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Longitudinal processing speed impairments in males with autism and the effects of white matter microstructure

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ABSTRACT

The present study used an accelerated longitudinal design to examine group differences and age-related changes in processing speed in 81 individuals with autism spectrum disorder (ASD) compared to 56 age-matched individuals with typical development (ages 6–39 years). Processing speed was assessed using the Wechsler Intelligence Scale for Children-3rd edition (WISC-III) and the Wechsler Adult Intelligence Scale-3rd edition (WAIS-III). Follow-up analyses examined processing speed subtest performance and relations between processing speed and white matter microstructure (as measured with diffusion tensor imaging [DTI] in a subset of these participants). After controlling for full scale IQ, the present results show that processing speed index standard scores were on average 12 points lower in the group with ASD compared to the group with typical development. There were, however, no significant group differences in standard score age-related changes within this age range. For subtest raw scores, the group with ASD demonstrated robustly slower processing speeds in the adult versions of the IQ test (i.e., WAIS-III) but not in the child versions (WISC-III), even though age-related changes were similar in both the ASD and typically developing groups. This pattern of results may reflect difficulties that become increasingly evident in ASD on more complex measures of processing speed. Finally, DTI measures of whole-brain white matter microstructure suggested that fractional anisotropy (but not mean diffusivity, radial diffusivity, or axial diffusivity) made significant but small-sized contributions to processing speed standard scores across our entire sample. Taken together, the present findings suggest that robust decreases in processing speed may be present in ASD, more pronounced in adulthood, and partially attributable to white matter microstructural integrity.

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1. Introduction

The ability to process implicit social cues and filter essential signals from a complex array of stimuli requires fast-paced integration of a large number of sensory inputs. Therefore, processing speed, or the speed at which we are able to perceive and react to stimuli in the environment, is a fundamental cognitive ability. Clinically, individuals with autism spectrum disorder (ASD) often demonstrate the need for increased time to process information and perform tasks, which appears to contribute to functioning in daily life. Research studies also have found evidence of slower processing speeds across the lifespan in individuals with ASD. On standardized Wechsler tests of intelligence, lower processing speed index scores have been reported in children, (Mayes & Calhoun, 2003, 2008; Oliveras-Rentas, Kenworthy, Roberson, Martin, & Wallace, 2012; Wechsler, 2003) adolescents, and adults with ASD (Spek, Schatorjé, Scholte, & van Berckelaer-Onnes, 2009). These slower processing speeds were associated with more severe ASD communication

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symptoms in high-functioning children with ASD (Oliveras-Rentas et al., 2012) and were found to be predictive of educational achievements in math, reading, and writing (Assouline, Foley Nicpon, & Dockery, 2011). These observations and results suggest that slower processing speed may be a common difficulty experienced by individuals with ASD and may relate to core ASD features, as well as educational and occupational prospects.

Although processing speed difficulties have been consistently reported in persons with ASD, little is known regarding how processing speed develops and changes with age in this population. In individuals with typical development, cross-sectional and longitudinal studies suggest rapid increases in processing speed during the first year of life (Rose, Feldman, & Jankowski, 2002), followed by continued increases through childhood and adolescence (Kail, 2007; Kail & Ferrer, 2007). Although very little is known about typical processing speed changes in middle age, processing speed appears to decline and may be related to other age-related declines in cognitive functions in older-adult populations (Salthouse, 1996; Salthouse & Ferrer-Caja, 2003, Silwinski & Buschke, 1999; Sternäng, Wahlin, & Nilsson, 2008; Zimprich & Kurtz, 2013). In both typically developing and patient populations, age-appropriate development of processing speed may be a critical predictor of a number of important cognitive and outcome measures. For example, processing speed may be a key predictor of general intelligence in typically developing adolescents (Coyle, Pillow, Snyder, & Kochunov, 2011), and in individuals with schizophrenia, processing speed may predict vocational outcome and social function (Sánchez et al., 2009). Therefore, understanding the longitudinal development of processing speed in persons with ASD may be a key element to better understanding and accommodating the needs of persons with ASD throughout the lifespan.

A better understanding of processing speed development in ASD may also elucidate underlying neural substrates contributing to the etiology of ASD. DTI studies in individuals with typical development suggest that processing speed may be associated with the white matter microstructure of a number of white matter tracts across the brain, including the bilateral anterior corona radiata, bilateral superior fronto-occipital fasciculus, bilateral superior longitudinal fasciculus, bilateral internal capsule, bilateral posterior cingulum, right inferior fronto-occipital fasciculus, and bilateral posterior corona radiata (Bendlin et al., 2010). In individuals with traumatic brain injury, processing speed was related to white matter microstructure of the superior longitudinal fasciculus (Turken et al., 2008), ventral striatum (Shah et al., 2012), as well as the corpus callosum and centrum semiovale (Kourtidou et al., 2012). Further, decreases in white matter integrity of the corpus callosum were related to decreases in processing speed in children with multiple sclerosis (Bethune et al., 2011) and in children and adults with ASD (Alexander et al., 2007). These results provide converging evidence across distinct samples and methodologies that the white matter microstructure of a number of tracts is likely involved in processing speed.

