and between subject effects. For both variables, we used a general

linear mixed effect model. Level one predictor variables included gain level (low, medium, or high visual gain). The level one fixed effect predictors included group (ASD vs. TD), age, and sex. All dichotomous variables (e.g., group and sex) were centered at zero. Age was converted to z-scores. Simple effect coding was used for gain level with one coding system used to represent low gain (0.67) versus medium and high gain (-0.33) and another to represent high gain (0.67) versus medium and low (-0.33). CoV was transformed using a log transformation due to a non-normal distribution. Given that FSIQ was significantly different between groups, we examined the association between FSIQ and each dependent variable (CoV and ApEn). FSIQ was not associated with either variable, thus it was not included in the models. Random intercepts of participant also were included in the models as they significantly improved model fit. A top-down approach was used with initial models including three-way interactions of group x gain x age, as well as all two-way interactions and main effect terms. To maintain the most parsimonious models and follow a hypothesis driven approach, additional three-way interactions were not included. Nested models were compared using likelihood ratio tests to determine whether each predictor improved the model fit. Variables that did not improve the model fit ($p>0.05$) were removed. For models with significant interaction effects, all lower-level interactions and main effects of variables included in the interaction were included in the final models (Hox et al., 2017).

For the fMRI task (Aim 2), group differences in cortical percent signal change were identified using AFNI's *3dLME* (Chen et al., 2013) with a two (group) x two (condition: right vs left hand) model with the group x condition interaction term for visual motion – rest contrasts. Visual motion dependent functional connectivity was identified using AFNI's *3dttest++* to conduct t-tests with group (ASD versus TD control) as the between-subject predictor for the

task-based contrast (visual motion-rest) separately for each condition (left and right hand). To examine the extent to which individual differences in visuomotor behavior were related to cortical percent signal change, we used general linear models for each ROI and gPPI comparison for the task-based contrast (visual motion-rest) in relation to visuomotor behavior quantified during laboratory testing (Aim 1). Group (ASD versus TD control) and visuomotor behavior (CoV or ApEn) were included as predictors as well as the group x visuomotor behavior interaction. Separate models were run for ApEn and CoV. To determine if variability differed across groups during the fMRI testing and therefore may contribute to differences in the amount of motion viewed during the visual motion condition, the standard deviation of the visual motion condition was compared between groups using an independent samples t-test.

To assess the relationships between visuomotor behavior and clinical symptoms (Aim 3), we conducted separate Spearman correlations between visuomotor outcomes (CoV and ApEn) and social-communication difficulties using the SRS-2 subscale and total t-scores. To measure the relationship between changes in visual gain on motor behaviors and measures of sensory differences we conducted separate Spearman correlations between change scores (e.g., differences in mean motor performance between middle and either high or low gain conditions) for each visuomotor precision gripping variable (CoV and ApEn) and the Child Sensory Profile 2 ($\leq$ age 14 years) or the Adolescent/Adult Sensory Profile (> age 14 years). For the Sensory Profile measures, we examined the quadrant raw scores (Seeking, Avoiding, Sensitivity, and Registration) and well as the visual domain score. We also examined the relationship between differences in brain activation and the Sensory Profile measures and the SRS-2 using separate Spearman correlations. Given the high number of correlations and to minimize Type I error, we used conservative cutoffs and only correlations of $r>0.5$ and $p<.05$ were considered significant.

Given the specific hypothesis regarding the associations between change in visuomotor behavior in response to changing visual gain and sensory sensitivity and registration as measured by the Sensory Profile, uncorrected results were interpreted.

Results

Behavioral Visuomotor Precision Grip Task

Individuals with ASD and TD controls showed similar MVCs (Table 1; ASD range: 15-119; TD Control range: 15-151). ASD participants showed a lower mean force across gain levels than TD controls [group main effect: $F(2, 1470)=33.67$, $p<.001$]. For both groups, mean force was similar across gain levels [gain level main effect: $F(2, 1469)=1.02$, $p=.36$].

Grip Force Variability

There were no differences in CoV between ASD and TD control participants. Male participants across both groups showed greater reductions in variability with increased age than female participants (age x sex: $\beta=0.13$, $SE=0.06$, $p=.024$; Table 4; Figure 1). Across groups, participants showed increased variability during the low and high gain conditions relative to the medium gain condition [visual angle (low vs. med + high gain) main effect: $\beta=0.08$, $SE=0.02$, $p<.001$; visual angle (high vs. med + low gain) main effect: $\beta=0.07$, $SE=0.02$, $p<.001$].

Approximate Entropy

ASD participants showed reduced force complexity relative to TD controls, and force complexity varied as a function of visual gain. The ASD group showed reduced complexity relative to controls during the low and medium visual gain conditions compared to the high gain condition [group x visual angle (low + med vs high gain): $\beta=0.04$, $SE=0.01$, $p=.007$], but no difference from controls when low gain was compared to medium and high gain [group x visual angle (low vs. med+high gain): $\beta=0.02$, $SE=0.01$, $p=.16$; Table 5; Figure 2]. Participants across

both groups showed greater force complexity at older ages (age main effect: β=0.06, SE=0.01, p<.001).

Brain Activation During Visual Motion Processing

We examined the variability of the visual motion condition viewed by participants separately for each hand. There was no difference in variability between the ASD and TD control groups for the right- (ASD: Mean = 0.85, SD= 0.61; TD Control: Mean= 0.68, SD=0.39) or left-hand conditions (ASD: Mean=0.76, SD=0.45; TD Control: Mean=0.68, SD=0.51). Across both groups, there was no significant difference in variability between the left-and right-hand conditions (Left: Mean= 0.72, SD=0.48; Right: Mean=0.77, SD=0.52).

Across groups, increased BOLD activation was seen in bilateral V5 during the visual motion condition relative to rest during the left-hand condition (Table 6). Similarly, during the right-hand condition, subthreshold increased BOLD activation was seen in right V5 (α <.07) and left V5 (α <.08).

BOLD activation in left thalamus extending to the left caudate nucleus showed a group x condition effect characterized by decreased activation in the TD control group relative to the ASD group during the right-hand condition (Table 7; Figure 3). Right dorsal intraparietal sulcus activation also varied as a function of group and condition, though this effect was below our significance threshold (α <.10). Right dorsal intraparietal sulcus showed increased activation in the ASD group relative to the TD control group during the right-hand condition and increased activation in the TD control group relative to the ASD group during the left-hand condition.

There was significant BOLD activation in the right caudate head extending towards the left caudate that varied as a function of group (Table 7; Figure 4). This increased activation was driven by the ASD group relative to TD controls.

BOLD activation across multiple regions differed as a function of hand tested (Table 7). Right primary motor cortex showed increased activation extending to right primary sensory cortex during the right-hand condition compared to the left-hand condition. Left primary motor cortex extending to the left primary sensory cortex and right cerebellum extending from lobules IV to V showed increased activation during the left-hand condition compared to the right-hand condition.

Functional Connectivity

Functional Connectivity Differences Between Individuals with ASD and TD Controls

No significant task-based functional connectivity differences were seen between groups.

