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Stressful Life Events and Daily Stressors Affect Awakening Cortisol Level in Midlife Mothers of Individuals with Autism Spectrum Disorders

Jen D. Wong, Ph.D., Marsha Mailick Seltzer, Ph.D., Jan S. Greenberg, Ph.D., and Jinkuk Hong, Ph.D.

Waisman Center, University of Wisconsin-Madison

David M. Almeida, Ph.D. and

Human Development and Family Studies, The Pennsylvania State University

Christopher L. Coe, Ph.D.

Psychology, University of Wisconsin-Madison

Abstract

Objectives—The current study examines the awakening cortisol level in midlife mothers ($M=51.4$ years old, $SD=8.4$) of individuals ($M=22.1$ years old, $SD=7.1$) with autism spectrum disorders (ASD) under stressful conditions that are not specific to the son or daughter's ASD symptoms.

Methods—In addition to completing a set of questionnaires and in-home interviews, 82 mothers from the Adolescents and Adults with Autism Study (AAA) participated in a Daily Diary Study.

Results—Findings from the multilevel models indicated that mothers who previously were exposed to no negative life events in the previous period had an increased awakening cortisol level on days following a greater number and more severe stressors, a normative stress response. In contrast, we observed a flatter cortisol level of daily stressors in mothers who experienced a greater number of negative life events in the previous period.

Conclusion—These findings highlight the sustained toll that global and everyday stressors have on awakening cortisol level of midlife and aging mothers of individuals with ASD.

Keywords

Stress; caregivers; cortisol

Introduction

Autism is an increasingly prevalent diagnosis, and individuals who have autism spectrum disorders (ASD) are affected throughout the life course (Happé & Charlton, 2011). In general, the life expectancy of individuals with developmental disabilities (DD) has risen over the years (e.g., Janicki, Dalton, Henderson, & Davidson, 1999), and many remain dependent on family members and services throughout adulthood (Seltzer, Krauss, Orsmond, & Vestal, 2000). According to Braddock et al. (2008), approximately 1.7 million adults with DD are being cared for by middle-age and older family caregivers. Autism is the most prevalent DD condition, but until recently research on the health and well-being of

aging parental caregivers has not specifically focused on this group (e.g., Pruchno & Meeks, 2004; Seltzer, Floyd, Song, Greenberg, & Hong, 2011; Yamaki, Hsieh, & Heller, 2009).

Parents of children and youth with ASD have elevated levels of stress and poorer well-being than parents of other types of DD conditions (Abbeduto et al., 2004). Studies consistently have shown that characteristics of ASD, particularly the son or daughter's behavior problems, are significant sources of stress for these parents (Davis & Carter, 2008), with high levels of behavior problems continuing into adulthood (Seltzer et al., 2010). Thus, midlife and aging parents of individuals with ASD experience elevated stress over decades, which highlights the need for more research on this group of caregivers.

Although factors directly related to the child's disability are stressful for parents of children with ASD, this parenting role is embedded in a larger social context. In addition to the unique challenges of parenting a son or daughter with ASD, these parents also are exposed to major negative life events (e.g., death of a family member) and daily stressors (e.g., arguments) that are experienced by everyone. In the current study, we examine how stressors not necessarily related to the child's disability are associated with maternal physiological functioning during midlife and older age. Specifically, we investigate how negative life events and daily stressors are associated with awakening cortisol level in a sample of middle-aged and older mothers of individuals with ASD.

Types of Stress: Life Events and Daily Stressors

Our study combines two distinct approaches to the study of stress and well-being. The first approach, the life events tradition (e.g., Holmes & Rahe, 1967), focuses on the global impact of life changes. Relatively infrequent in occurrence, major life events, such as death of a family member or marital separation, often result in long-term changes in lifestyle, residence, financial well-being, and social relations (Neugarten, 1979; Wheaton, 1990) and lead to distress, constraining other areas of life (Pearlin, Schieman, Fazio, & Meersman, 2005). A number of studies of families of individuals with ASD have examined the *psychological* effects of negative life events (Barker et al., 2010). However, little is known about the *physiological* effects of life events for parents of individuals with ASD, which is one focus of the present study.

