Understanding and Supporting Puberty in Autistic Girls and Boys

Blythe A. Corbett, Ph.D.
James G. Blakemore Chair and Professor,
Vanderbilt University Medical Center
Autism Research Institute
21st of November 2024

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Outline

Autism Spectrum Disorder
Developmental: Adolescence, Puberty
Physiological: HPA and HPG
Psychological: Mental Health
Biobehavioral: Interactions
Hormonal: Sex and Gender
Social: Peers

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Autism Spectrum Disorder (ASD)

DSM-V Criteria

- **Social Communication**
  - Social emotional reciprocity
  - Nonverbal communication
  - Developing and maintaining relationships
- **Restricted Repetitive Patterns of Behavior, Interests or Activities**
  - Stereotyped or repetitive movements
  - Insistence on sameness
  - Restricted, fixed interests
  - Hyper- Hypo-reactivity to sensory stimuli

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Developmental

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Adolescence

- Adolescence is a time of significant psychological, social, emotional and hormonal changes (Spear, 2000; Steinberg, 2005) with greater emphasis on psychosocial development including peer relationships.

- Characterized by transitions and changes in identities as youth experiment and explore *who* they are, *what* they like, and *how* this interacts with their environment or others (Katz-Wise et al., 2023).

- Stages include early (10-14 years), middle (15-17 years) and late adolescence/young adulthood (17 – 24).

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Puberty

Puberty refers to biological maturation contributing to significant changes in morphology, cognition, emotion regulation and physiological stress that leads to reproductive capacity and psychosocial development (Spear, 2000; Steinberg, 2005).

External Development: The emergence of secondary sexual characteristics distinguishing the sexes signals the onset of puberty, involving breast development (*thelarche*) in females and genitals (*gonadarche*) in males and pubic hair (*pubarche*) in both sexes.

Internal Development: Endocrine axis orchestrating gonadal steroid production and adrenal androgen production.

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Early Onset Risks

Deviations in pubertal timing can enhance the risk for mental health problems (Ge, 2009; Graber, 1997; Kaltiala-Heino, 2003; Negriff, 2011; Waylen, 2004).

Increased risk factor for females (Marceau, 2014; Mendle, 2007) for depression (e.g., Angold, 2003; Conley; Ge, 2001;Llewellyn, 2012;Rierdan, 1991), suicidality (Graber, 1997) and anxiety (Patton, 1996).

These mental health conditions have a higher prevalence in adolescents with ASD (e.g., Gotham, 2015; Kuusikko, 2008; White, 2009).

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Theoretical Models of Timing & Tempo Effects

Maturational Deviance - states differences in normative development in timing or tempo lead to greater psychological distress and behavioral issues (Petersen, 1980).

Hormonal Influence - suggests that the increase in hormones due to maturational changes HPA axis (cortisol) and HPG axis (estradiol, testosterone) can lead to greater risk for psychopathology (Angold, 1999).

Contextual Amplification - emphasizes the social context, interpersonal relations can facilitate or impede pubertal maturation (Ge, 2009).

Accentuation hypothesis - posits that life transitions accentuate underlying emotional and behavioral predispositions during these periods of heightened novelty and uncertainty (Caspi, 1991).

Hormone Sensitivity - early puberty and pubertal increases in psychiatric symptoms are both caused by an elevated neurobiological sensitivity to natural hormone flux (Owens, 2020)

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Puberty & ASD

Limited research has focused on the adolescent transition and pubertal development (Picci, 2015), even though autistic individuals show poor adaptation to developmental transitions (Taylor, 2010; 2017).

Previous studies have reported improvement in some areas in puberty (e.g., Anderson, 2011; Brown, 1969; Rutter, 1970; Seltzer, 2004).

Yet, social withdrawal often intensifies (Anderson, 2011) and third of youth experience significant psychosocial problems (Billstedt, 2005; Gillberg, 1987).

Onset of menses often accompanied by challenges with emotion regulation (Burke, 2010; Obaydi, 2008) and heightened sensory experiences (Hamilton, 2011;Steward, 2018).

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Pubertal Measurement -Tanner Staging

A brief, standardized physical exam conducted by trained study physicians developed by Marshall and Tanner (1969, 1970).