Because of the number of tracts likely involved, it is possible that a metric of whole-brain white matter microstructure may predict processing speed more accurately than the white matter microstructure of any individual tract. Indeed, in older individuals with typical development, a measure of higher radial diffusivity (RD) across all lobes of the brain was found to be associated with executive function and processing speed measures (Jacobs et al., 2013). Furthermore, two studies have found that a composite white matter integrity factor (i.e., a combination of FA, RD, MD, and axial diffusivity (AD) across eight major tracts, or an aggregation of the white matter integrity of healthy looking white matter tracts) was more predictive of processing speed than when the individual tracts were treated as single predictors (Penke et al., 2010; Venkatraman et al., 2011). Given that white matter microstructure atypicalities have been commonly reported in ASD (see Travers et al., 2012 for a review), investigating white matter microstructure as a predictor of processing speed is essential to better understand the links between the behavioral and the neural manifestations of ASD.

To examine the intersection among possible processing speed differences in ASD, age-related development of processing speed, and white matter contributions to processing speed, the present study longitudinally examined age-related processing speed changes in 81 individuals with ASD and 56 age-matched individuals with typical development from childhood to mid-adulthood (6–39 years old). Additional analyses examined whether whole-brain white matter FA, MD, RD, and AD predicted processing speed in a subset of participants who underwent multiple DTI scans.

2. Materials and method

2.1. Design

As part of a 13-year longitudinal study, the current study employed an accelerated longitudinal design (i.e., cohort-sequential design) (Harezlak, Ryan, Giedd, & Lange, 2005; Nesselroade & Baltes, 1979), which simultaneously measured individual longitudinal changes in processing speed across multiple age cohorts. Data were collected at four separate time points: Pre-Time 1 (henceforth called Time 0), Time 1, Time 2, and Time 3. Processing speed data were collected at Time 0, Time 1, and Time 3. DTI scans were collected at Time 1, Time 2, and Time 3. Therefore, in the context of the broader longitudinal study, the current study analyzes processing speed data from Time 0, Time 1, and Time 3, and the DTI data are analyzed for Time 1 and Time 3. See Fig. 1 for a depiction of the accelerated longitudinal design.

2.2. Participants

Participants for this study included 81 males with ASD and 56 males with typical development between the ages of 6.3 and 39.8 years. These participants were selected from the broader longitudinal neuroimaging study (109 ASD and 80 typically developing controls [TDC]) based on processing speed data completeness and age matches (three processing speed assessments were excluded in participants with ASD over 40 years of age because there were no typically developing matched controls in that age range). In the broader longitudinal study, the retention rate (at least two scans and two assessments) was 85% for the group with ASD and 71% for the group with typical development. The participants with ASD were rigorously diagnosed based on Autism Diagnostic Interview-Revised (Lord, Rutter. & Le Couteur, 1994), Autism Diagnostic Observation Scale-General (Lord et al., 2000), Diagnostic Statistical Manual-IV (APA, 1994), and International Statistical Classification of Diseases and Related Health Problems (ICD-10) criteria. Participants with ASD met criteria for a lifetime diagnosis of autistic disorder, Asperger's syndrome, or pervasive developmental disorder not otherwise specified

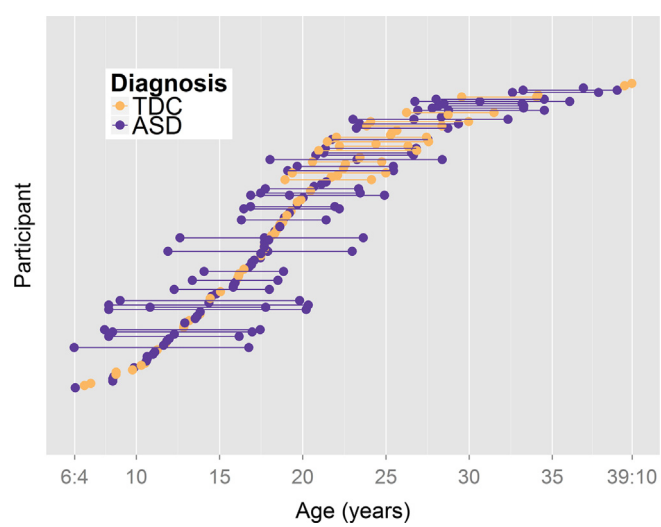

Fig. 1. Depiction of accelerated longitudinal design, including the age at each processing speed assessment and the number of processing speed assessments for each participant within each group (autism spectrum disorder [ASD] and typically developing controls [TDC]).

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