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Temporal patterns, heterogeneity, and stability of diurnal cortisol rhythms in children with autism spectrum disorder☆

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ABSTRACT

The current study used a multifaceted approach to assess whether children with ASD have a distinctive diurnal rhythm of cortisol that differentiates them from typically developing (TD) peers and whether sub-groups of ASD children can be identified with unique diurnal profiles. Salivary cortisol was sampled at four time points during the day (waking, 30-min post-waking, afternoon, and evening) across three days in a sample of 36 children with autism spectrum disorder (ASD) and 27 typically developing (TD) peers. Between-group comparisons on both mean levels and featural components of diurnal cortisol indicated elevated evening cortisol and a dampened linear decline across the day in the ASD group. No differences were evident on the cortisol awakening response (CAR). Group-based trajectory modeling indicated that a subgroup (25%) of ASD children demonstrated an attenuated linear decline while the cortisol trajectory of the second subgroup was indistinguishable from that of the TD group. Intraclass correlations indicated that, when aggregated across days, cortisol measures were generally stable over the interval assessed. There were few significant relations between cortisol measures or sub-groups and measures of stress, temperament, and symptoms. Results encourage follow-up studies to investigate the functional significance, heterogeneity and longer-term stability of diurnal cortisol profiles in children with ASD.

1. Introduction

Individuals with autism spectrum disorder (ASD) demonstrate profound impairments in social interaction, communication, and stereotypic behaviors (APA, 2013) that are often manifest as difficulty responding to changes in daily routines. These difficulties may be related to atypical functioning of the hypothalamic-pituitary-adrenal (HPA) axis. Indeed, it is well known that novelty, unpredictability, and change increase activation of the HPA axis and are associated with heightened levels of cortisol (e.g., Gunnar et al., 1988; Levene et al., 1989). Because cortisol is crucial for homeostatic regulation and the ability to adapt to environmental challenges, it is important to assess whether children with ASD have a distinctive cortisol signature that differentiates them from typically developing (TD) peers.

The focus of the present study was the diurnal rhythm of cortisol secretion, the functional form of which is well characterized across individuals. Cortisol is highest in the morning upon waking, and an estimated 77% of people experience a sharp rise in cortisol 30-min post waking, referred to as the cortisol awakening response (CAR) (Pruessner et al., 1997; Wust et al., 2000). The CAR has been conceptualized as a preparatory phenomenon as individuals anticipate daily events and challenges that may occur throughout the course of the day (Fries et al., 2009). The CAR is followed by a steady decline of cortisol levels throughout the day until it reaches a nadir in the evening (Anders, 1982; Weitzman et al., 1971). Together, the CAR and subsequent decline are the two dominant featural components of the diurnal rhythm of cortisol secretion.

One study of children and adolescents with and without ASD found that there were no significant differences in the overall amount of daily cortisol secretion (Marinovic-Curin et al., 2008),

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thus suggesting the importance of studying more specific components of the diurnal cycle. Indeed, while afternoon levels of cortisol appear comparable between children with and without ASD, elevated evening cortisol levels in children with ASD have been reported (Corbett et al., 2008) that have been associated with measures of daily stress and sensory sensitivity (Corbett et al., 2009).

Other investigations have focused on the featural components of the diurnal cycle. To date, studies have yielded no differences between ASD and TD children in the CAR (Corbett and Schupp, 2014; Marinovic-Curin et al., 2008; Zinke et al., 2010) and mixed findings regarding differences in the slope of the peak-to-trough decline of cortisol throughout the day. Some studies have reported no between-group differences (Brosnan et al., 2009; Corbett et al., 2006; Kidd et al., 2012), while others have reported a dampened linear decline in the ASD group (Corbett et al., 2008; Corbett et al., 2009).

The present study was designed to provide a more complete and nuanced picture of cortisol differences between children with ASD and TD peers and, in the process, elucidate factors that might account for inconsistent results in previous studies. One source of variation in prior findings could be differences in the data-analytic procedures used to assess variations in the functional form of cortisol across the day. We used a more comprehensive approach than previous studies by including assessments of both changes in mean levels over time and of specific featural components of the cortisol rhythm (i.e., the CAR and linear decline in cortisol from morning through evening). In addition, to enhance sensitivity of measurement, we used the precise times at which cortisol was sampled as a predictor in our featural models.