The second approach focuses on everyday or 'quotidian' stressors (e.g., Almeida, 2005), which are defined as the routine challenges of day-to-day living, including arguments with a family member or unexpected deadlines. Life events and daily stressors differ in terms of frequency and may also have differential effects on well-being and health. Major life events occur less frequently and tend to have a more distal impact on well-being and physical health, whereas daily stressors tend to have a more proximal effect (Almeida, 2005). Furthermore, the two types of stressors may interact, such that the impact of daily stressors may be magnified in the context of exposure to negative life events. This is the central hypothesis of the present study.

Cortisol

Cortisol is the main hormone product of the hypothalamic-pituitary-adrenocortical (HPA) axis and is considered to be a primary marker of biological stress reactivity (Adam & Gunnar, 2001). Under routine conditions, cortisol facilitates normal adaptation to the environment and the maintenance of homeostasis through various processes including glucose level stabilization, cell metabolism, and inflammatory responses (Heim, Ehlert, & Hellhammer, 2000). Under conditions of threat or distress, the HPA axis activates and secretes cortisol into the bloodstream (Dickerson & Kemeny, 2004). Dysregulated cortisol is implicated in a host of psychological, physiological, and physical health conditions,

including depression, immune disorders, and cardiovascular disease (Bhattacharyya, Molloy, & Steptoe, 2008; McEwen et al., 1997).

While the cortisol literature has focused more on cortisol awakening response (referring to the increase in cortisol release observed over the first 30 minutes post awakening and often is assessed by the difference between cortisol levels at 30 minutes post-awakening and upon awakening) than other measurements of cortisol reactivity, research examining the magnitude of cortisol awakening response continues to be mixed (see Chida & Steptoe, 2009 and Fries, Dettenborn, & Kirschbaum, 2009 for review). This may be the case because a portion of the population does not exhibit the cortisol awakening response (see Wust et al. 2000 who observed cortisol awakening response in only 75% of their sample of healthy adults) masking the linkages between stressors and cortisol reactivity.

In addition, awakening cortisol levels are more responsive than cortisol levels assessed later in the day to subtle changes in the HPA axis associated with environmental stressors and psychiatric conditions such as chronic fatigue syndrome, depression, and sleep disturbance (e.g., Backhaus, Junghanns, & Hohagen, 2004; Dahlgren, Kecklund, Theorell, & Akerstedt, 2009). Prior research (e.g., Dahlgren et al., 2009) also has showed that low cortisol levels in the morning are associated with anxiety, symptoms of exhaustion, and poor health the day before. By focusing on awakening cortisol levels, we can better understand the time-order effects of stressors on next day's cortisol. Unlike cortisol level at awakening, cortisol values later in the day are likely to be influenced by same-day events, confounding the examination of the effect of prior-day events on next day cortisol values later in the day since these effects may be affected by ongoing stress during the second day. In this regards, the examination of cortisol levels at awakening also may provide us with clearer insights to cortisol reactivity to stressors for this sample of caregivers than the magnitude of cortisol awakening response.

Stressors and Cortisol

Stressors represent challenges and demands that trigger a response from the HPA axis. Whereas acute stressors (e.g., daily stressors) typically lead to a temporary increase in cortisol (see Miller, Chen, & Zhou, 2007, for a review), a reduced or blunted pattern of cortisol response often is observed in individuals with a history of chronic stressors (e.g., burnout, post-traumatic stress disorders; Neeck, Federlin, Graef, Rusch, & Schmidt, 1990; Yehuda, 2000). As a consequence, the literature on stress and cortisol responsiveness has been mixed, with some studies reporting increased cortisol levels (e.g., Nicolson, 2004) and others documenting blunted cortisol response (e.g., Bloch, Peleg, Koren, Aner, & Klein, 2007). In this study, we are interested in the effects of both negative life events and daily stressors on the awakening cortisol level of mothers of individuals with ASD.

