



Published in final edited form as:

J Intellect Dev Disabil. 2018 ; 43(1): 20–28. doi:10.3109/13668250.2017.1310824.

The Role of Context in Psychosocial Stress among Adolescents with Autism Spectrum Disorder: Piloting a Semi-structured, Videogame-based Paradigm

Blythe A. Corbett^{*,1,2,3}, Scott D. Blain¹, and E. Kale Edmiston³

¹Vanderbilt University, Department of Psychiatry

²Vanderbilt University, Department of Psychology

³Vanderbilt Brain Institute

Abstract

Background: Autism Spectrum Disorder (ASD) is characterised by altered social patterns, often associated with increased stress. While puberty is associated with increased stress, there is limited research on stress response to **social interaction** in adolescents with ASD. The study investigated stress response to semi-structured, videogame-based interaction in adolescents with and without ASD, and the impact of puberty.

Method: Twelve adolescents with ASD and 12 typically developing (TD) peers participated in a semi-structured, videogame-based **social interaction**. Stress was measured via salivary cortisol.

Results: There were no significant between-group differences in cortisol. Pubertal development was correlated with cortisol in ASD ($r = -0.901$, $p < 0.0001$), but not TD ($r = 0.022$, $p = 0.949$).

Conclusions: Findings contribute to a fuller picture of the developmental trajectories of physiological stress in ASD, including the importance of context, structure, and puberty. The current investigation underscores the necessity of incorporating varied social contexts when assessing stress and **social interaction**.

Keywords

Autism Spectrum Disorder; Stress; Puberty; Adolescence; Social Interaction; Cortisol

*Correspondence to Blythe Corbett: PMB 40, 230 Appleton Way Nashville, TN 37203. blythe.corbett@vanderbilt.edu, addresses of other authors: scott.d.blain@vanderbilt.edu, kale.edmiston@vanderbilt.edu.

Author Note:

All of the authors listed have made significant contribution to the study and generation of the manuscript, and approve the manuscript for submission.

The authors have no conflicts of interest to declare and the funding body imposes no known restrictions on free access or publication of research data.

Introduction

Social Interaction in Autism Spectrum Disorder

Autism spectrum disorder (ASD) is characterised by deficits in multiple domains of social functioning (APA, 2013). At the social-cognitive level, these deficits include impaired face processing (Lozier et al., 2014) and theory of mind (Castelli et al., 2002). Social impairments in ASD also impact behavior; compared to typically developing (TD) peers, youth with ASD exhibit decreased quantity and quality of peer interaction (Lord and MaGill-Evans, 1995; Bauminger et al., 2003). Such difficulties in social interaction are often associated with increased stress and anxiety (Simon and Corbett, 2013; Schupp et al., 2013).

One important stress system, thought to be dysregulated in many individuals with ASD, is the hypothalamic pituitary adrenal (HPA) axis (Taylor & Corbett, 2014). The HPA-axis responds to novel situations perceived as threatening and leads to the release of glucocorticoid hormones, such as cortisol (Coplan et al., 1996). **Thus, measuring salivary cortisol concentration provides a non-invasive, reliable metric of HPA activity (Kirschbaum & Hellhammer, 1994). Salivary cortisol has been used to measure stress response in youth with ASD and TD peers, measuring reactivity to various social interaction paradigms (e.g., Gunnar et al., 2003; Lopata et al., 2008).**

Compared to TD children, youth with ASD exhibit a greater salivary cortisol response to a variety of social settings, including introduction to a novel peer in an educational setting (Lopata et al., 2008) and playing with same-aged peers on a playground (Author Citation, 2010). Nonetheless, specific context appears to play a role, and highly-structured social contexts may be less stressful for youth with ASD; compared to TD peers, children with ASD show a blunted cortisol response to the Trier Social Stress Test (TSST)-Child Version, a structured story telling paradigm (Lanni et al., 2012). In contrast, social interaction paradigms that are less structured and focus on open-ended, naturalistic peer interaction appear to elicit a stronger stress response in youth with ASD (Author Citation, 2010; 2012).

One validated protocol for investigating social interaction in **high-functioning** ASD is the Peer Interaction Paradigm (PIP; Author Citation, 2012). The PIP involves a semi-structured, 20-minute playground interaction in which a participant engages in play with two gender- and age-matched peers. **The paradigm includes both periods of free, unsolicited peer interaction, as well as solicited play (facilitated by an age-matched confederate). The periods of solicited play include a variety of cooperative play activities, including games involving playground equipment (e.g., playing on swings, hide-and-seek) and toys (e.g., ball toss).** Research utilizing the PIP suggests that, compared to TD peers, children with ASD display a heightened and longer-lasting cortisol response to peer interaction (Author Citation, 2010; 2012; 2014). While the PIP provides a valuable methodology for studying social interaction and stress reactivity in children with ASD, the protocol's ecological validity is limited by participant age. **By comparison, there are very few standardized behavioral paradigms that exist for examining social interaction among adolescents, with or without ASD.**

ASD and Pubertal Development

Adolescence refers to a period of social and cognitive maturation of the child brain into its adult form. Adolescence, which is marked by the onset of puberty, is an essential phase for both physiological and psychosocial development. In addition to an increased importance and complexity of social interactions and peer relationships (Roisman et al., 2004), adolescence is associated with development of the HPA-axis and alterations to the stress response (Romeo, 2010, for review). During the developmental adolescent period, there is an apparent maturation of the circadian rhythm revealing higher basal cortisol levels in older adolescents (Adam, 2006; Walker et al., 2001; Gunnar et al., 2009). Developmental differences have been shown on several physiological indices of arousal (Stroud, 2009) including increased cortisol in anticipation of a social stressor (Sumter, 2010). As such, compared to pre-pubescent children, adolescents display increased cortisol response to psychosocial stressors (Gunnar et al., 2009; Stroud et al., 2009), particularly in the earliest stages of puberty (Di Luigi et al., 2006).

