Review

Biological Psychiatry: CNNI

An Altered Scaffold for Information Processing: Cognitive Control Development in Adolescents With Autism

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ABSTRACT

We investigated how cognitive neuroscientific studies during the last decade have advanced the understanding of cognitive control from adolescence to young adulthood in individuals with autism spectrum disorder (ASD). To do so, we conducted a selective review of the larger structural, resting-state, and diffusion-weighted imaging studies of brain regions and networks related to cognitive control that have been conducted since 2007 in individuals with ASD and typical development (TYP) in subjects 10 to 30 years of age that examined how these regions and networks support behavioral and task-based functional magnetic resonance imaging performance on tasks assessing cognitive control. Longitudinal structural studies reveal overgrowth of the anterior cingulate cortex and slower white matter development in the parietal cortex in adolescents with ASD compared with TYP. Cross-sectional studies of the salience, executive control, and default mode resting-state functional connectivity networks, which mediate cognitive control, demonstrate patterns of connectivity that differ from TYP through adolescence. Finally, white matter tracts underlying these control-related brain regions continue to show reduced diffusion properties compared to TYP. It is thus not surprising that cognitive control task performance improves less during adolescence in ASD compared with TYP. This review shows that a cognitive neuroscientific approach produces insights about the mechanisms of persistent cognitive control deficits in individuals with ASD from adolescence into young adulthood that are not apparent with neuropsychological methods alone, and it draws attention to the great need for longitudinal studies of this period in those with ASD. Further investigation of anterior cingulate cortex and frontoparietal neural circuits may help specify pathophysiology and treatment options.

Keywords: Adolescent development, Autism, Cognitive control, Executive functions, Neuroimaging, Young adulthood

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Cognitive control—the maintenance of situational context and inhibition of prepotent responding to permit the goal-directed behavior (1)—is a key component in the National Institute of Mental Health Research Domain Criteria project (RDoC) (2). As specified by RDoC, cognitive control consists of three broad components: working memory or cue/context maintenance, inhibition of prepotent response tendencies, and set-shifting, task switching, or cognitive flexibility.

In perhaps the most influential theory of the neural mechanisms governing cognitive control, Miller and Cohen (3) proposed that the prefrontal cortex (PFC) is specialized for the representation and maintenance of situational context that provides top-down biasing to facilitate information flow from relevant neural systems. This model has provided a foundation for the development of testable mechanistic hypotheses using cognitive neuroscientific versus clinical neuropsychological measurements (4). Hypotheses then can be verified using functional magnetic resonance imaging (fMRI) studies. These studies have localized control processes to the dorsolateral PFC (DLPFC), ventrolateral PFC, anterior PFC, anterior cingulate cortex (ACC), and parietal cortices (5,6), and have generated insights about how control is evoked in response to ACC-generated conflict signals (7), timing differences in neural circuit recruitment (8), and basal ganglia–PFC interactions that guide reward-driven learning (9).

In typical development (TYP), adolescence is considered a critical period for the development of mature thought and action (10). This has not been well-examined in individuals with autism spectrum disorder (ASD). To help fill this gap in understanding, we selectively reviewed structural, resting-state, diffusion-weighted, and task-based fMRI studies of brain regions and networks subserving cognitive control in individuals with ASD. Peer-reviewed and published scientific papers written in English between 2007 and 2017 were identified through a computerized literature search using Google Scholar and PubMed. Search terms used across all studies included autism, cognitive control, adolescence, young adulthood, and MRI. Other terms, including brain structure, default mode network, salience network, executive control network, diffusion, DTI, cue/context maintenance, response inhibition, set shifting, and task switching, were also used in their respective sections. To be included, studies also had to have a

Table 1. Summary of Structural Neuroimaging Studies in ASD

Study, Year	*n*	Age, Years, Mean ± SD	Method	Finding(s)
Bonilha *et al.*, 2008 (14)	ASD, 12; TYP, 16	ASD, 12.4 ± 4; TYP, 13.2 ± 5	Whole-brain voxel-based morphometry	ASD > TYP, DLPFC and parietal gray matter; ASD < TYP, frontal and parietal white matter
Nordahl *et al.*, 2007 (15)	ASD,[a] 15; TYP, 29	ASD, 12.3 ± 3.2; TYP, 11.8 ± 2.6	Cortical folding	ASD > TYP, intraparietal sulcal depth
Hua *et al.*, 2013 (16)	ASD, 13; TYP, 7	ASD, 12.0 ± 2.3; TYP, 12.3 ± 2.4; two MRI time points, 2.9 ± 0.9 year interval	Longitudinal brain growth	ASD < TYP, white matter growth in parietal lobe; ASD > TYP, gray matter expansion in ACC
Wallace *et al.*, 2015 (17)	ASD, 17; TYP, 18	ASD, 17.4 ± 2.4; TYP, 17.5 ± 1.5; two MRI time points, 1.7 ± 0.8 year interval	Longitudinal cortical thickness and surface area	ASD > TYP, cortical thinning in superior parietal cortex