The work of Smith and colleagues (2010) demonstrated that mothers of adolescents and adults with ASD are exposed to more daily stressors than mothers of similarly-aged children without disabilities. They found that, during an eight-day diary study, mothers of adolescents and adults with ASD reported more days with at least one stressful event (65% of days vs. 43%) than the comparison group. Recently, research has shown that the stress of parenting an adolescent or adult with disabilities is associated with a pattern of hypocortisolism. Comparing parents of individuals with disabilities and without disabilities, Seltzer and colleagues (2009) found that parents of grown children with disabilities exhibited a flatter cortisol decline across the day when they spent more time with their son or daughter, a pattern not evident in the comparison group. In another study, mothers of sons and daughters with ASD exhibited significantly lower levels of cortisol at all collection points (e.g., awakening, 30 minutes post awakening, bedtime) than mothers of typically developing sons and daughters after controlling for maternal age, prescription medications

usage, and saliva collection time (Seltzer et al., 2010). The same study also found that mothers of sons and daughters with ASD had a less pronounced (more blunted) cortisol awakening response on the morning after their adult child with ASD had more behavior problems, provided that the son or daughter had a history of clinically significant behavior problems (Seltzer et al., 2010). These studies highlight the toll of *child-related stressors* on an important neuroendocrine process in parents of children with DD, resulting in lower levels and more blunted slopes of cortisol at various times throughout the day. However, less is known about the adrenal hormone activity of such parents under stressful conditions that are *not specific* to the child's symptoms. Only one study has examined the physiological effects of such life events (Seltzer, Barker et al., 2011) in mothers of children with fragile X, and found that mothers with a specific genotype had a blunted cortisol response when exposed to negative life events. However, that study did not examine the effects of daily stress.

The Current Study

In the current study, we examine how general life stress may influence awakening cortisol level of midlife mothers -- above and beyond the stressors directly related to the son or daughter with ASD. Specifically, we extend past work by examining how both exposure to negative life events and the experience of daily stressors are associated with awakening cortisol level in mothers of individuals with ASD. We hypothesize that negative life events and daily stressors will work in combination, rather than independently, to predict maternal awakening cortisol level. We base this prediction on the prior work of Seltzer and colleagues (2010) who found that the association between daily behavior problems and cortisol secretion in mothers of adolescents and adults with ASD was moderated by the child's history of behavior problems. By extension, we hypothesized that the association between daily stressors and awakening cortisol level in these mothers would be moderated by previous exposure to negative life events. Specifically, those mothers who previously were exposed to fewer negative life events would have higher awakening cortisol levels on days following more stressors. In contrast, we predict a pattern of blunted cortisol level on days following more daily stressors for mothers who previously were exposed to more negative life events.

To further the understanding of the different aspects of the daily stressor characteristics on awakening cortisol level, we also examine the interactive effect of *appraisal* of stressor severity and negative life events on awakening cortisol level. Similar to the pattern expected for the interactive effect of *number* of daily stressors and negative life events, we predict that mothers who previously were exposed to fewer negative life events would have higher awakening cortisol levels on days following *more severe* daily stress. We also predict that mothers who previously were exposed to greater numbers of negative life events would exhibit lower awakening cortisol levels on days following more severe daily stress.

Methods

Participants

Participants were selected from the ongoing longitudinal study of Adolescents and Adults with Autism (the AAA study; Barker et al., 2011; Seltzer et al., 2003). Mothers were recruited through agencies, schools, clinics, and the media. To qualify for the study, families met the following three criteria: (a) included a child 10 years of age or older; (b) child received an independent diagnosis of ASD from a professional, as reported by parents; and (c) scores on the Autism Diagnostic Interview-Revised (ADI-R; Lord, Rutter, & Le Couteur, 1994; Rutter, Le Couteur, & Lord, 2003), administered by research staff, were consistent with the parental report of an ASD.