Given that dysregulation of the HPA-axis is common in ASD even during childhood (Taylor & Corbett, 2014), adolescence poses a particularly important time for the study of psychosocial stress, in such vulnerable populations. Despite the obvious clinical relevance, few studies have explored social interaction and stress in adolescents with ASD. Behavioral research suggests that high-functioning adolescents with ASD have difficulties adapting behaviour and utilizing social skills in differing social contexts (Ratto et al., 2010). Compared to TD peers, adolescents with ASD may be less able to down regulate the stress response using regulatory behavioral mechanisms (Author Citation, 2016). Nonetheless, similar to findings of blunted cortisol response to the TSST-C in children with ASD (Lanni et al., 2013), adolescents with **high-functioning** ASD exhibit a blunted cortisol response to the TSST—a classic mock job interview paradigm to induce social evaluative threat (Author Citation, 2016). On the other hand, stress response to **less formal social** interaction has not been directly investigated in adolescents.

The Current Study

As noted, previous research shows that children with ASD exhibit a particularly heightened cortisol response to peer interaction (Author Citation, 2010; 2013). Furthermore, pubertal maturation has a significant impact on the stress response (Gunnar et al., 2009; Stroud et al., 2009). Nonetheless, no studies to date have systematically investigated HPA-axis response to **social interaction** in adolescents with ASD. Thus, the present pilot study sought to investigate **social interaction and stress** in **high-functioning** adolescents with/without ASD, using a novel semi-structured, videogame-based paradigm. **A videogame was chosen as the context for the interaction because such games are a common leisure activity for adolescents (both TD and with ASD), increasing the similarity of the paradigm to a real life social scenario (Mazurek, 2013). Furthermore, videogames provide a semi-structured context, which allows for flexibility and naturalistic social interaction among participants, while providing a limited amount of structure and goal-oriented framing. The chosen activity mirrors the playground games (e.g., ball toss and joint swinging) that have been incorporated into validated peer interaction paradigms for younger children (Author Citation, 2010; 2012; 2014).**

Goals of the current study were to assess group differences in cortisol, during participation in the videogame-based social interaction. Furthermore, we sought to examine the relation between stress and pubertal development. We hypothesised that youth with **high functioning** ASD would show greater salivary cortisol response to the **videogame-based interaction**, compared to TD **peers**. Furthermore, we anticipated that salivary cortisol response would be negatively correlated with pubertal development, in light of the peak in cortisol reactivity associated with early adolescence (Di Luigi et al., 2006).

Methods

Participants

Participants included adolescents between 13 to 17 years of age who had demonstrated pubertal onset. The sample consisted of 12 unmedicated individuals with ASD (1 female) and 12 age-matched participants with typical development (3 females, for demographics, see Table 1). All participants were medication free due to the significant impact that many medications have on cortisol levels (Granger et al., 2009). The Institutional Review Board approved this study. Informed consent was obtained from parents prior to participation in the study and assent was obtained from participants. Recruitment efforts included distribution of Institutional Review Board-approved flyers to university clinics, area schools, and resource centers, as well as the use of university and local autism listserv resources.

Procedure

The study required two visits to the University setting and three continuous days of home saliva sampling conducted between visits one and two. Visit 1 consisted of diagnostic and neuropsychological testing, which included confirmation of ASD diagnosis, completion of study measures (outlined below), as well as parent and participant instruction in home saliva sampling methods.

Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999).—The WASI is a measure of cognitive ability that provides an estimated Full Scale IQ score based on two verbal and two nonverbal performance subtests. All participants completed the WASI and were required to have a Full-Scale IQ of at least 70. **See Table 1 for participant IQ information.**

The Pubertal Development Scale (PDS).—The PDS (Petersen, 1988) is a parent report measure of the degree of physical development including growth in height, growth of body hair, skin changes/acne, and overall development compared to peers. It also includes voice deepening and facial hair questions for boys. Scores range from 1: “change has not yet begun” to 4: “development complete”. All participants had a mean score of at least 2, indicating pubertal onset.

Autism Diagnostic Observations Schedule Version II (ADOS-II, Lord et al., 2012).—Adolescents with ASD completed the ADOS-II, Schedule 3 or 4, depending on developmental appropriateness, to confirm the presence of ASD. The ADOS was administered by **research-reliable** clinicians. In the instance of first-time diagnoses, the

Autism Diagnostic Interview-Revised (ADI-R, Lord et al., 1994) was also administered to a parent. All ASD participants met ADOS-II criteria for ASD with a total ADOS score greater than 7. Two participants who had ADOS-II scores of 6 were included in the study and were determined to have ASD on the basis of developmental history, SCQ scores, ADI, and clinical judgment (BAC, CN). **The ADOS has demonstrated high research reliability and ability to differentiate between individuals with and without ASD (Zander et al., 2015).**

The Social Communication Questionnaire (SCQ).—The SCQ (Rutter, 2003), is a brief parent-report questionnaire that assesses for past and present behaviors indicative of ASD, including social communication abilities and restricted and repetitive behaviors or interests. In the present study, the SCQ was used as a screening tool to rule out ASD in the TD group and to corroborate ASD diagnosis obtained via the ADOS. SCQ scores greater than or equal to 15 are thought to indicate ASD. No TD participant had a SCQ score greater than or equal to 10 on the SCQ. **Reliability estimates of the SCQ from previous studies have been as high as .87 (Krug et al., 1980).**