Two measures with 5 stages:

Genitals (G1-G5 for males) and **Breasts** (B1-B5 for females) (GB stage)

Pubic hair (P1-P5 for both genders) (PH stage)

For our studies we use visual inspection only to be consistent with original Tanner staging and to maximize participation.

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Parent- and Self-Report Pubertal Assessment Measures

Pubertal Development Scale (PDS; Petersen et al. 1988). A widely-used parent-report questionnaire of pubertal status examining growth, skin changes, pubic hair and breast/voice changes across gender. Also, menses status in females.

Gender-Specific Self-Assessment Questionnaire (GSSQ; Rasmussen et al. 2015). Based on Tanner Stage gender-specific illustrations and text represented in female and male anatomical drawings.

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Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-019-04132-w

ORIGINAL PAPER

Pubertal Development Measurement in Children With and Without Autism Spectrum Disorder: A Comparison Between Physical Exam, Parent- and Self-Report

Blythe A. Corbett[1,2] · Rachael A. Muscatello[1] · Yasas Tanguturi[1] · Emily McGinn[1] · Sara Ioannou[1]

Participants: N=200 (TD 78; ASD 122) ages 10-13 (134 Males, 66 Females).

Concordance: between self- and parent-report compared to physical exam.

Self-report: concordance slight-to-fair (κ=.17-.32).

Parent-report: slight-to-moderate (κ=.21-.44), ASD group somewhat lower than TD group.

Pubertal assessments by parent or child are not reliable indices of precise pubertal staging;

Important to measure parent and child "perceived" development for comparison.

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Pubertal Timing During Early Adolescence: Advanced Pubertal Onset in Females with Autism Spectrum Disorder

Blythe A. Corbett, Simon Vandekar, Rachael A. Muscatello, and Yasas Tanguturi

Autism Research 000: 1–14, 2020

N = 239 ages 10-to-13; ASD=137, 35 females; TD=102, 45 females

Physical exam based on pubertal stage of genital/breast (GB) and pubic hair (PH).

Statistics: linear regression using main effects of sex and age-by-sex interactions in TD and ASD groups, and main effects of diagnosis and diagnosis-by-age interactions in males and females, controlling for body mass index, SES, and race.

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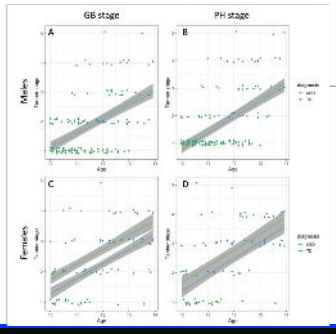

Diagnosis modeled separately for sex, no difference in males (t = 1.329, P = 0.186, rdf = 143).

Autistic females showed significantly earlier pubertal development (t = 1.97, P = 0.053, rdf = 70).

Analysis of menses revealed autistic females had significantly earlier onset than TD (t = −2.56, P = 0.018, rdf = 21).

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HHS Public Access
Author manuscript
Autism Res. Author manuscript; available in PMC 2023 October 01.

Published in final edited form as:
Autism Res. 2022 October ; 15(10): 1894–1908. doi:10.1002/aur.2786.

Examination of Pubertal Timing and Tempo in Females and Males with Autism Spectrum Disorder compared to Typically Developing Youth

Blythe A. Corbett, Ph.D.[1,2,3], Rachael A. Muscatello, Ph.D.[1], Ahra Kim, M.P.H.[4], Simon Vandekar, Ph.D.[4], Sara Duffus, M.D.[5], Sloane Sparks, DNP, PMHNP[1], Yasas Tanguturi, M.D.[1]

Years/Ages Y1 = aged 10-13; Y2 = aged 11-14; Y3 = aged 12-15
Timing is the onset of puberty
Tempo is the pace or progression through puberty

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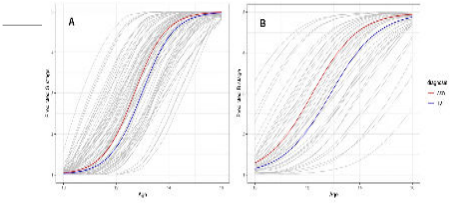
Timing & Tempo in TD & ASD Youth in Genital and Breast Development in Males and Females – between 10-16 years *(Corbett et al., 2022)*



(A) Male participants with ASD showed earlier G stage by ~ 3.43 months but not significant. (B) **Females with ASD showed earlier B stage by ~ 8.28 months**. Little evidence for differences in tempo for B or PH stage.