Relationships Between Behavioral Performance, Brain Activation, and ASD Symptoms

BOLD Activation Associated with Visuomotor Behavior

Group (β = -0.35, SE=0.12, p=.005) and ApEn (β = -1.10, SE=0.51, p=.03) were associated with left thalamus activation during the right-hand condition indicating that the ASD group showed greater activation in the left thalamus than controls and that greater left thalamus activation was associated with lower ApEn across groups.

TD participants showed a negative association between BOLD activation and ApEn in the intraparietal sulcus during the left-hand condition, but this relationship was not significant for the ASD group (group x ApEn interaction: β = -1.48, SE=0.75, p=.054). TD controls also showed greater intraparietal sulcus activation than the ASD group (group main effect: β=0.83, SE=0.29, p=.006). Further, there was a positive association between BOLD activation in the intraparietal sulcus during the left-hand condition and CoV in TD controls, but no relationship in the ASD group (group x CoV interaction: β = 0.71, SE=0.31, p=.02).

Clinical Associations with Visuomotor Behavior and Brain Activation in ASD

Increased social communication difficulties on the SRS-2 were associated with decreased ApEn (r_s=-0.53, p=.002; Figure 5; Table 8). Increased change in ApEn from medium to high gain levels was associated with increased self-reported sensory sensitivity as measured by the Adolescent/Adult Sensory Profile, though this relationship did not reach significance (r_s=0.40, p=.066; Figure 6; Table 9).

Increased BOLD activation in the right caudate during the right-hand condition was associated with decreased social awareness (r_s=-0.58, p=.008; Figure 7a; Table 10) and decreased restricted and repetitive patterns of behaviors (r_s=-0.62, p=.004; Figure 7b) as measured by the SRS-2. Increased BOLD activation in the right caudate during the right-hand condition was associated with decreased registration as measured by the caregiver-report Sensory Profile (r_s=-0.83, p=.005; Figure 7c; Table 11).

Discussion

Studying visual motion effects on visually guided motor behavior and the neurophysiology of visual motion processing in ASD, we document several novel findings. First, decreases in force complexity were more severe in ASD compared to TD controls when visual gain was degraded suggesting an increased reliance on visual feedback to control precision motor behaviors. Second, visual motion sensitive brain regions, including V5, showed similar levels of brain activation and functional connectivity for individuals with ASD and TD controls. We found increased caudate activation in ASD during visual motion processing which suggests greater reliance on subcortical networks to suppress unwanted motor behaviors given that the fMRI task also involved a visuomotor behavior component. Third, we found that decreased force complexity was associated with more severe social communication difficulties in ASD suggesting that disruptions in visual motor integration may contribute to social communication

impairments. We also found that increased caudate activation was associated with less severe autistic symptoms suggesting that greater recruitment of subcortical regions involved in motor suppression and inhibition may result in a suppression of other core ASD symptoms. Finally, we found that increased change in force complexity from medium to high gain was associated with increased sensory sensitivity in ASD indicating that hyper-reactivity to visual stimuli during motor behavior is associated with greater sensory hypersensitivities suggesting overlapping visuomotor neural networks.

Visually Guided Motor Behavior in ASD

We found that individuals with ASD showed greater motor impairments than TD controls during a visually guided precision gripping task suggesting a reduced ability to translate visual feedback to precision motor behaviors (Mosconi et al., 2015; Wang et al., 2015). Specifically, we found that individuals with ASD showed reduced complexity relative to controls only during the lower visual gain conditions indicating that they may be overly reliant on visual relative to non-visual sensory feedback (e.g., haptic, proprioceptive) to make precision motor behaviors. Over reliance on visual feedback in ASD has been demonstrated in studies comparing motor performance during conditions of static versus dynamic visual feedback. Lidstone et al. (2020) found that individuals with ASD showed greater difficulties modulating motor behaviors compared to TD controls when tracking a visual target (i.e., dynamic visual feedback) relative to static visual feedback (e.g., individuals pressed a force transducer to reach a static target box). These findings, taken together, suggest specific disruptions in visual motor integration in ASD. Further, the present study did not find differences in visuomotor behavior during higher visual gain conditions, which contrasts with our previous studies showing increased variability at higher visual gain conditions (Lepping et al., 2022; Mosconi et al., 2015). Differences between

studies may reflect the narrower range of visual gain levels used in the present study indicating that individuals with ASD may show impairments in precision gripping only when visual gain is more significantly increased, relative to the high visual gain condition used in the present study.

Studies also have documented that individuals with ASD show an altered ability to effectively integrate multiple types of sensory feedback to coordinate movements. During a similar precision gripping task, Shafer et al., (2021) found that individuals with ASD and TD controls showed similar changes in force variability when visual feedback was manipulated. However, when somatosensory feedback was manipulated, only TD controls showed disruptions in motor performance while individuals with ASD showed similar performance with and without the somatosensory disruption. These findings suggest that individuals with ASD rely more heavily on visual feedback than somatosensory feedback during precision manual motor behaviors and show a reduced ability to integrate multiple types of sensory information to effectively control continuous motor actions. Studies also have shown an increased reliance on proprioceptive feedback relative to visual feedback during motor learning in ASD (Haswell et al., 2009; Izawa et al., 2012) and that increased reliance on proprioceptive feedback is associated with more severe impairments in motor functioning, social interaction, and imitation (Haswell et al, 2009). These findings indicate that different motor behaviors involve differing patterns of sensory reliance and provide converging evidence for a bias towards integration of uni-sensory information to adjust motor behaviors rather than integrating multisensory information in ASD.

Visual Motion Brain Activation in ASD

Based on previous studies showing abnormal activation in motion sensitive cortices in ASD (Robertson et al., 2014; Samson et al., 2012; Takarae et al., 2014), we predicted that individuals with ASD would show abnormal activation in areas V1, V3, and V5 during visual

motion. However, we found similar increases in activation in motion sensitive regions across groups during visual motion perception indicating that participants were sensitive to the visual motion presented during the task. Therefore, differences in motion perception and precision visuomotor behaviors across groups were not due to differences in the function of motion sensitive extrastriate cortex. The null findings in the extrastriate cortex are consistent with previous studies showing intact visual motion perception abilities in ASD (Jones et al., 2011; Manning et al., 2015) and a previous study showing similar connectivity between V1 and V5 during a visual motion task (Brieber et al., 2010). Our null findings indicate that differences in visuomotor behaviors found during the present study are not due to differences in dorsal pathway function and may instead be due to difference in visuomotor-cerebellar or striatal networks. Another possible explanation is that that visual motion perception impairments may only be seen in a subset of individuals with ASD demonstrating the need for further studies characterizing sensory differences in ASD.