The Social Responsiveness Scale Second Edition (SRS-2).—The SRS (Constantino, 2012) is a parent-report questionnaire used to assess the presence of ASD symptoms across the following domains: Social Awareness, Social Motivation, Social Cognition, Social Communication, and Restrictive and Repetitive Behaviors. A total t-score was calculated for each participant. The SRS identifies the severity of ASD symptoms and also can be used to differentiate social impairments in ASD from those that occur in other diagnoses. No TD participant had a t-score greater than 50. **The SRS has high reliability as demonstrated through previous studies that indicate an alpha reliability level of .91 (Moul et al., 2015).**

Home Saliva Sampling Procedure

Our procedure for home saliva sampling is well-established and has been described in detail elsewhere (Author Citation, 2008; 2014). Participants provided four samples per day on three continuous weekdays between Visit 1 and Visit 2, for a total of twelve at home samples. Samples were collected at waking, thirty minutes post waking, in the afternoon between one and four pm, and before bedtime. Participants passively drooled into a test tube through a straw, providing a minimum one mL of saliva for each sample, kept refrigerated at home until Visit 2.

Wii™ Bowling Interaction Paradigm

Visit 2 consisted of the semi-structured, videogame-based social interaction paradigm. For this paradigm, one participant with ASD and an age-matched TD participant played a Nintendo® Wii™ Bowling (Nintendo®, 2006) video game with a third, typically developing confederate participant for twenty minutes. **The system was set up and the game cued up before participant arrival. Avatars were preselected for each participant, representing players “1,” “2,” and “3.” The room was void of extraneous materials and contained a table that supported the television monitor and game system. Remote controls were placed on the table and used by each participant.** At arrival, the ASD and TD participants were kept separate and provided a saliva sample after allowing for five minutes of

acclimation to the laboratory setting. Lab personnel then directed the participants to the Wii™ room, where they were met by an age- and sex-matched confederate peer to begin play. The confederate peer was a TD adolescent selected and trained by lab personnel to facilitate play and provide a supportive environment as well as structure to the twenty-minute paradigm. The confederate introduced him or herself to both the TD and ASD study participants and invited them to play Wii™ Bowling. Lab personnel then excused themselves from the room and observed the play interaction from behind a two-way mirror. **During the interaction, the confederate peer facilitated joint play of the videogame and periodically solicited conversation with the participants (both ASD and TD). For example, the confederate would ask questions or attempt to begin a conversation once per minute, if natural conversation was not already occurring.**

The entire paradigm was also video recorded by a camera placed behind the video game console. After twenty minutes, lab personnel entered the room to end the play paradigm and escort the TD and ASD study participants to separate sampling rooms. Salivary cortisol samples were obtained, one immediately after the paradigm, one ten minutes after the end of the paradigm, a third sample twenty minutes after the end of the paradigm, a fourth sample forty minutes after the end of the paradigm, and a final sample one hour after the end of the paradigm (see Figure 1). In total, six samples were taken on the day of the paradigm.

Salivary Cortisol Assay

The salivary cortisol assay was performed using a Coat-A-Count® radioimmunoassay kit (Siemens Medical Solutions Diagnostics, Los Angeles, CA) modified to accommodate lower levels of cortisol in human saliva relative to plasma. Saliva samples, which had been stored at -20°C, were thawed and centrifuged at 3460 rpm for 15 minutes to separate the aqueous component from mucins and other suspended particles. All samples were replicated. The coated tube from the kit was substituted with a glass tube into which 100 µl of saliva, 100 µl of cortisol antibody (Location Blinded), and 100 µl of ¹²⁵I-cortisol were mixed. After incubation at 4°C for 24 hours 100 µl of normal rat serum in 0.1% PO4/EDTA buffer (1:50) and precipitating reagent (PR81) were added. The mixture was centrifuged at 3460 rpm for 30 minutes, decanted, and counted. Serial dilution of samples indicated a linearity of 0.99. **Interassay coefficient of variation was 1.62%.**

Statistical Analysis Plan

Demographics and neuropsychological measures.—Independent sample t-tests were used to test for significant differences between the ASD and TD participants with regards to age, pubertal development, IQ, SCQ, and SRS scores, as well as afternoon basal salivary cortisol levels.

Cortisol.

As expected, descriptive statistics showed right skewness in the salivary cortisol data. All data was log transformed (base 10) to align with the relative normality assumptions of repeated measures ANOVA (Lanni et al., 2012; Richdale and Prior, 1992).

Levene's Test for Homogeneity of Variances was performed to determine if there were differences in variability between groups in salivary cortisol measures during the videogame-based social interaction paradigm.

ANOVA was performed to determine if the baseline cortisol values (mean afternoon over three days of home sampling and first sample taken at arrival on the day of the **Videogame-based interaction**) were comparable between the ASD and TD groups.

In order to determine if there was a physiological response to the paradigm in each diagnostic group, paired sample t-tests were performed separately in the log-transformed ASD and TD samples using the two samples taken immediately after the Wii™ interaction paradigm ended. Results were considered significant at a two-tailed $p < 0.05$.

Finally, repeated measures ANCOVA was used to analyze diagnostic effects on salivary cortisol during the **videogame-based interaction** with the salivary cortisol values at each of the six time points on the day of the **videogame-based interaction** paradigm as factors. Average afternoon basal salivary cortisol from the three days of home sampling was included as a covariate of no interest in the model. Results were considered significant at a two-tailed $p < 0.05$.

Pubertal Effects.