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Pubertal Timing Summary and Considerations

Females with ASD evidence advanced pubertal onset relative to TD females and ASD males.

Pubertal onset sets into motion a cascade of events which may magnify and further complicate an already vulnerable trajectory, especially in females.

Early onset risks may involve psychosocial (e.g., peer relations (Graber, 2004;Hamilton, 2014), biological (e.g., hormones, Apter, 1983; Dahl, 2004) and environmental effects (e.g., paternal absence, low SES (Bogaert, 2005; Ellis, 2000; Mendle, 2007; Obeidallah, 2000).

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Physiological

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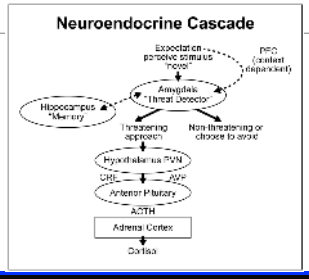
Hypothalamic Pituitary Adrenal (HPA) Axis



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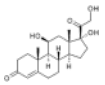
Cortisol

- Widely used biological marker of diurnal regulation and stress
- Elevations occur in response to novel and unpredictable situations
- Sequestered in saliva
- Noninvasive sampling
- Detectable changes in saliva after 20 min (e.g., response to a stressor)



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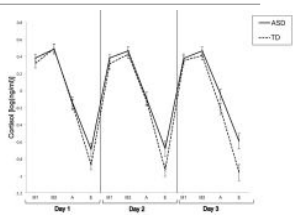
Diurnal Regulation Cortisol

- Peak concentrations in the morning, sharp decline, nadir in the evening.
- Autistic children shown more variable and dysregulated rhythms (Corbett, 2006; 2008; 2009; Hoshino, 1987;Tomarken, 2015).
- Elevated evening children compared to TD peers (Corbett, 2009;Tordjman, 2014), contributing to a blunted slope in a subgroup of children (Tomarken, 2015) .



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HPA Axis and Adolescence

- The dynamic adolescent period is marked by significant physiological changes in the regulation and responsivity of the HPA axis.
- Developmental changes result in elevations in diurnal basal cortisol levels (Barra, 2015) and higher cortisol in response to perceived stressors (Gunnar, 2009) .

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CAMBRIDGE UNIVERSITY PRESS

Regular Article

The developmental trajectory of diurnal cortisol in autistic and neurotypical youth

Blythe A. Corbett, Trey McGonigle, Rachael A. Muscatello, Jinyuan Liu and Simon Vandekar

Investigating diurnal cortisol by examining:

Aim 1) cortisol expression longitudinally over the pubertal transition between autistic and neurotypical youth,

Aim 2) the trajectory of diurnal cortisol and the unique contributions of age vs. puberty

Aim 3) potential sex differences

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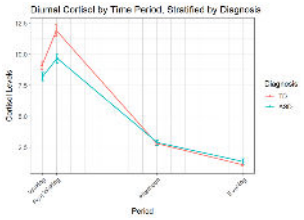
Mean diurnal cortisol levels over the course of the day stratified by Diagnosis



As hypothesized, autistic compared to TD youth demonstrate a shallower diurnal slope and elevated evening cortisol.

Differences were in the context of higher cortisol and flatter rhythms based on age and pubertal development.

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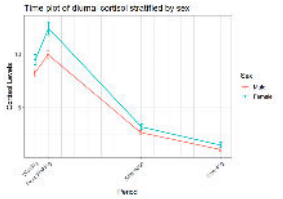
Mean diurnal cortisol levels over the course of the day stratified by sex



Sex-based differences emerged - females in both groups had higher cortisol, flatter slopes, and higher evening cortisol than males.

HPA maturation is impacted by age, puberty, sex, as well as an ASD diagnosis.

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Psychological

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Adolescence and Mental Health

- In general population, half of people who will suffer from mental illness will have their onset by 14 years of age (Kessler et al., 2005).
- Adolescence is a pivotal transition for youth with ASD, a condition characterized by difficulty with social competence and poor adaptability to change, including developmental transitions.
- The timing of the release of pubertal hormones contributes to individual differences in sex-biased psychopathological conditions, including depression.