Heterogeneity within the ASD group is another factor that might account for inconsistencies across studies. It is well-known that ASD is highly heterogeneous across multiple domains (for recent reviews, see, e.g., Jeste and Geschwind, 2014; Lenroot and Yeung, 2013). Previous studies have generally reported that groups of children with ASD have more variability in diurnal cortisol values (Corbett et al., 2006; Corbett et al., 2008; Hoshino et al., 1987; Richdale and Prior, 1992; Yamazaki et al., 1975) and parents of ASD patients demonstrate heterogeneity in daily cortisol profiles (Dykens and Lambert, 2013). To our knowledge, however, no prior studies have explicitly assessed whether sub-groups of ASD children can be identified based on distinct patterns of the diurnal rhythm of cortisol. We used group-based trajectory modeling (GBTM; Nagin, 2005; Jones and Nagin, 2007) to assess whether subgroups could be identified that displayed distinct trajectories of cortisol across the day. To understand potential causes of differences in cortisol measures between ASD and TD children and any ASD subgroups identified, we assessed the relation between cortisol and measures of daily stress, trait anxiety, and sensory sensitivity, as well as demographic and symptomatic features.

One limitation of previous studies on HPA functioning in ASD is the failure to assess psychometric properties of cortisol measures that may also account for differences across studies, or in the specific pattern of effects observed in a given study. There are several reasons why an examination of reliability, stability, and variability is important. First, if basal cortisol levels truly reflect individual differences in HPA functioning, they should demonstrate the temporal stability expected of an individual difference measure. Second, because increased measurement error tends to attenuate relations with external variables (e.g., Nunnally and Bernstein, 1994), patterns of significant and non-significant correlations and group differences could be linked to differences in the reliability of the different measures of diurnal cortisol that can be extracted. Third, it is important to assess whether prior evidence for greater variability of cortisol within the ASD group is due to greater variability between individuals (perhaps due to subgroup heterogeneity) or greater fluctuations on a within-subjects basis. For all these reasons, we additionally compared the TSD and AD groups on the stability and variability of cortisol measures.

In sum, the current study examined characteristics of diurnal cortisol variation in a sample of children with and without ASD by assessing mean differences at different times of day, featural components of the diurnal rhythm, subgroup heterogeneity in cortisol trajectories, and psychometric properties (i.e., stability and variability) of cortisol.

2. Method

2.1. Participants

The participants consisted of 63 unmedicated, healthy children between the ages of 7 and 16 years old, 36 with ASD (30 males, mean age = 10.20, SD = 1.96), and 27 TD controls (23 males, mean age = 9.71, SD = 1.54). Diagnoses were made in accordance with the Diagnostic and Statistical Manual (DSM-IV) criteria (APA, 2013) and were confirmed by a previous diagnosis by a psychologist, psychiatrist, or behavioral pediatrician with ASD expertise, clinical judgment at the time of participation (by BAC or another doctoral level psychologist experienced in the diagnosis of ASD), and the ADOS (Lord et al., 2000), administered by research-reliable personnel. Inclusion in the study required an estimated IQ of 70 or higher (see Table 1).

The Vanderbilt University Institutional Review Board approved the study. Prior to participation in the study, parents provided informed written consent and participants provided verbal assent. Participants were recruited by IRB approved flyers and established recruitment systems (e.g., clinics, resource centers, support groups, school, and recreational facilities).

3. Measures

The diagnostic and parent report measures and salivary cortisol collection training were administered during one visit to the University.

3.1. Autism diagnostic observation schedule (ADOS)

Autism Diagnostic Observation Schedule (ADOS) (Lord et al., 2000) is a semi-structured interview used to assess diagnostically characteristic behaviors of ASD. Test-retest reliability for the domains include social (.78), communication (.73), social communication (.82), and restricted, repetitive behavior (.59). Internal consistency for all domains and modules ranges from .47 to .94 (Lord et al., 2000).

3.2. Wechsler abbreviated scale of intelligence (WASI)

Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) is a measure of general intelligence used to estimate intellectual functioning. Reported test-retest reliabilities range from .76 to .85 for each subtest, and are .95 for the full-scale estimated IQ (Wechsler, 1999).

3.3. Stress Survey Schedule (SSS)

Stress Survey Schedule (Groden et al., 2001) is a parent-report measure of stress designed for individuals with autism and other developmental disabilities. The measure consists of 60 daily stress-related items rated on a five-point Likert scale and includes eight dimensions of stress. Internal consistency correlations range from 0.70 to 0.87. Based on evidence indicating linkages between cortisol