To assess for relationships between pubertal development and stress responsivity to **videogame-based interaction**, we employed Pearson partial correlation analyses within each diagnostic group between PDS scores and each participant's peak cortisol value, controlling for mean baseline afternoon cortisol levels. Results were considered significant at a two-tailed $p < 0.05$.

Results

There were no significant differences in age, pubertal development, verbal, performance, or full scale IQ between groups. There were, as expected, significant differences in SCQ and SRS scores between groups.

Levene's Test demonstrated no significant differences between groups in cortisol sample variability (all p values > 0.20). ANOVA showed no significant between-group differences in baseline cortisol values (mean afternoon cortisol and cortisol upon arrival on the day of the videogame-based paradigm ($F = 0.627$, $p = 0.437$)).

Paired sample t-tests of the immediately pre- and immediately post-interaction cortisol values indicated no significant increase in cortisol in the TD group ($t = 0.958$, $p = 0.361$) or the ASD group ($t = -0.421$, $p = 0.682$).

Repeated measures ANOVA revealed no significant differences between groups in salivary cortisol across all six samples when controlling for mean home afternoon cortisol ($F = 0.272$, $p = 0.608$).

Correlational analyses revealed a significant correlation between pubertal development and cortisol reactivity ($r = -0.54$, $p = 0.01$). However, cortisol reactivity was not significantly correlated with age ($r = -0.33$, $p = 0.15$). Partial correlation analyses revealed a significant negative correlation between pubertal development and peak cortisol following the videogame-based interaction in the ASD ($r = -0.85$, $p < 0.001$), but not the TD group ($r = 0.03$, $p = 0.94$, see figure 2). This correlation of cortisol and development in ASD also held true at time-points corresponding to the middle ($r = -0.73$, $p = 0.01$) and 20 minutes post play ($r = -0.77$, $p = 0.005$).

Discussion

Compared to TD peers, children with ASD oftenc exhibit altered patterns of stress in response to social interaction, including increased cortisol response to peer interaction (Lanni et al., 2012; Schupp et al., 2013; Lopata et al., 2008). While adolescence is an extremely important phase for the development of both social relationships and the HPA-axis, the effects of pubertal development on stress response to **social interaction** has not been **thoroughly** investigated, in adolescents with ASD. Thus, the current study attempted to investigate group differences in cortisol response to a **videogame-based social interaction** in adolescents with and without ASD, as well as the impact of pubertal development.

Findings show no significant between-group differences in salivary cortisol reactivity, in response to the **videogame-based interaction** task. The lack of group differences, while contrary to our hypotheses, may stem from the particular social context of the videogame-based task. Specifically, while previous work has shown significantly greater cortisol response to peer interaction on a playground in children with ASD (Author Citation, 2010; 2012), the current task was much more structured in nature. Whereas the PIP allows participants to freely explore a large playground area and does not center on a particular social activity, the current Wii™ bowling task is clearly focused on the videogame, providing greater structure and predictability. These negative findings could also be seen as compatible with the strong restricted interests/behaviors characteristic of ASD (APA, 2013). In other words, the lack of stress response in the children with ASD may reflect their ease with more repetitive, consistent and predictable features the videogame-based task provides.

Lack of group differences in cortisol response is underscored by previous research suggesting divergent patterns of stress reactivity in differing social contexts (i.e. social evaluative threat vs. informal **interaction with peers**), between ASD and TD youth (Author Citation, 2012). Namely, compared to TD peers, children with ASD show a blunted cortisol response to the TSST-C (Lanni et al., 2012; Jansen et al., 2000; Levine et al., 2012) and a similar trend is seen in adolescents with ASD (Author Citation, 2016). In relation to the TSST and the original PIP, the current videogame-based paradigm may exemplify an intermediary in terms of structure, more structured than the free-form PIP but less structured than a formal interview. Consequently, while the current paradigm may not be explicitly evaluative enough to be considered threatening by TD participants, the elements of structure and goal-orientedness may have led to less stress in the ASD group, causing neither group to exhibit a significant cortisol response.

While there were no significant between-group differences in cortisol response, there were group differences in the partial correlations between puberty and cortisol response. Specifically, even though cortisol response was not associated with pubertal development in TD participants, there was a significant negative correlation between pubertal development and cortisol in the ASD group suggesting down regulation of cortisol as participants with ASD mature. Previous research in TD individuals shows that, compared to older adolescents, those in the earliest stages of puberty exhibit a more pronounced salivary cortisol response (Di Luigi et al., 2006). It is relevant to point out that Di Luigi and colleagues reported a negative correlation between pubertal development and cortisol reactivity in a group of typically developing male participants, but the participants' mean age (13.3) was younger than the current study's sample (14.9). Thus, the majority of typically developing participants in the current study may have already passed the peak-stress phase of adolescence. On the other hand, participants with ASD showed a very strong negative association between pubertal development and stress response. These results may suggest a developmental lag in stress response development, for adolescents with ASD.

Findings add to previous literature demonstrating altered development trajectory of the stress response, in ASD. Such alterations appear present across childhood and adolescence (Lanni et al., 2012; Schupp et al., 2013; Author Citation, 2016), but may stabilise in adulthood (Jansen et al., 2006). For instance, young (8–9 years) children with ASD actually show less cortisol reactivity to peer interaction than young TD children, while the opposite pattern holds true for older (10–12 years) children (Schupp et al., 2013). Furthermore, age has been shown to be a moderator of cortisol reactivity in pre-pubescent children with ASD, with cortisol response significantly increasing with age in ASD, but not TD children (Author Citation, 2010). Altered patterns of development also appear for stress response to more structured social contexts. Studies utilizing variations of the TSST found that, while children and adolescents with ASD show blunted cortisol response to social evaluative threat (Lanni et al., 2012; Author Citation, 2016) adults with ASD appear to exhibit a typical stress response (Jansen et al., 2006). Paired with current results and work utilizing the PIP (Author Citation, 2010; 2012; 2014), this suggests a possibly lagged/inverted trajectory of the stress response in ASD. Namely, individuals with ASD may show exaggerated cortisol response to peer interaction during youth, which peaks at puberty, but then takes on a more typical pattern moving into adolescence and adulthood. On the other hand, cortisol response to social evaluative threat may be attenuated in youth with ASD, but takes on a more typical pattern of elevation with age (Author Citation, 2016). Alternatively, this trajectory may be altered or exaggerated rather than delayed, per se. Longitudinal designs would allow for the fuller elucidation of such developmental trends.