We also found that individuals with ASD showed greater caudate activation than TD controls during visual motion in contrast to rest reflecting an increased need for motor suppression after completing a motor task. During this fMRI paradigm, participants first completed a motor condition and then viewed their previous motor performance but were instructed not to press. Blocks during which participants were pressing during the visual motion condition were excluded from analyses. Therefore, all participants included were successful in inhibiting their motor response during blocks of trials included in the analyses. Increased caudate activation in the ASD group suggests that greater cognitive resources were required to inhibit or suppress the planned motor behavior when instructed to passively view motion. This finding may also suggest increased involvement in motor preparation and planning as the caudate and other

anterior basal ganglia nuclei are involved in early stages of visuomotor planning (Prodoehl et al., 2009; Wasson et al., 2010). Our finding of increased activation to inhibit motor behaviors is consistent with evidence showing that basal ganglia circuits are involved in the inhibition and suppression of unwanted behaviors and that inhibitory control is essential to achieve coordinated movements in a changing environment (Subramanian et al., 2017). Additionally, there is evidence of deficits in inhibitory control in ASD (Christ et al., 2007; Mosconi et al., 2009; Schmitt et al., 2018) associated with altered fronto-striatal white matter organization (Langen et al., 2012). Our findings indicate that in order to have similar performance to controls during this visual motion task, individuals with ASD show altered striatal activation suggesting greater difficulty inhibiting a planned motor movement.

Our finding of increased caudate activation in ASD is consistent with studies showing altered basal ganglia structure and function in ASD. The basal ganglia are made up of several subcortical nuclei including caudate, putamen, nucleus accumbens, globus pallidus, and subthalamic nucleus (Subramanian et al., 2017). These regions are involved in a range of sensorimotor and cognitive tasks including motor learning and initiation (Graybiel, 2008; Hikosaka et al., 2002), sensory processing and integration (Graybiel, 1998; Jin & Costa, 2015; Yin, 2010), and inhibitory control (i.e., the ability to inhibit prepotent responses; Jahanshahi et al., 2015; Langen et al., 2012). Within ASD, postmortem studies of the basal ganglia reveal greater volumes of the caudate nucleus and nucleus accumbens (Wegiel et al., 2014), yet structural MRI studies have been inconsistent. Some studies have found no difference in caudate volumes between ASD and controls (Harden et al., 2003; Sato et al., 2014; Sears et al., 1999), yet other studies have shown increased caudate volumes in ASD relative to TD controls after controlling for total cerebral volume (Hollander et al., 2005; Langen et al., 2007). There is also

evidence of functional differences within the basal ganglia in ASD including increased fronto-striatal circuit activation, including caudate nucleus activation, in individuals with ASD relative to controls during eye movements (Takarae et al., 2007) and increased putamen activation during visuomotor behavior in ASD relative to controls (Unruh et al., 2019). These findings demonstrate an atypical organization of subcortical networks involved in visuomotor control and automatic sensorimotor behaviors and an increased reliance on subcortical circuits in ASD.

In contrast, we also found that the TD control group showed lateralized differences in thalamus activation relative to ASD characterized by decreased left hemisphere thalamic activation during the right-hand condition. Thalamic nuclei serve as a relay for sensory and motor signals from the body to the cerebral cortex (Ding et al., 2010). Thalamic cortico-striatal circuits are involved in the suppression of motor behavior and the regulation of these circuits supports shifting attention and suppressing motor behavior in the presence of salient sensory stimuli (Ding et al., 2010). In the context of the present visual motion study, the lateralized deactivation in TD controls relative to ASD suggests that the ASD group and TD controls may rely on different regions within the thalamic cortico-striatal circuit to achieve a similar outcome of motor suppression. We also found that decreased thalamic activation during the right-hand condition was associated with increased complexity across groups suggesting that reduced activation is associated with improved precision visuomotor behaviors, which was seen particularly in the control group. These findings provide further evidence of altered organization of subcortical networks involved in visuomotor behavior and visual motion processing.

TD controls also showed increased activation in the intraparietal sulcus during the left-hand condition but slightly decreased activation during the right-hand condition relative to ASD, though this difference in activation was subthreshold. This region is involved in motion

perception (Salillas et al., 2008; Wattam-Bell et al., 2010) and reduced activation in ASD during the left-hand condition suggests possible disruptions in higher level motion processing in ASD. Further, during the left-hand condition, increased activation was associated with decreased complexity and increased variability in TD controls, with no relationship in ASD. This relationship suggests that overactivation of the intraparietal sulcus is associated with worse visuomotor behaviors, but only in TD controls.

Functional Connectivity in ASD

Given evidence of disrupted connectivity in ASD impacting visual, sensory (Cardon et al., 2017; Oldehinkel et al., 2019), and sensorimotor networks (Khan et al., 2015; Oldehinkel et al., 2019), we examined task-based functional connectivity during motion perception. We predicted reduced connectivity between visual processing regions V1 and V5 in ASD versus TD controls. However, we found no significant differences in task based functional connectivity with V1, V3, or V5 between ASD and TD controls. This null finding suggests that differences seen in the integration of visual feedback to make precision motor behaviors may be due to alterations in connectivity within visuomotor networks rather than connectivity between basic sensory regions involved in the processing of visual motion. Evidence of altered connectivity in ASD during a visuomotor precision gripping task with varying levels of visual gain has shown that visuomotor deficits in ASD are associated with atypical functional connectivity of the posterior parietal, premotor, cerebellar, and striatal circuits, which are involved in translating sensory feedback into precise motor behaviors (Lepping et al., 2022).

Another possible explanation for the null functional connectivity findings within visual motion processing regions is that basic sensory connectivity differences during visual motion perception may be present in only a subset of individuals with ASD. Given the heterogeneity

within ASD, it is possible that individuals with basic sensory connectivity differences were not reflected in the present study. These results are consistent with a previous study showing that individuals with ASD had similar V1-V5 connectivity as controls (Brieber et al., 2010). This study by Brieber et al. (2010) was conducted in a sample of autistic individuals with above average IQs. It is possible that differences in connectivity with basic visual regions may be more pronounced in individuals with more significant autistic symptoms or comorbid intellectual disabilities. However, these individuals are often excluded from fMRI studies due to behavioral difficulties and difficulties completing task-based fMRIs. Future studies should include individuals with ASD with comorbid intellectual disabilities and a wider range of symptom severity to reflect the broader population and determine whether basic visual sensory connectivity differences may impact visual motion perception in a subset of individuals.

Associations Between ASD Symptoms, Visuomotor Impairments, and Brain Activation

We found that reduced complexity across visual gain conditions was associated with more severe social communication difficulties in ASD. One hypothesis is that early alterations in sensory and motor development in ASD may contribute to the development of autistic symptoms (Castartelli et al., 2016; Gliga, 2014; Hannant et al., 2016). This theory suggests that disruptions in the ability to integrate and interpret visual information to carry out motor behaviors may contribute to difficulties imitating others' actions and interpreting and predicting social motor behaviors (e.g., gestures) resulting in impairments in social skills and social awareness (Lidstone & Mostofsky, 2021). Further, children with fine motor delays early in development are at a greater risk for developing ASD by age three years (Landa & Garrett-Mayer, 2006) and motor impairments and deficits in gestures are increased in children with ASD compared to children with other neurodevelopmental disorders (Dewey et al., 2007; Mostofsky et al., 2007). Autistic

symptoms also are associated with reduced white matter integrity within visual processing regions in siblings who developed autism suggesting that alterations in connectivity within visual processing regions may contribute to increased risk and early development of ASD symptoms (Girault et al., 2022). These findings suggest that early visual motor impairments are associated with and may contribute to the development of core ASD symptoms later in life including social and communication difficulties.