ACC, anterior cingulate cortex; ASD, autism spectrum disorder; DLPFC, dorsolateral prefrontal cortex; MRI, magnetic resonance imaging; TYP, typical development.

[a]These individuals were diagnosed with Asperger syndrome according to DSM-IV criteria.

mean of >10 participants per group (e.g., a two-group study where one group had 9 participants and the other had 11 participants was included). Given the relative lack of longitudinal studies of ASD during the adolescence to young adulthood period, many comparisons are of cross-sectional studies, although greater weight was given to existing longitudinal studies when drawing inferences about findings.

COMPONENTS OF THE SCAFFOLD

Structural Neuroimaging of Cognitive Control–Related Brain Regions

Cortical gray matter volume increases during childhood, peaks around puberty, and then begins to decline across adolescence and adulthood (9). Frontal and parietal regions reach peak volume around 12 years of age in males and about a year earlier in females (11). Increases and decreases in volume pre- and postadolescence are steeper for the parietal lobe than for the frontal lobe. In TYP, decreases in volume within the cognitive control network during adolescence and adulthood are associated with increased performance on tasks of executive functioning and emotion identification (12).

Several cross-sectional structural MRI studies have evaluated global cortical gray and white matter differences between adolescents with ASD compared with age-matched TYPs [see (13)]. Since 2007, there has been one study that used whole-brain voxel-based morphometry (a technique involving comparing differences in brain anatomy using volumetric MRI scans across groups) that identified volume increases in both the DLPFC and the superior and interior parietal lobule, as well as decreased white matter volume across all cerebral lobes in those with ASD compared with TYP (14). Differences in the folding of the cerebral cortex (gyrification) also have been reported in the frontal lobe and intraparietal sulcus in individuals with ASD compared with TYP (15).

More recently, evidence from two longitudinal studies suggests that there are between-group differences in the structure of cognitive control–related brain regions. Hua *et al.* (16) evaluated youth with ASD from late childhood into adolescence. They reported abnormal overgrowth versus the pruning typically found during adolescence in the ACC and slower white matter development in the parietal lobe in those with ASD compared with TYP. Wallace *et al.* (17) evaluated cortical thickness (a brain morphometric measure used to assess the combined thickness of the layers of the cerebral cortex) and surface area in slightly older adolescents with ASD beginning at 17 years of age and then again at 19 years of age. They noted accelerated cortical thinning in the superior parietal cortex in ASD compared to TYP. Table 1 presents the two cross-sectional structural, voxel-based morphometry, and cortical folding studies and two longitudinal studies of white and gray matter and cortical thickness development that were published before 2017. While older studies are ambiguous, two recent longitudinal studies suggest that the rate of development in key cognitive control regions is implicated in ASD. However, no studies include both males and females with ASD. Figure 1A shows the brain regions implicated in structural studies.

Resting-State Functional Neuroimaging Studies of Cognitive Control in ASD

Resting-state fMRI (rsfMRI) examines the correlation in blood oxygen level–dependent signal between brain regions during periods of quiet rest. This is referred to as functional connectivity (FC) (18). A reliable set of rsfMRI networks (19) emerges during adolescence, when there is a strengthening of FC within networks (integration) and decreased FC between networks (segregation). This culminates in the establishment of a mature intrinsic functional brain architecture in young adulthood (20–22). Atypical connectivity between three specific intrinsic functional networks—the default mode network (DMN), the salience network (SN), and the executive control network (ECN) (23)—is central to disorders involving cognitive control impairments, and these networks are the focus of this selective review.

Most rsfMRI studies in ASD have examined the DMN, which includes the posterior cingulate cortex/retrosplenial cortex and medial prefrontal cortex, and which demonstrates robust FC at rest and during self-referential processing (Figure 1B) (24). Children with ASD demonstrate aberrant FC within the DMN and greater FC between the DMN and other intrinsic functional networks (25–27) than those with TYP. During adolescence, DMN connectivity does not increase to the same extent in ASD