While our results can be interpreted with a focus on development and/or social context, findings may also be contextualised in research showing greater prevalence of videogame playing in child/adolescent boys with ASD, compared to TD peers (Mazurek & Engelhardt, 2013a; Mazurek & Engelhardt, 2013b; Orsmond & Kuo, 2011; Shane et al., 2008). If experience with videogames provided a framework of familiarity and organization, this context may have served as a buffer against the perception of threat typically associated with peer interaction. If it is the case that videogames (and/or the structure they offer) provide a buffer against psychosocial stress in ASD, videogames may serve as a useful context for

interventions targeting anxiety, stress, and social skills in youth with ASD. Such methods could be particularly useful as youth with ASD show strong preference for video- and computer- based material (Corbett et al., 2005; Charlop and Milstein, 1989; Charlop-Christy et al., 2000).

Already, interventions based on videogames and other interactive technologies have been used for improving multiple domains of cognition and behaviour in ASD (Blum-Dimaya et al., 2010; Gotsis et al., 2010; Liu et al., 2008). Videogames and other adaptive technologies have also shown promise as components of social skills interventions for ASD (Madsen et al., 2008; Picard & Goodwin, 2008; Piper et al., 2006). Such videogame-based interventions could possibly add to a body of novel interventions for ASD using interactive methods such as physical exercise (Petrus et al., 2008, for review) and theatre (Author Citation, 2016). Nevertheless, precaution is needed, particularly in regard to encouraging general use of consumer videogames, as videogame overuse may be associated with maladaptive behaviour and disrupted patterns of attention in ASD (Mazurek & Engelhardt, 2013b). Thus, much further research is required before the merits of such interventions can be fully assessed.

Limitations

One obvious limitation to the current study is the small sample size. Twelve participants per group limits statistical power and the ability to detect any group differences, which may be present. Furthermore, while the current study sought to investigate group differences in stress response to **social interaction with peers**, the structured, goal-oriented nature of the current paradigm may characterise a specific social context that individuals with ASD do not find particularly stressful. Thus, future studies should address this limitation by exploring stress reactivity in a variety of social contexts, differing in scope and structure (e.g., job interview, videogame-based task, “networking/hang-out” simulation). Additionally, while the current study suggests that pubertal development may play a significant role in stress reactivity among adolescents with ASD, a greater range of ages (including participants before and after puberty) is needed to fully examine these effects. These future directions would serve to more fully illustrate the nature of psychosocial stress and its developmental trajectory, in ASD and TD youth.

Summary

Findings of the current study indicated no significant group differences in salivary cortisol response to a **videogame-based interaction** paradigm. Neither group showed significant elevation in salivary cortisol, compared to baseline, which suggests that adolescents with ASD may not find the particular social context stressful, possibly due to its structured, goal-oriented nature. These findings also have broader implications and underscore the importance of exploring **social interaction** and stress in multiple social contexts that vary in structure and scope. While there were no overall group differences, pubertal development had differential effects on stress response in ASD vs. TD participants. This reveals further insights into alterations in the developmental trajectory of the psychosocial stress response in ASD, possibly related to developmental delay and/or exaggeration. All in all, the current study adds to a small, but growing body of work exploring **social interaction** and stress

response in adolescents with ASD, while introducing a novel semi-structured, videogame-based social interaction paradigm.

Acknowledgments:

The authors would like to thank the families for their participation in this study.

This work was supported by NIMH R01 MH085717 (Corbett).

