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Elevated Morning Testosterone Levels in Prepubertal Adolescents as a Potential Indicator of Early Pubertal Onset in Autism Spectrum Disorder (ASD)

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Introduction: Puberty is characterized by significant physical and psychological changes, which may be especially challenging for individuals with autism spectrum disorder (ASD). Although the etiology of ASD remains uncertain, studies have suggested imbalances in hormones, such as testosterone, may modulate the autism phenotype. While differences in fetal and postnatal testosterone have been reported, there is limited literature regarding testosterone variations during adolescence in ASD. We investigated morning salivary testosterone levels in youth with ASD and typical development (TD) to explore hypothesized hormonal differences, expecting elevated levels in ASD compared to TD.

Methods: Youth with ASD (n=120) and TD (n=89), ages 10 to 13 years, were enrolled as part of a longitudinal study on pubertal development. Physician examination determined development using the Tanner scales (Stage 1-5), where stage 1 indicates prepuberty and stage 5 represents full physical sexual maturation. Salivary testosterone was collected in the morning immediately upon waking and averaged across three days. Diagnostic (ASD/TD) and sex (male/female) differences were examined using general linear models with pubertal stage and age as covariates. Participants were further categorized as "prepubertal" (Tanner stage 1) or "pubertal" (Tanner stage \geq 2), and differences within groups were considered.

Results: Males demonstrated significantly higher salivary testosterone compared to females ($F(1,192)=9.04$, $p=0.003$) when controlling for age and Tanner stage. There was no significant effect for diagnosis ($p>0.05$), indicating youth with and without ASD had similar morning testosterone levels. However, when groups were dichotomized on pubertal development, prepubertal ASD youth had higher testosterone relative to their TD peers ($F(1,95)=6.65$, $p=0.01$). Although the interaction of diagnosis and sex was not significant, pairwise comparisons indicated prepubertal females with ASD had elevated testosterone compared to TD females ($p=0.02$) and ASD males ($p=0.05$). ASD and TD youth in the pubertal group were not statistically different ($p>0.05$).

Discussion: Fetal androgens, such as testosterone, may contribute to the autism phenotype, yet little research has examined group differences during the pubertal transition, a particularly challenging period for youth with ASD. Notably, prepubertal youth with ASD showed elevated testosterone. Previously, early pubertal onset based on physical exam in this sample was reported in females with ASD. Hormonal changes may occur prior to physical signs of puberty, suggesting sex hormones might serve as an earlier marker of advanced pubertal timing in ASD females. Early puberty has been linked to negative social, behavioral, and mental health outcomes; therefore, future research should examine the role of testosterone in pubertal timing and autism symptom presentation, particularly as it relates to the biopsychosocial changes associated with pubertal development.

Keywords:

Autism spectrum disorders, Puberty, Testosterone