We also found that greater changes in complexity with increasing visual gain were associated with elevated self-reported sensory sensitivity in autistic individuals; yet this relationship was not present with caregiver reported sensory sensitivity. This relationship suggests that deficiencies in processing sensory information may contribute to motor behavioral impairments in ASD, and that these sensory processing issues relate to core clinical sensory disruptions. The association implicates underlying visuomotor neural networks responsible for the integration of sensory feedback to adjust motor commands (Shafer et al., 2021) and suggests that this shared visuomotor networks may underpin both precision visuomotor impairments and sensory hypersensitivities, particularly within the visual domain. Additionally, the differing findings between self- and caregiver-reported sensory sensitivities emphasizes the importance of measuring sensory symptoms across multiple informants. It is especially important to gather self-report measures of sensory symptoms given the difficulty of others reporting on an internal process.

Further, our results show that increased activation in the right caudate was associated with less severe autistic symptoms including decreased social awareness difficulties and restricted and repetitive behaviors. Given the active role that the basal ganglia play in motor suppression and inhibition (Jahanshahi et al., 2015; Langen et al., 2012) and the increased

activation needed to suppress motor behaviors during this task, this association between increased caudate activation and less severe autistic symptoms suggests that individuals who show the greatest activation may be better able to inhibit other unwanted behaviors, including repetitive behaviors or inappropriate social behaviors. We also found that increased caudate activation was associated with a greater ability to attend to relevant sensory cues. In addition to playing a role in the suppression of motor behaviors, increased caudate activation may be involved in the processing of visual feedback suggesting that individuals with ASD with greater caudate activation also show more awareness of sensory cues in the environment and fewer core ASD symptoms.

Limitations and Future Directions

There are several limitations with the present study. First, our sample was limited to individuals with an IQ > 70. This limits the generalizability of our findings to the broader sample of individuals with ASD and reflects the need for a larger and more diverse sample of autistic individuals. An important next step will be to conduct laboratory and task-based fMRI and connectivity studies with a sample of autistic individuals across cognitive abilities and levels of support needs. To complete task-based fMRIs, modifications to procedures may be needed to include individuals with comorbid intellectual disabilities as described by Nordahl et al., (2016). Another limitation of the present study was the age range of participants. Given the restrictions on data collection due to COVID-19, the age range for this study was expanded to include a wider range of older individuals. To effectively examine developmental changes in visual motion perception and its impact on motor behavior, particularly early in childhood when these key sensory regions are still developing, a larger sample across younger ages is needed. This may

include a longitudinal study design or a cross-sectional design that includes a larger number of participants across each age.

One limitation of the fMRI study was the experimental design of our visual motion task. Our results showed greater activation in subcortical regions including the caudate and thalamus which suggests increased activation due to motor suppression. Given that participants viewed the visual motion after completing a motor task, they appeared to be using significant cognitive resources to suppress the motor response. A pure visual motion task in which participants are not also completing a motor task will allow for a more precise measure of basic visual regions involved in motion perception.

A final limitation was in our assessment of clinical sensory symptoms in ASD. Given the expanded age range, participants completed two different versions of the Sensory Profile (i.e., self- and caregiver-report) and we were unable to combine scores across groups resulting in smaller samples for each measure. Further, given limitations of caregiver-reported measures of sensory symptoms, future studies should use more quantitative or observational measures of sensory symptoms in addition to multiple informant reports to better understand the association between visuomotor behaviors and brain activation with dimensional measures of these common and impairing clinical symptoms.

Conclusions

The present study demonstrates that individuals with ASD show a reduced ability to integrate visual feedback during a precision gripping task, particularly when visual gain is degraded, suggesting an overreliance on visual feedback during motor control. We also found no differences between groups in activation or connectivity of key visual motion processing regions suggesting that differences in visuomotor behaviors may be due to differences within visuomotor

or striatal networks, rather than basic sensory processing regions among individuals with ASD. Finally, we found that deficits in visually guided motor behaviors were associated with core ASD symptoms implicating shared neural mechanisms underlying visual motor integration and core ASD symptoms.

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Appendix

Table 1

Demographic and Clinical Characteristics of Participants Who Completed the Laboratory Visuomotor Precision Gripping Task

	N (%Male)[a]	Age	FSIQ	PIQ	VIQ	% Right-Handed[a]	MVC
ASD	59 (66)**	16.1 (5.5)	104.1 (14.4)**	104.3 (15.5)*	101.9 (13.3)*	88%	50.3 (23.2)
TD Controls	44 (39)**	17.0 (6.8)	111.8 (10.6)**	111.1 (11.3)*	108.3 (9.5)*	84%	57.2 (32.4)

Note. Data are reported as mean (standard deviation).

[a] % Male and % Right-handed were compared across groups using a chi-squared test.

**p<0.01; *p<0.05.

Abbreviations: FSIQ, Full-Scale IQ; PIQ, Performance IQ; VIQ, Verbal IQ.

Table 2

Racial and Ethnic Demographic Characteristics of Participants

	ASD (N=59)	TD Controls (N=44)
Race		
White	49 (83.1)	34 (77.3)
Black or African American	0 (0)	2 (4.5)
Asian	1 (1.7)	0 (0)
Native Hawaiian or Other Pacific Islander	1 (1.7)	0 (0)
American Indian or Alaskan Native	2 (3.4)	0 (0)
More than One Race	5 (8.5)	7 (15.9)
Other or Unknown	1 (1.7)	1 (2.3)
Ethnicity		
Hispanic or Latino	50 (84.7)	34 (77.3)
Not Hispanic/Latino	8 (13.6)	9 (20.5)
Unknown	1 (1.7)	0 (0)

Note. Data are reported as number (percentage). Race and ethnicity were compared across groups using a chi-squared test.

Table 3

Demographic and clinical characteristics of participants who completed both the fMRI visual motion and laboratory visuomotor precision gripping tasks

	N (%Male)[a]	Age	FSIQ	PIQ	VIQ	% Right-Handed[a]
ASD	38 (55)	17.7 (6.1)	105.0 (14.7)**	105.2 (15.6)*	104.3 (13.3)	84%
TD Controls	33 (39)	18.1 (6.8)	113.5 (10.6)**	112.6 (10.2)*	109.2 (9.6)	85%

Note. Data are reported as mean (standard deviation).

[a] % Male and % Right-handed were compared across groups using a chi-squared test.

**p<0.01; *p<0.05.

Abbreviations: FSIQ, Full-Scale IQ; PIQ, Performance IQ; VIQ, Verbal IQ.