References

- Adam EK (2006). Transactions among adolescent trait and state emotion and diurnal and momentary cortisol activity in naturalistic settings. *Psychoneuroendocrinology*, 31(5), 664–679. [PubMed: 16584847]
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC.
- Bauminger N, Shulman C, & Agam G (2003). Peer interaction and loneliness in high-functioning children with autism. *Journal of autism and developmental disorders*, 33(5), 489–507. [PubMed: 14594329]
- Blum-Dimaya A, Reeve SA, Reeve KF, & Hoch H (2010). Teaching children with autism to play a video game using activity schedules and game-embedded simultaneous video modeling. *Education and Treatment of Children*, 33(3), 351–370.
- Castelli F, Frith C, Happé F, & Frith U (2002). Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. *Brain*, 125(8), 1839–1849. [PubMed: 12135974]
- Charlop MH and Milstein JP (1989) Teaching autistic children conversational speech using video modeling. *Journal of Applied Behavior Analysis* 22(3): 275–285. [PubMed: 2793634]
- Charlop-Christy MH, Le L, et al. (2000) A comparison of video modeling with in vivo modeling for teaching children with autism. *Journal of autism and developmental disorders*, 30(6): 537–552. [PubMed: 11261466]
- Constantino JN, & Gruber CP (2012). *Social Responsiveness Scale Los Angeles*: Western Psychological Services.
- Coplan JD, Andrews MW, Rosenblum LA, Owens MJ, Friedman S, Gorman JM, Nemeroff CB (1996). Persistent elevations of cerebrospinal fluid concentrations of corticotropin-releasing factor in adult nonhuman primates exposed to early-life stressors: implications for the pathophysiology of mood and anxiety disorders. *Proceedings of the National Academy of Sciences*, 93(4), 1619–1623.
- Corbett BA, & Abdullah M (2005). Video modeling: why does it work for children with autism? *Journal of Early and Intensive Behavior Intervention*, 2(1): 2.
- Di Luigi L, Baldari C, Gallotta MC, Perroni F, Romanelli F, Lenzi A, & Guidetti L (2006). Salivary steroids at rest and after a training load in young male athletes: relationship with chronological age and pubertal development. *International journal of sports medicine*, 27(9), 709–717. [PubMed: 16944399]
- Gotsis M, Piggot J, Hughes D, & Stone W (2010, 6). SMART-games: a video game intervention for children with Autism Spectrum Disorders. In *Proceedings of the 9th International Conference on Interaction Design and Children* (pp. 194–197). ACM.
- Granger DA, Hibel LC, Fortunato CK, & Kapelewski CH (2009). Medication effects on salivary cortisol: Tactics and strategy to minimize impact in behavioral and developmental science. *Psychoneuroendocrinology*, 34(10), 1437–1448. [PubMed: 19632788]
- Gunnar MR, Sebanc AM, Tout K, Donzella B, & van Dulmen MM (2003). Peer rejection, temperament, and cortisol activity in preschoolers. *Developmental Psychobiology*, 43(4):346–368. [PubMed: 15027418]
- Gunnar MR, Wewerka S, & Frenn K (2009). Developmental Changes in Hypothalamus-pituitary-adrenal Activity over the Transition to Adolescence: Normative Changes and Associations with Puberty. *Developmental Psychopathology*, 21, 69–85.

- Jansen LMC, Gispens-de Wied CC, Van der Gaag RJ, Ten Hove F, Willemsen-Swinkels SWM, Hartevelde E, & Van Engeland H (2000). Unresponsiveness to psychosocial stress in a subgroup of autistic-like children, multiple complex developmental disorder. *Psychoneuroendocrinology*, 25(8), 753–764. [PubMed: 10996471]
- Jansen LM, Gispens-de Wied CC, Wiegant VM, Westenberg HG, Lahuis BE, & Van Engeland H (2006). Autonomic and neuroendocrine responses to a psychosocial stressor in adults with autistic spectrum disorder. *Journal of autism and developmental disorders*, 36(7), 891–899. [PubMed: 16865550]
- Kirschbaum C, & Hellhammer DH (1994). Salivary cortisol in psychoneuroendocrine research: recent developments and applications. *Psychoneuroendocrinology*, 19(4), 313–333. [PubMed: 8047637]
- Krug DA, Arick J, & Almond P (1980). Behavior checklist for identifying severely handicapped individuals with high levels of autistic behavior. *Journal of Child Psychology and Psychiatry*, 21(3), 221–229. [PubMed: 7430288]
- Lanni KE, Schupp CW, Simon D, & Corbett BA (2011). Verbal ability, social stress, and anxiety in children with autistic disorder. *Autism*, 1362361311425916.
- Liu C, Conn K, Sarkar N, & Stone W (2008). Physiology-based affect recognition for computer-assisted intervention of children with Autism Spectrum Disorder. *International journal of human-computer studies*, 66(9), 662–677.
- Lopata C, Volker MA, Putnam SK, Thomeer ML, & Nida RE (2008). Effect of social familiarity on salivary cortisol and self-reports of social anxiety and stress in children with high functioning autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 38(10), 1866–1877. [PubMed: 18483844]
- Lord C, & McGill-Evans J (1995). Peer interactions of autistic children and adolescents. *Development and Psychopathology*, 7(04), 611–626.
- Lord C, Rutter M, Le Couteur A (1994). Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord* 24:659–685. [PubMed: 7814313]
- Lord C, Petkova E, Hus V, Gan W, Lu F et al., (2012). A multisite study of the clinical diagnosis of different autism spectrum disorders. *Arch Gen Psychiatry* 69:306–313. [PubMed: 22065253]
- Lozier LM, Vanmeter JW, & Marsh AA (2014). Impairments in facial affect recognition associated with autism spectrum disorders: a meta-analysis. *Development and psychopathology*, 26(4), 933–945. [PubMed: 24915526]
- Madsen M, El Kaliouby R, Goodwin M, & Picard R (2008, 10). Technology for just-in-time in-situ learning of facial affect for persons diagnosed with an autism spectrum disorder. In *Proceedings of the 10th international ACM SIGACCESS conference on Computers and accessibility* (pp. 19–26). ACM.
- Mazurek MO, & Engelhardt CR (2013a). Video game use in boys with autism spectrum disorder, ADHD, or typical development. *Pediatrics*, 132(2), 260–266. [PubMed: 23897915]
- Mazurek MO, & Engelhardt CR (2013b). Video game use and problem behaviors in boys with autism spectrum disorders. *Research in Autism Spectrum Disorders*, 7(2), 316–324.
- Moul C, Cauchi A, Hawes DJ, Brennan J, & Dadds MR (2015). Differentiating autism spectrum disorder and overlapping psychopathology with a brief version of the Social Responsiveness Scale. *Child Psychiatry & Human Development*, 46(1), 108–117. [PubMed: 24604214]
- Nintendo®. (2006). *Wii Sports™* Kyoto, Japan: Nintendo® Co., Ltd.
- Orsmond GI, & Kuo HY (2011). The daily lives of adolescents with an autism spectrum disorder Discretionary time use and activity partners. *Autism*, 15(5), 579–599. [PubMed: 21697194]
- Petersen AC, Crockett L, Richards M, Boxer A (1988). A self-report measure of pubertal status: Reliability, validity, and initial norms. *Journal of Youth and Adolescence*, 17:117–133. [PubMed: 24277579]
- Picard RW, & Goodwin M (2008). Developing innovative technology for future personalized autism research and treatment. *Autism Advocate*, 50(1), 32–39.
- Piper AM, O'Brien E, Morris MR, & Winograd T (2006, 11). SIDES: a cooperative tabletop computer game for social skills development. In *Proceedings of the 2006 20th anniversary conference on Computer supported cooperative work* (pp. 1–10). ACM.

