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Cognitive Deficits and Association with Autism Spectrum Disorder and Attention Deficit Hyperactivity Disorder in 22q11.2 Deletion Syndrome

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Abstract : 22q11.2 Deletion Syndrome (22q11.2DS) is caused by the deletion of approximately 60 genes on chromosome 22 and is associated with high rates of neurodevelopmental disorders such as Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD). The presentation of these disorders in 22q11.2DS is reported to be comparable to idiopathic forms and therefore presents a valuable model for understanding mechanisms of neurodevelopmental disorders. Cognitive deficits are thought to be a core feature of neurodevelopmental disorders, and possibly manifest in behavioural and emotional problems. There have been mixed findings in 22q11.2DS on whether the presence of ADHD or ASD is associated with greater cognitive deficits. Furthermore, the influence of developmental stage has never been taken into account. The aim was therefore to examine whether the presence of ADHD or ASD was associated with cognitive deficits in childhood and/or adolescence in 22q11.2DS. We conducted the largest study to date of this kind in 22q11.2DS. The same battery of tasks measuring processing speed, attention and spatial working memory were completed by 135 participants with 22q11.2DS. Wechsler IQ tests were completed, yielding Full Scale (FSIQ), Verbal (VIQ) and Performance IQ (PIQ). Age-standardised difference scores were produced for each participant. Developmental stages were defined as children (6-10 years) and adolescents (10-18 years). ADHD diagnosis was ascertained from a semi-structured interview with a parent. ASD status was ascertained from a questionnaire completed by a parent. Interaction and main effects of cognitive performance of those with or without a diagnosis of ADHD or ASD in childhood or adolescence were conducted with 2x2 ANOVA. Significant interactions were followed up with t-tests of simple effects. Adolescents with ASD displayed greater deficits in all measures (processing speed, $p = 0.022$; sustained attention, $p = 0.016$; working memory, $p = 0.006$) than adolescents without ASD; there was no difference between children with and without ASD. There were no significant differences on IQ measures. Both children and adolescents with ADHD displayed greater deficits on sustained attention ($p = 0.002$) than those without ADHD. There were no significant differences on any other measures for ADHD. Magnitude of cognitive deficit in individuals with 22q11.2DS varied by cognitive domain, developmental stage and presence of neurodevelopmental disorder. Adolescents with 22q11.2DS and ASD showed greater deficits on all measures, which suggests there may be a sensitive period in childhood to acquire these domains, or reflect increasing social and academic demands in adolescence. The finding of poorer sustained attention in children and adolescents with ADHD supports previous research and suggests a specific deficit which can be separated from processing speed and working memory. This research provides unique insights into the association of ASD and ADHD with cognitive deficits in a group at high genomic risk of neurodevelopmental disorders.

Keywords : 22q11.2 deletion syndrome, attention deficit hyperactivity disorder, autism spectrum disorder, cognitive development
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