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J Res Autism Spectr Disord. 2020 Sep;77:101613. doi: 10.1016/j.rasd.2020.101613.
Epub 2020 Jul 17.

Higher depressive symptoms in early adolescents with Autism Spectrum Disorder by self- and parent-report compared to typically-developing peers

Jessica M Schwartzman [1], Blythe A Corbett [1 2]

Depressive symptoms are higher in male and female early adolescents with ASD than their TD peers based on self-report.

Parents of adolescents with ASD also report higher depressive symptoms.

Screening and intervention for depressive symptoms in ASD should occur during early adolescence.

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Original Article

autism

Autism
1–14
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DOI: 10.1177/13623613211023885
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SAGE

Diagnostic- and sex-based differences in depression symptoms in autistic and neurotypical early adolescents

Jessica M Schwartzman[1], Zachary J Williams[1,2,3] and Blythe A Corbett[1,2]

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Participants: Included 212 autistic and neurotypical early adolescents.

Results: ASD and female sex-assigned-at-birth pose elevated risks for depression during adolescence.

- Depressive symptoms related to interpersonal problems, negative self-esteem, and beliefs of worthlessness, suggest intervention targets

- Autistic males and females endorsed similar severity and type of depressive symptoms, yet unique differences emerged when compared to sex-matched neurotypical peers.

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Biobehavioral

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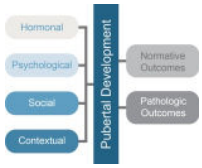
Propose a Biopsychosocial Model of Pubertal Development in ASD



Considers the influence of **hormonal** (HPA, HPG), **psychological** (emotional, behavioral), **social** (competence, relations) and **contextual** (familial) factors that can impact this developmental period.

A framework in which to rigorously and comprehensively examine the complexities of puberty and autism.

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Molecular Autism

RESEARCH Open Access

Trajectory of depressive symptoms over adolescence in autistic and neurotypical youth

Blythe A. Corbett, Rachael A. Muscatello, Trey McGonigle, Simon Vandekar, Christina Burroughs and Sloane Sparks

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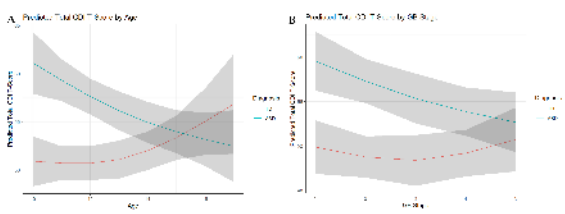

ASD group evidenced elevated depressive scores in early adolescence and puberty ($p<0.001$) and decreased during middle adolescence and puberty. Females higher than males in both groups ($p=0.001$).
TD group showed the opposite trend with an increase in depression symptoms with advancing development.

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ASD and Depression Summary

- Results reveal significant differences in autistic youth showing higher depression symptoms earlier in development (age, pubertal stage), then decreasing during later in development

- TD youth show the opposite pattern.

- Sex differences were observed in both groups, females showing higher symptoms of depression.

- Findings suggest a period of quiescence in depressive symptomology that may be influenced by biopsychosocial factors.

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Hormonal

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Testosterone and ASD

The etiology of ASD is uncertain, imbalances in hormones, such as testosterone, may modulate the autism phenotype (e.g., Baron-Cohen, 2006).

Differences in fetal and postnatal testosterone have been reported, there is limited literature regarding testosterone variations during adolescence in ASD.

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Molecular Autism

RESEARCH Open Access

Salivary testosterone in male and female youth with and without autism spectrum disorder: considerations of development, sex, and diagnosis

Rachael A. Muscatello[1], Emma Bafaljoo[2], Karan K. Mirpuri[2], Ahra Kim[1], Simon Vandekar[3] and Blythe A. Corbett[1,4]*

Investigated morning salivary testosterone levels in youth with ASD (*n* = 140) and TD (*n* = 104), ages 10 to 13 years

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Results and Interpretation

Youth with ASD showed significantly elevated testosterone concentrations compared to TD peers ($p<0.05$).

A significant age-by-sex interaction emerged with distinct developmental slopes for males and females ($p<0.05$).

At younger ages, females had higher testosterone, until ~ 11.5 years when levels plateau.