Table 4

MLM Showing Significant Predictors of CoV for the Visuomotor Precision Gripping Task

Fixed Effect Estimates	Estimate (SE)	*t*	*p*
Level 1 Variables			
Intercept	-1.11 (0.03)	-41.80	<.001
Visual Angle (Low vs Med + High)	0.08 (0.02)	5.60	<.001
Visual Angle (Low + Med vs High)	0.07 (0.02)	4.73	<.001
Level 2 variables			
Age	-0.16 (0.03)	-5.427	<.001
Sex	-0.06 (0.05)	-1.12	.26
Interaction Variables			
Age x Sex	0.13 (0.06)	2.30	.02
Random Effects Variance	Variance (SD)		
Level 1 Residual	0.06 (0.23)		
Level 2 Intercept	0.07 (0.26)		

Table 5

MLM Showing Significant Predictors of ApEn for Sustained Precision Grip Task

Fixed Effect Estimates	Estimate (SE)	*t*	*p*
Level 1 Variables			
Intercept	0.34 (0.01)	33.10	<.001
Visual Angle (Low vs Med + High)	-0.07 (0.01)	-9.84	<.001
Visual Angle (Low + Med vs High)	-0.023 (0.01)	-3.41	<.001
Level 2 variables			
Group	-0.02 (0.02)	-0.98	.331
Age	0.06 (0.01)	5.80	<.001
Interaction Variables			
Group x Visual Angle (Low vs Med + High)	0.02 (0.01)	1.41	.158
Group x Visual Angle (Low + Med vs High)	0.04 (0.01)	2.69	.007
Random Effects Variance	Variance (SD)		
Level 1 Residual	0.01 (0.11)		
Level 2 Intercept	0.01 (0.10)		

Table 6

Brain Regions Showing Significant Activation Combined Across ASD and TD Control Groups During Visual Motion – Rest

	Cluster size (Voxels)	Peak Z-statistic	Peak activation location (MNI)		
			X	Y	Z
Left hand condition					
R V5/MT	961	5.07	-50	71	-2
L V5/MT	553	5.16	53	71	5
Right hand condition					
R V5/MT	294	5.45	-44	65	5
L V5/MT	282	5.22	44	77	5

Note. Voxel-wise $p<0.01$; $\alpha<0.05$; clusters ≥ 365 were retained. Peak activation location is in MNI (Montreal Neurologic Institute) coordinate space.

Abbreviations: R, right; L, left; V5/MT, middle temporal visual area.

Table 7

Brain Regions Showing Significant Group, Condition, or Group x Condition Interactions in Activation in the Linear Mixed Effects Model (3dLME)

	Cluster size (Voxels)	Peak F-value	Peak activation location (MNI)		
			X	Y	Z
		Group (main effect)			
R caudate	101	16.82	-17	-35	-5
		Condition (main effect)			
R M1	318	19.91	-41	26	62
L M1	134	16.02	41	17	53
R cerebellum lobules IV-V	100	27.09	-14	56	-17
		Group x Condition			
L thalamus	169	21.25	17	20	14
R IPS	53	12.91	-35	50	35

Note. Voxel-wise $p<0.01$; $\alpha<0.05$; clusters ≥ 56 were retained. Peak activation location is in MNI (Montreal Neurologic Institute) coordinate space.

Abbreviations: R, right; L, left; IPS, intraparietal sulcus; M1, primary motor cortex.

Table 8

Association Between Visuomotor Precision Gripping and Social Communication Symptoms Measured Using the SRS-2 in ASD

	CoV	ApEn
Social Awareness	0.36	-0.47
Social Cognition	0.20	-0.21
Social Communication	0.41	-0.53*
Social Motivation	0.04	-0.14
RRBs	0.30	-0.37
Total Score	0.38	-0.49

Note. $p<0.05$*.

Abbreviations: SRS-2, Social Responsiveness Scale, Second Edition; CoV, coefficient of variation; ApEn, approximate entropy; RRBs, restricted and repetitive behaviors.

Table 9

Association Between Visuomotor Precision Gripping and Sensory Symptoms Measured Using the Caregiver- and Self-Report Sensory Profile in ASD

		CoV (Med vs. Low Gain)	CoV (Med vs High Gain)	ApEn (Med vs Low Gain)	ApEn (Med vs High Gain)
Caregiver-Report	Seeking	0.23	-0.14	-0.17	-0.02
	Avoiding	0.07	0.03	-0.19	-0.03
	Sensitivity	0.01	-0.05	-0.10	-0.03
	Registration	-0.08	-0.08	-0.06	0.10
	Visual Processing	0.03	-0.08	-0.05	0.02
Self-Report	Registration	-0.03	-0.18	0.04	0.16
	Seeking	-0.26	-0.18	0.13	0.08
	Sensitivity	-0.02	-0.35	0.07	0.40~
	Avoiding	-0.30	-0.18	0.19	0.22
	Visual Processing	-0.05	-0.17	-0.03	0.22

Note. ~p=.066.

Abbreviations: CoV, coefficient of variation; ApEn, approximate entropy; Med, medium.

Table 10

Association Between Brain Activation and Social Communication Symptoms Measured Using the SRS-2 in ASD

	Left Thalamus (RC)	Left Thalamus (LC)	IPS (RC)	IPS (LC)	Right Caudate (RC)	Right Caudate (LC)
Social Awareness	-0.30	-0.12	-0.05	-0.24	-0.58**	0.10
Social Cognition	0.10	-0.29	-0.38	-0.14	-0.29	-0.06
Social Communication	-0.27	-0.28	-0.15	-0.25	-0.46	-0.03
Social Motivation	0.06	-0.14	-0.32	-0.09	-0.07	-0.11
RRBs	-0.28	-0.12	-0.15	-0.07	-0.62**	-0.09
Total Score	-0.13	-0.30	-0.25	-0.30	-0.49	-0.06

Note. **p<0.01.

Abbreviations: SRS-2, Social Responsiveness Scale, Second Edition; RC, right hand condition; LC, left hand condition; IPS, intraparietal sulcus.

Table 11

Association Between Brain Activation and Sensory Symptoms Measured Using the Caregiver- and Self-Report Sensory Profile in ASD

