**Title:** Examination of Pubertal Timing in Early Adolescence Reveals Advanced Pubertal Onset in Girls with Autism Spectrum Disorder

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**Introduction:** Puberty refers to biological maturation contributing to significant changes in morphology, cognition, emotion regulation and physiological stress. Puberty is influenced by biobehavioral factors resulting in normative, precocious or delayed pubertal onset. Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder with impairment in reciprocal social communication and poor adaptation to change; thus, the onset and course of puberty may be a pivotal transition. The cross-sectional prospective study measured pubertal timing to examine hypothesized differences for group (ASD vs. Typical development (TD)) and sex (female vs. male).

**Methods:** Participants included 239 children between 10-to-13 years, 137 with ASD (mean age = 11.43, 35 females and 102 males) and 102 with TD (mean age = 11.72, 44 females and 58 males) participants. Pubertal assessment consisted of a brief, standardized physical exam conducted by trained and licensed study physicians. Subsequently, 234 youth completed the pubertal exam conducted by study physicians. Pubertal onset (Tanner stage >1) was modeled separately in TD and ASD using logistic regression with a nonlinear age-by-sex interaction, controlling for body mass index (BMI).

**Results:** In TD children, there was strong evidence for age (p=0.001; Chisq=13.41; df=2), but weak evidence for differences in pubertal onset for male and female (p = 0.776; Z=0.284). In ASD, there was a main effect for both age (p<0.001, Chisq=16.88, df=2) and sex (p =0.002, Z=3.046). Analysis based on sex, suggest early pubertal onset in ASD females relative to TD (p=0.062, Z=1.86), but not in males (p=0.872, Z=-0.161). Approximately 79% of the females with ASD started puberty by age 11 in contrast to 53% in TD females. ASD diagnosis was strongly related to increased anxiety and depression.

**Discussion:** Girls with ASD evidence advanced pubertal onset relative to ASD males and TD females. The earlier onset can extend the adolescent period thereby lengthening the divergence between the social environment, neural development and hormonally-responsive motivational and affective behaviors. Thus, the relative emotional reactivity, cognitive imbalance and incongruence with physical maturation can contribute to enhanced risk for mental health problems. Findings underscore the need for an enhanced understanding of pubertal development in ASD, as differences to the timing or tempo may have significant developmental consequences.

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