Male testosterone rapidly increases and surpass females.

Testosterone may play a unique role in ASD, especially during periods of dynamic hormonal changes, such as puberty.

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Social

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Social, Identities and Gender Diversity

Adolescence is often characterized by **transitions and changes in identities** as youth experiment and explore who they are, what they like, and how this interacts with their environment or others (Katz-Wise et al., 2023).

Gender identity pertains to an individual's **innate sense of gender**, which may or may not align with their sex-assigned at birth (ASAB).

Gender diversity is a broad term referring to an individual's experience of their gender as being different from assigned sex at birth.

Research suggests higher prevalence of gender diversity (i.e., gender dysphoria or gender incongruence) in individuals diagnosed with ASD or autistic traits compared to non-autistic peers (e.g., Bouzy, et al., 2023; Kallitsounaki, et al., 2023).

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autism

Original Article

Greater gender diversity among autistic children by self-report and parent-report

Blythe A Corbett[1], Rachael A Muscatello[1], Mark E Klemencic[1], Millicent West[1], Ahra Kim[1] and John F Strang[2,3]

Sample: Y1 sample included 140 with ASD (age=11.42; 104 males, 36 females) and 104 TDs (age=11.71; 58 males, 46 females).

Measure: The Gender Diversity Screening Questionnaire (GDSQ) is a self-report (GDSQ-S) and parent-report (GDSQ-P) screener.

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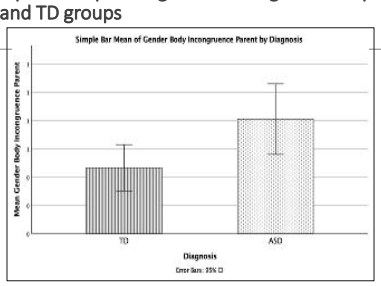
GDSQ parent-report of gender incongruence experiences in ASD and TD groups



Parents of autistic children reported significantly more **gender-body incongruence** experienced by their child than parents of TD children.

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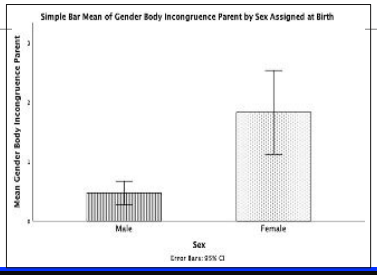
GDSQ parent-report of gender incongruence for ASD group



Within-group analysis showed parents of **autistic females-assigned-at-birth** reported significantly more **gender-body incongruence** than autistic males-assigned-at-birth.

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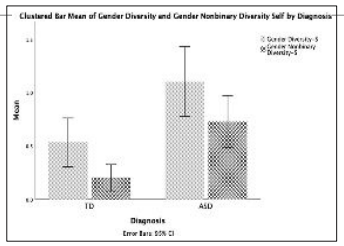
GDSQ self-report of gender nonbinary and gender incongruence experiences in ASD and TD



Autistic children endorsed higher rates of **Binary Gender Diversity** (less identification with ASAB more with other sex) and **Nonbinary Gender Diversity** (identification as neither) compared to TD peers.

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Received: 12 January 2024 | Accepted: 12 April 2024
DOI: 10.1002/aur.3141

RESEARCH ARTICLE

Gender diversity in autistic and neurotypical youth over adolescence and puberty: A longitudinal study

Blythe A. Corbett[1,2,3] | Rachael A. Muscatello[1,2] | Melissa Cyperski[1] | Eleonora Sadikova[1] | E. Kale Edmiston[4] | Trey William McGonigle[5] | Rachel Calvosa[1] | Simon Vandekar[5]

Examine the impact of diagnosis (ASD, TD), sex (AFAB, AMAB), and developmental level (age, pubertal stage) on GDSQ-P and GDSQ-S over time.

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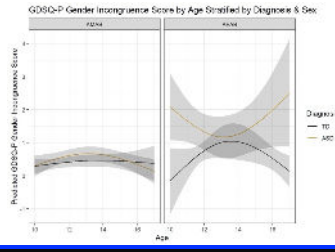
GDSQ-P Gender Incongruence Score by Age Stratified by Diagnosis and Sex



Gender Incongruence was significantly different, p=0.014, showing higher incongruence for autistic AFAB at age 10, decreasing between age 12-14 years.