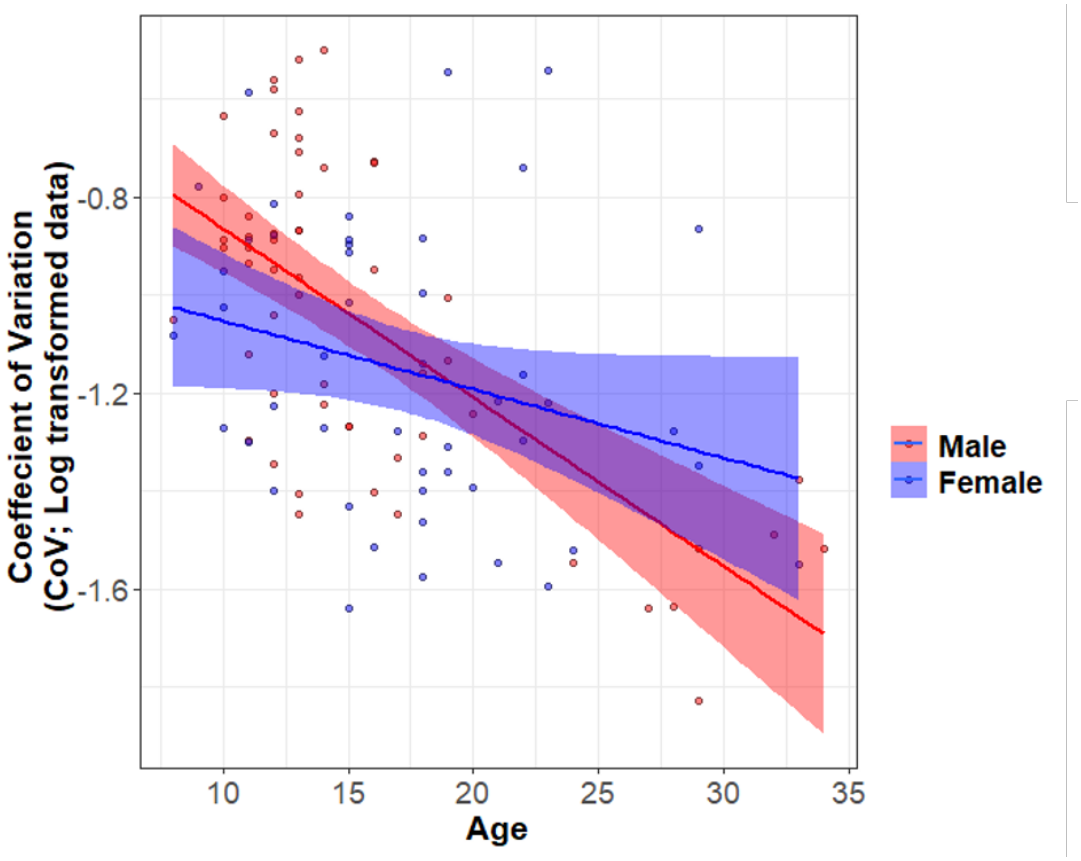
		Left Thalamus (RC)	Left Thalamus (LC)	IPS (RC)	IPS (LC)	Right Caudate (RC)	Right Caudate (LC)
Caregiver-Report	Seeking	0.21	-0.21	0.06	-0.10	-0.49	-0.23
	Avoiding	0.17	-0.13	-0.37	-0.10	-0.35	0.26
	Sensitivity	0.01	-0.35	0.09	-0.36	-0.54	-0.14
	Registration	0.10	-0.53	0.32	-0.18	-0.83**	-0.47
	Visual Processing	0.07	-0.13	0.17	-0.44	-0.28	0.27
Self-Report	Registration	0.21	-0.41	0.06	0.02	0.14	-0.43
	Seeking	-0.05	0.28	0.20	0.001	-0.14	-0.23
	Sensitivity	0.04	-0.20	0.004	-0.31	0.20	-0.37
	Avoiding	0.15	-0.04	0.39	-0.35	0.45	-0.42
	Visual Processing	0.07	0.06	0.32	-0.40	0.36	-0.41

Note. $p<0.01$**.

Abbreviations: RC, right hand condition; LC, left hand condition; IPS, intraparietal sulcus.

Figure 1

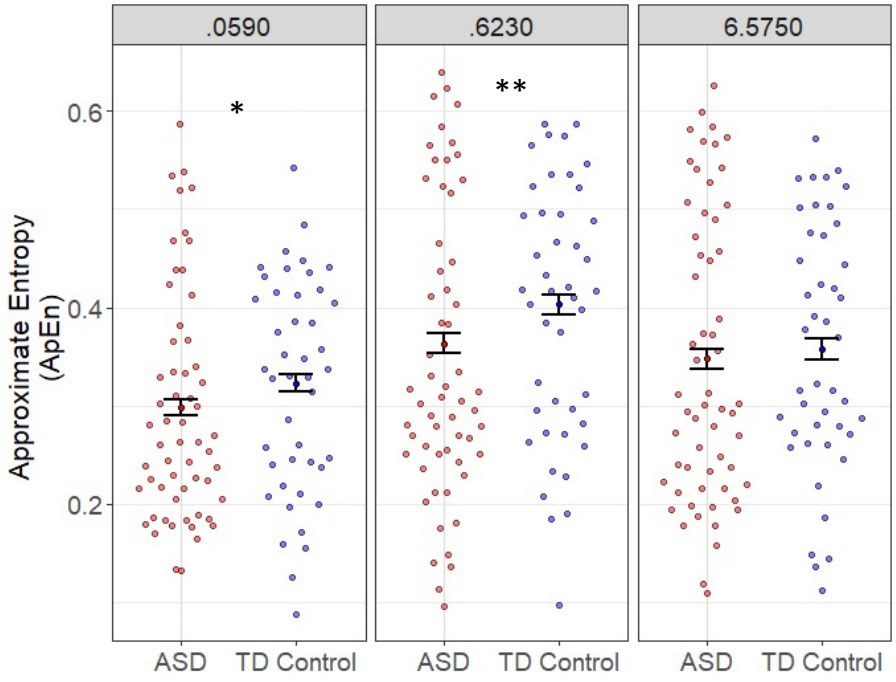
Sustained Force Variability for Individuals with ASD and TD Controls Varies as a Function of Age and Sex



Note. During the precision gripping task, males across both groups showed greater reductions in variability across age than female participants.

Figure 2

Sustained Force Complexity During Precision Gripping for Individuals with ASD and TD Controls Across Visual Feedback Conditions



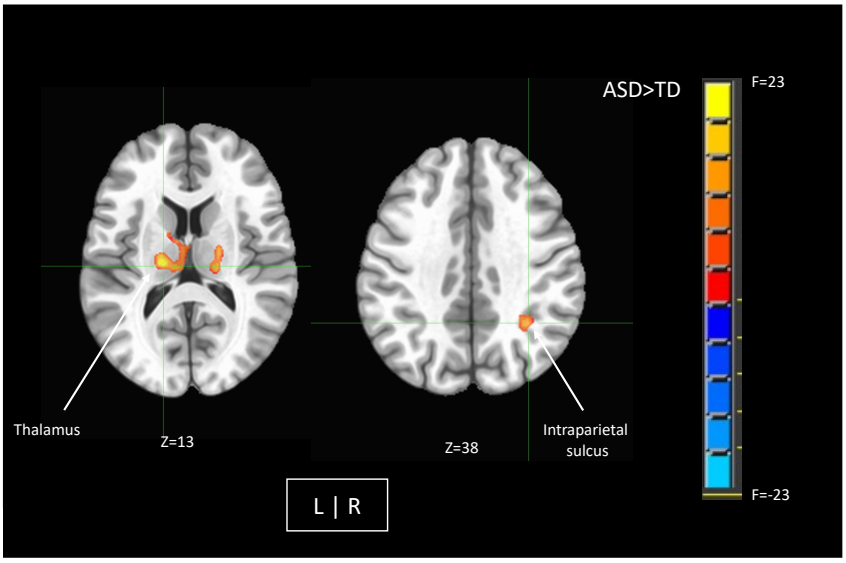
Note. ASD participants showed reduced force complexity relative to controls during the low and medium visual gain conditions, but not during the high visual gain condition.