- Ratto AB, Turner-Brown L, Rupp BM, Mesibov GB, & Penn DL (2011). Development of the contextual assessment of social skills (CASS): A role play measure of social skill for individuals with high-functioning autism. *Journal of autism and developmental disorders*, 41(9), 1277–1286. [PubMed: 21287253]
- Richdale AL, & Prior MR (1992). Urinary cortisol circadian rhythm in a group of high-functioning children with autism. *Journal of autism and developmental disorders*, 22(3), 433–447. [PubMed: 1400105]
- Romeo RD (2010). Adolescence: a central event in shaping stress reactivity. *Developmental psychobiology*, 52(3), 244–253. [PubMed: 20175102]
- Roisman GI, Masten AS, Coatsworth JD, & Tellegen A (2004). Salient and emerging developmental tasks in the transition to adulthood. *Child development*, 75(1), 123–133. [PubMed: 15015679]
- Rutter M (2003). Categories, dimensions, and the mental health of children and adolescents. *Annals of the New York Academy of Sciences*, 1008, 11–21. [PubMed: 14998868]
- Schupp CW, Simon D, & Corbett BA (2013). Cortisol responsivity differences in children with autism spectrum disorders during free and cooperative play. *Journal of autism and developmental disorders*, 43(10), 2405–2417. [PubMed: 23430177]
- Simon DM & Corbett BA (2013). Examining associations between anxiety and cortisol in high functioning male children with autism. *Journal of Neurodevelopmental Disorders*, 5, 32. [PubMed: 24216056]
- Shane HC, & Albert PD (2008). Electronic screen media for persons with autism spectrum disorders: Results of a survey. *Journal of autism and developmental disorders*, 38(8), 1499–1508. [PubMed: 18293074]
- Stroud Laura R., Foster Elizabeth, Papandonatos George D., Handwerker Kathryn, Granger Douglas A., Kivlighan Katie T., & Niaura Raymond. (2009). Stress Response and the Adolescent Transition, Performance versus Peer Rejection Stressors. *Developmental Psychopathology*, 21(1), 47–68.
- Sumter SR, Bokhorst CL, Miers AC, Van Pelt J, & Westenberg PM (2010). Age and puberty differences in stress responses during a public speaking task: do adolescents grow more sensitive to social evaluation? *Psychoneuroendocrinology*, 35(10), 1510–1516. [PubMed: 20541871]
- Taylor JL, & Corbett BA (2014). A review of rhythm and responsiveness of cortisol in individuals with autism spectrum disorders. *Psychoneuroendocrinology*, 49, 207–228. [PubMed: 25108163]
- Walker EF, Walder DJ, & Reynolds F (2001). Developmental changes in cortisol secretion in normal and at-risk youth. *Development and psychopathology*, 13(03), 721–732. [PubMed: 11523856]
- Wechsler D (1999). Wechsler abbreviated scale of intelligence Psychological Corporation.
- Zander E, Willfors C, Berggren S, Choque-Olsson N, Coco C, Elmund A, ... & Linder J (2016). The objectivity of the Autism Diagnostic Observation Schedule (ADOS) in naturalistic clinical settings. *European Child & Adolescent Psychiatry*, 25, 769–780. [PubMed: 26584575]