TD AFAB evidence inverse trend.

AMAB were stable.

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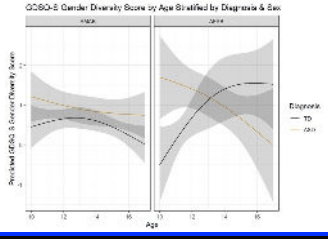
GDSQ-S Gender Diversity Score by Age Stratified by Diagnosis and Sex



- A significant diagnosis by sex-assigned-at-birth by age interaction for GDSQ-S Gender Diversity, p=0.002
- Higher scores in autistic AFAB youth over adolescence, and TD AFAB showing initially lower, then increasing levels over adolescence.
- AMAB were largely stable.

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Summary of Findings

The significant diagnostic, developmental and sex-based differences indicate AFAB youth experience greater gender diversity that evolves over development.

Gender identity formation is nuanced and may be influenced by pubertal progression, hormonal patterns and psychosocial factors.

Results underscore the need for enhanced understanding of the unique, dynamic profiles of females-assigned-at-birth.

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Overarching Summary of ASD Findings

Autistic females enter puberty earlier than TD females and ASD/TD males, putting them at risk for psychological, physical and social challenges.

Higher rate, earlier onset of depression in ASD, especially autistic females.

Greater prevalence of gender diversity in ASD, especially AFAB.

Need to comprehensively measure psychological variables based on self-report, parent-report and clinical-report.

Adolescence/pubertal development is not necessarily linear, we need to identify factors of risk and resiliency to elucidate and support this dynamic transition.

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Model

Autism Spectrum Disorder

Developmental: Adolescence/Puberty

Physiological: HPA and HPG

Psychological: Mental Health

Biobehavioral: Interactions

Hormonal: Sex and Gender

Social: Peers

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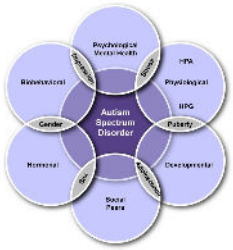

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Renewal– Pubertal Development Study

Longitudinal Study of Boys and Girls 8 – 13 years of age with ASD, TD and Intellectual Disability
R01 MH111599-06A1

Aim 1: Pubertal: To examine the timing, tempo and course of puberty based on physical development, hormones and menstrual cycle.

Aim 2: Psychosocial: To examine reciprocal social communication and internalizing symptoms at the onset and over the course of puberty.

Aim 3: Physiological: To simultaneously examine physiological characterization of social functioning at the level of the CNS, HPA and PNS during naturalistic social interactions

SENSE Lab

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Current Research - Female Development Study

Longitudinal Study of Girls 6 – 12 years of age with ASD, TD and Intellectual Disability
R01 HD107695

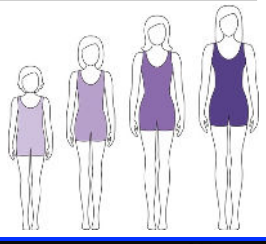
Pubertal: Timing, Tempo, Sex, Gender

Physiological – RSA, Cortisol

Social: ERP Hyperscanning

Hormonal: Estradiol, Testosterone, DHEAS

SENSE Lab
Making SENSE of Adolescence



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Acknowledgements

We thank the children and families who participate in our research!

Current Funding

NICHD R01 107695

NIMH R01 111599-061A

NIMH R33 120149

Previous Relevant Funding

NIMH R01 114906

NIMH R01 111599

NIMH R34 MH097793

NIMH R01 MH085717

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SENSE Lab Members & Key Collaborators

Rachel Calvosa, B.S.
Melissa Cyperski, Ph.D.
Jon Ebert, Psy.D.
Kale Edmiston, Ph.D.
Sasha Key, Ph.D.
Ahra Kim, MPH
Mark Klemencic, B.S.

SENSE Lab

Rachael Muscatello, Ph.D.
Trey McGonigle, B.S.
Jessica Schwartzman, Ph.D.
Sloane Sparks, DNP, PMHNP
Jaclyn Tamaroff, MD
Simon Vandekar, Ph.D.
Yasas Tanguturi, MD

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Thank you!

SENSE Lab
Making SENSE of Adolescence

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