*p<0.05, **p<0.01.

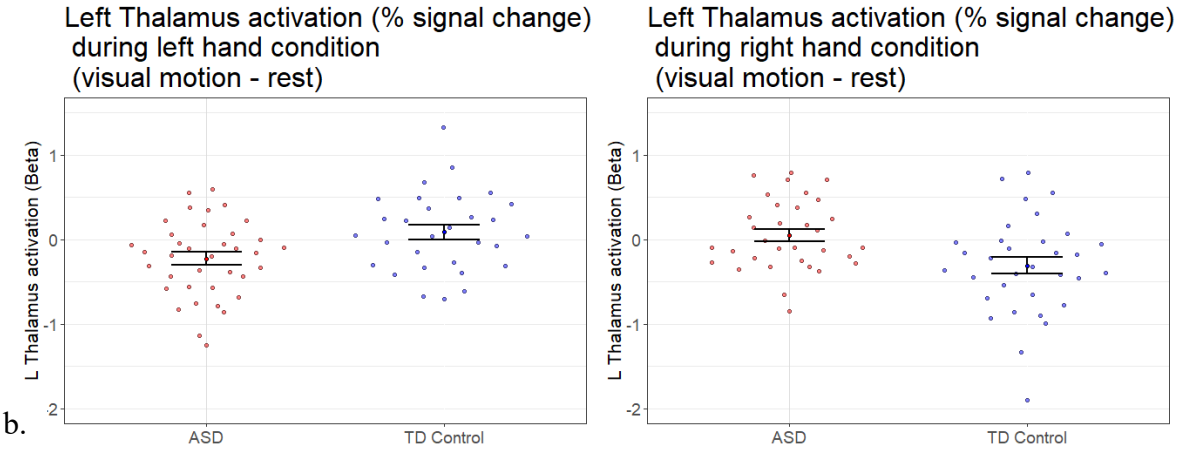
Figure 3

Brain Activation During Visual Motion Perception in Contrast to Rest Varies as a Function of Group and Hand Condition

a.



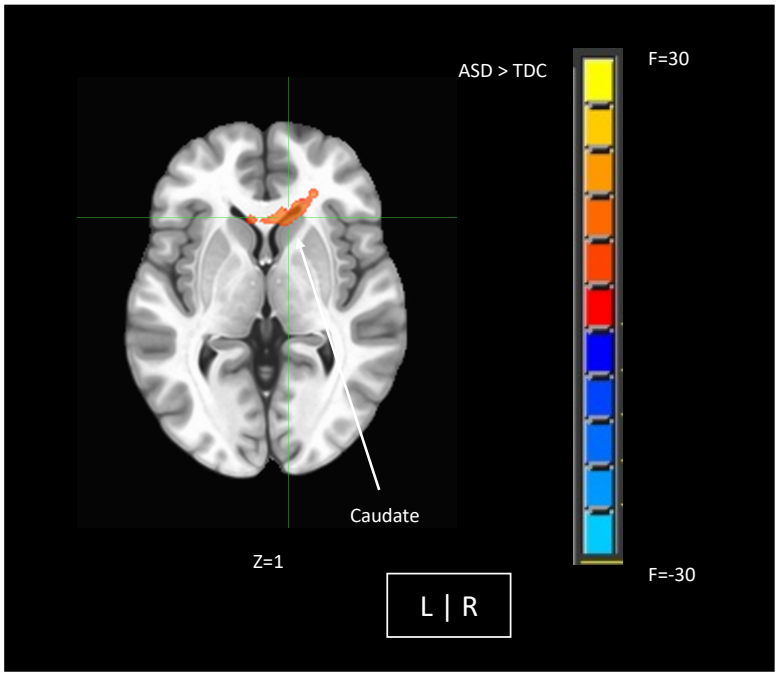
b.



Note. (a) Axial slices showing regions with activation that varied by group and condition. The color bar ranges from F=-23 to F=23 with an activation threshold of $\alpha < 0.05$, corrected for multiple comparisons. (b) TD controls showed reduced activation in the left thalamus during the right-hand condition.

Figure 4

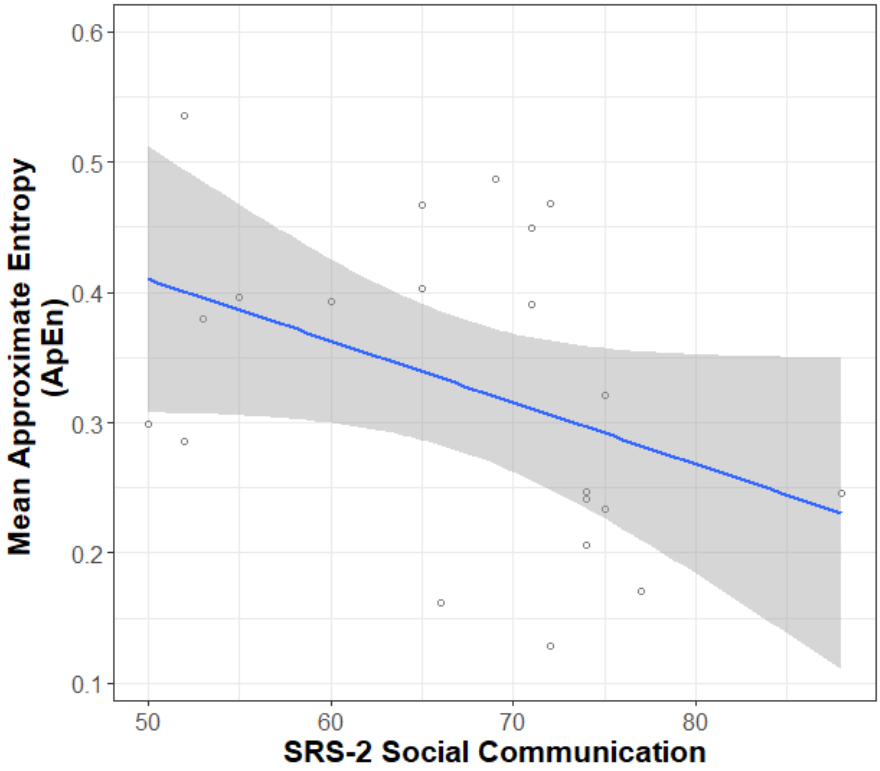
Brain Activation During Visual Motion Perception in Contrast to Rest in Individuals with ASD and TD Controls



Note. Axial slice showing the region with activation that varied by group. The color bar ranges from F=-30 to F=30 with an activation threshold of $\alpha < 0.05$, corrected for multiple comparisons. Individuals with ASD showed increased right caudate activation when viewing visual motion in contrast to rest compared to typically developing controls.