Timeline Video Game Interaction

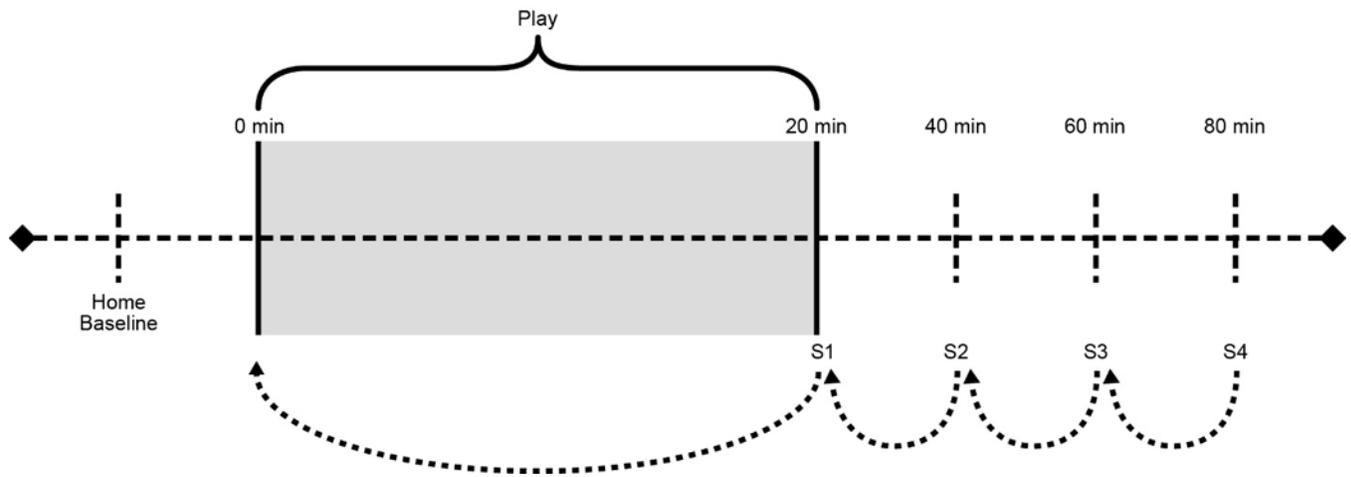


Figure 1.
 Timeline for the Semi-structured, Videogame-based Interaction
 Note: Timeline for the 20 minute play period including the salivary cortisol sampling.
 Cortisol levels correspond to time-points 20 minutes prior to sampling, because of cortisol's 20 minute lag time.

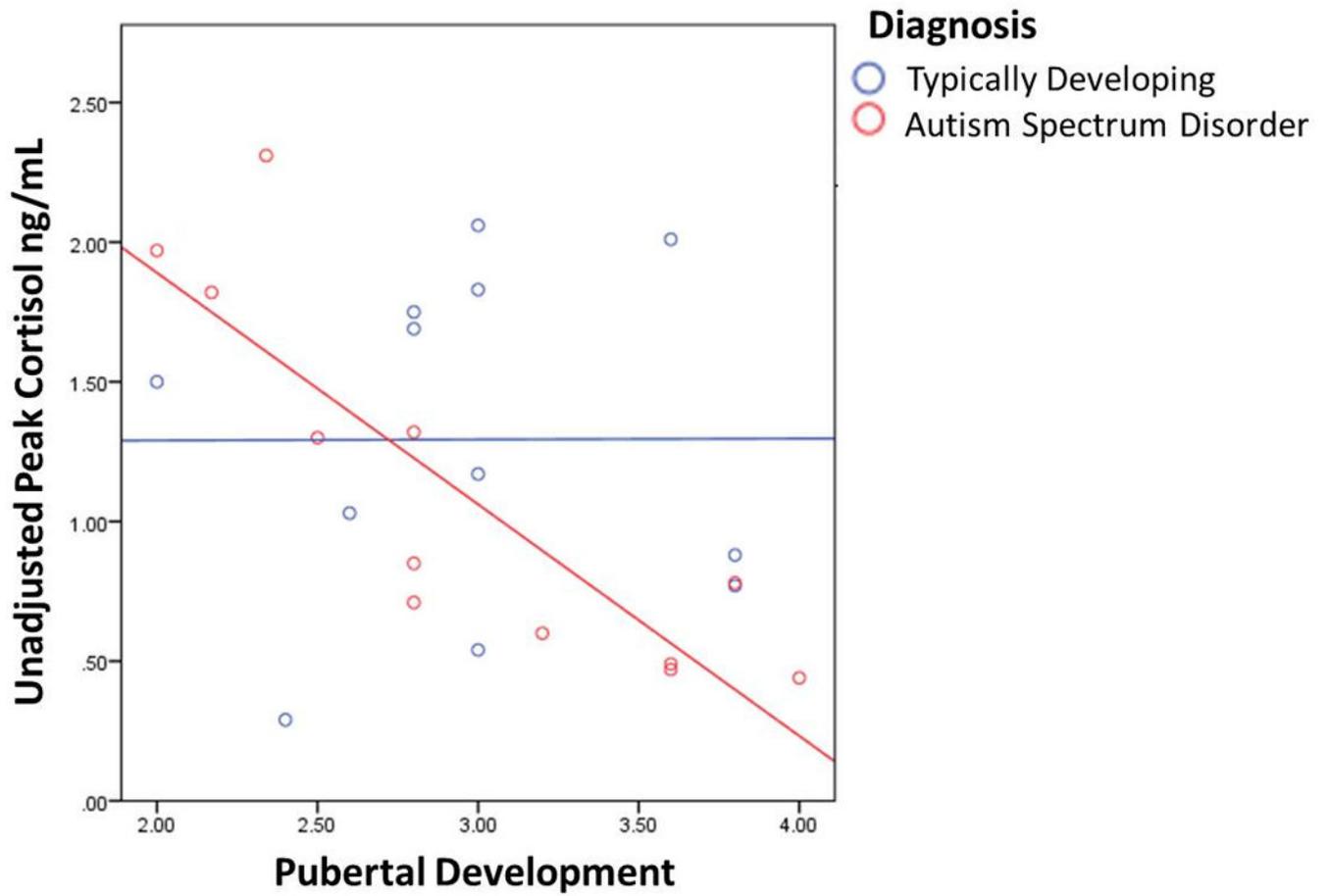


Figure 2. Negative Correlation between Pubertal Development and Cortisol during Videogame-based Interaction in Adolescents with ASD

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1.

Participant Demographics

Group (N)	Age	PDS	VIQ	PIQ	FSIQ	SCQ	SRS
TD (12)	14.89 (1.32)	2.98 (0.54)	115.18 (16.68)	110.45 (12.84)	114.27 (14.67)	2.50 (2.20)	43.33 (3.45)
ASD (12)	14.90 (1.74)	2.97 (0.67)	98.83 (25.60)	100.17 (19.24)*	99.67 (23.31)	22.08 (11.27)**	77.42 (11.35)**

TD = Typical development, ASD = Autism Spectrum Disorder, VIQ = Verbal IQ, PIQ = Performance IQ, FSIQ = Full Scale IQ, SCQ = Social Communication Questionnaire, SRS = Social Responsiveness Scale

*
p < .05.

**
p < 0.0001