Figure 5

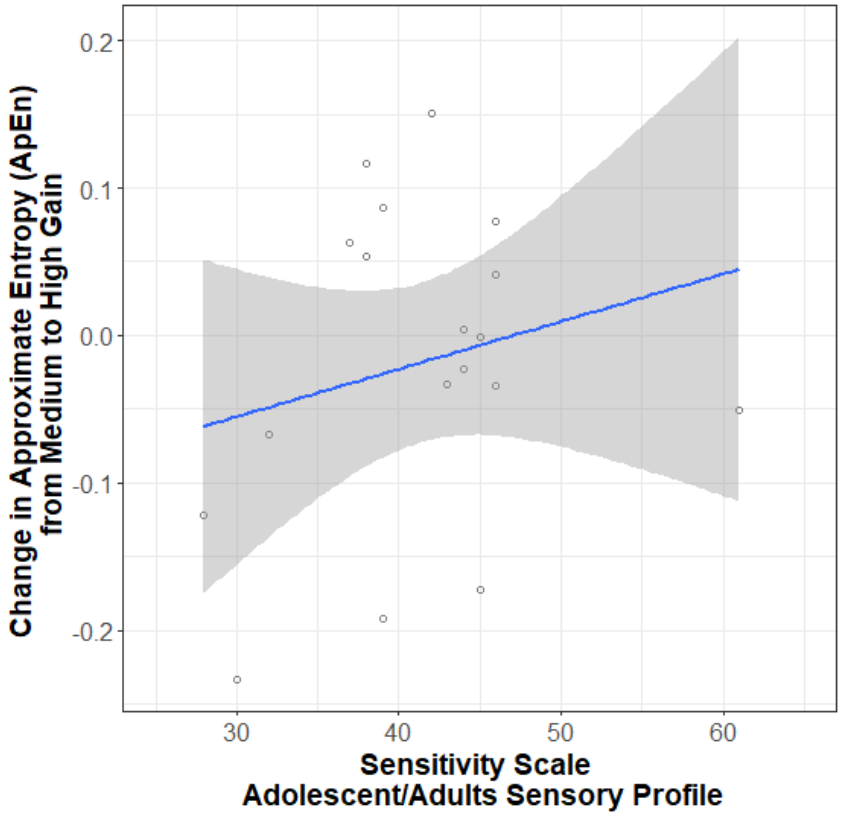
Reduced Force Complexity was Associated with Greater Social Communication Difficulties in ASD



Note. There was a negative relationship between social communication difficulties as measured by the SRS-2 and force complexity in individuals with ASD (r_s=-0.53, p<.05).

Figure 6

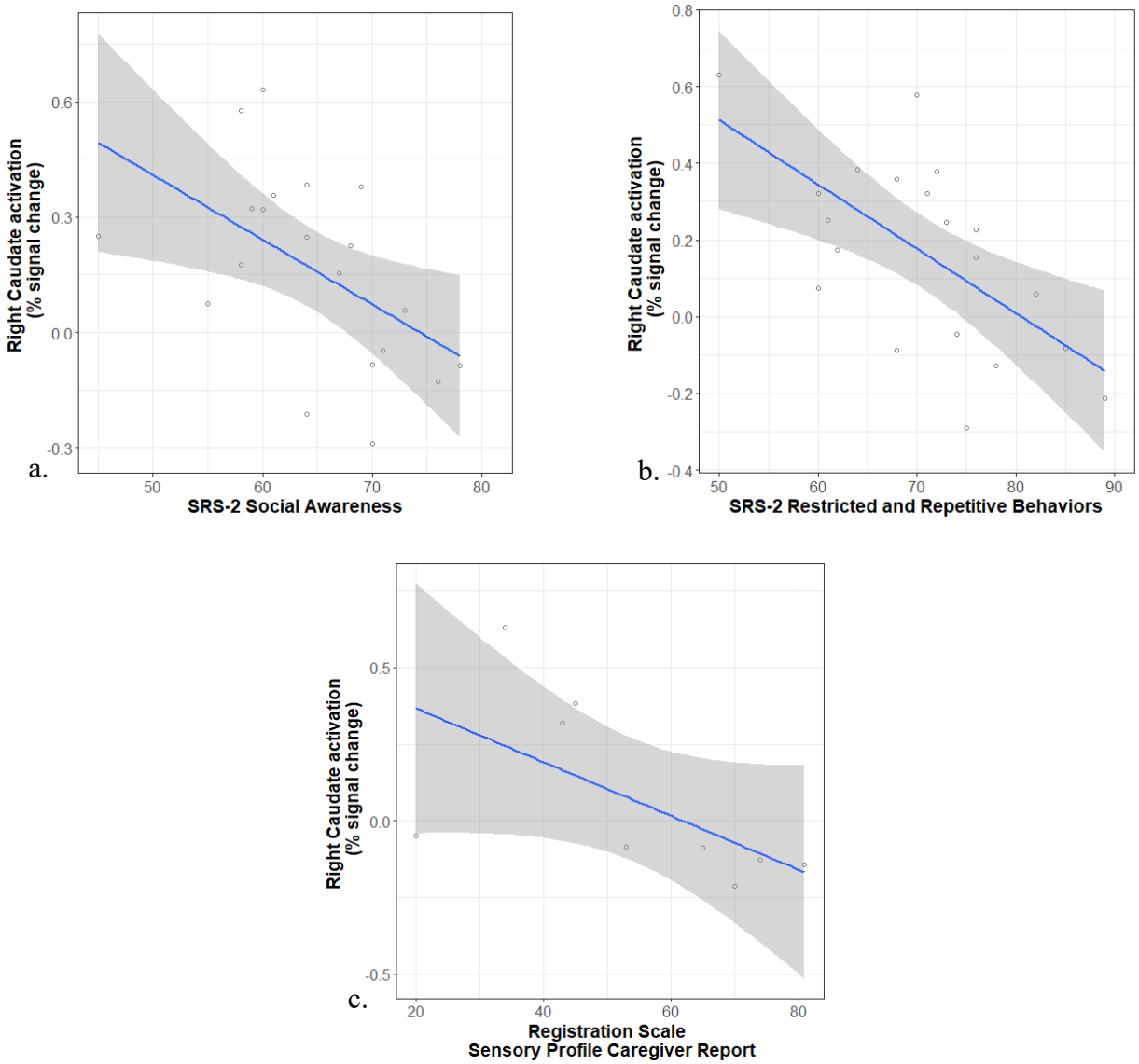
Increased Change in ApEn was Associated with Greater Self-Reported Sensory Sensitivities in ASD



Note. Individuals with ASD showed increased self-reported sensory sensitivities associated with increased change in ApEn from medium to high gain (r_s=0.40, p=.066).

Figure 7

Right Caudate Activation During the Right-Hand Condition in ASD was Associated with Less Severe Social Communication and Sensory Symptoms in ASD



Note. In individuals with ASD, decreased right caudate activation during the right-hand condition was associated with (a) more severe social awareness difficulties (r_s=-0.58, p<.01), (b) more severe restricted and repetitive behaviors (r_s=-0.62, p<.01), and (c) reduced caregiver-reported sensory registration (i.e., reduced missing of sensory input; r_s=-0.83, p<.01).