At the beginning of the study in 1998, families of 406 individuals with ASD participated. Data were collected primarily from mothers in their homes eight times between 1998 and 2011 (see Barker et al., 2011; Seltzer, Greenberg et al., 2011, for study methods description). During 2006 and 2007, the AAA Daily Dairy Study was conducted with mothers whose son or daughter with ASD still lived at home with her. By the time of the Daily Dairy Study, 136 individuals with ASD remained co-resident with their parents. Six mothers were unreachable and 34 declined participation. Of the 96 mothers in the Daily Dairy Study, three declined saliva collection and seven did not provide complete data on medication use, which was needed for the present analysis. Because of the associations between sleep-related factors and cortisol responsiveness (Fries et al., 2009), one mother who reported staying awake for more than 20 hours and waking up after 12 noon on all saliva collection days was excluded. Three mothers did not provide information on the Life Events Checklist, thereby resulting in a final sample of 82 mothers with adolescents or adults with ASD for the present analyses. Analyses of mothers included in this study and those who did not participate showed that the two groups did not differ significantly by age, education, marital status, or household income, or the age, gender, or behavior problems of the individual with ASD. Mothers who were not included in this study were significantly more likely to be working than those included.

Procedure

The present analyses utilized data from two waves (Times 4 and 5) of the AAA study. At Time 4 (2004), mothers completed a set of self-administered questionnaires before participating in an in-home interview. The present analyses specifically focused on measures from the self-administered questionnaires (i.e., the Life Events Checklist, maternal education, child's behavior problems).

At Time 5 (2006-2007), mothers participated in the Daily Dairy Study, which consisted of telephone interviews on eight consecutive evenings. Lasting 15 to 25 minutes, the daily telephone interview included questions about experiences in the previous 24 hours. Questions focused on time use, daily stressors, positive events, mood, and physical symptoms (Almeida, Wethington, & Kessler, 2002). The Daily Dairy interviews were conducted by The Pennsylvania State University's Survey Research Center.

On Days 2 through 5 of the Dairy Diary Study, mothers provided four saliva samples each day. A week prior to the telephone interview, participants received a Home Saliva Collection Kit. Each kit included 16 numbered and color-coded salivettes (Sarstedt, Nümbrecht, Germany), which contained a small absorbent wad about $\frac{3}{4}$ of an inch long, an instruction sheet, and a sample collection time log. Respondents were instructed to record the exact time they provided each saliva sample on the log. Respondents were instructed to collect their first saliva sample before eating, drinking, or brushing their teeth, not to consume any caffeinated products before taking their subsequent samples throughout the day, and to store all samples in the refrigerator (Almeida, Piazza, & Stawski, 2009).

Measures

Negative Life Events—At Time 4 of the AAA study, mothers reported whether they or their spouse or a child had experienced a range of life events in the past 12 months. Derived from Abidin's (1986) Life Stress Scale of the Parenting Stress Index, the 21-item Life Events Checklist consisted of positive and negative events. We focused only on negative events because of our interest in examining the impact of stress on maternal cortisol levels. The 11 negative items used in this study pertained to marital dissolution, finances (e.g., went deeply into debt), substance abuse, deaths, health problems, and caring for an aging parent. The final item (caring for an aging parent) was added to the life events list in Abidin's

Checklist by the AAA study investigators. The most commonly reported events were health problems (42.7%), caring for an aging parent (26.8%), and death of a family member (24.4%). The items were summed to create a *total negative life events* score. Only 4.8% of the sample reported experiencing more than 4 negative life events. To reduce skew, the total negative life events score was capped at 4, with 4 representing 4 or more negative life events. Due to the design of the AAA study, the Life Events Checklist was administered prior to the Daily Diary Study. Because of the time lapse between the assessments of life events and daily stressors, the life events assessed in this study reflect events that occurred two to three years prior to the measurement of daily stress and cortisol level. Therefore, we controlled for the duration of time that elapsed between the experience of life events and the measurement of daily stressors (see below).

Salivary Cortisol—Saliva samples at awakening, 30 minutes post awakening, before lunch, and before bedtime were assayed for cortisol at Time 5. Cortisol concentrations were quantified with a commercially available luminescence immunoassay (IBL, Hamburg, Germany), with intra-assay coefficients of variation below 5% (Dressendorfer, Kirschbaum, Rohde, Stahl, & Strasburger, 1992). In this study, we focused on the cortisol level at the awakening point because we were interested in the lagged effect of stress experienced the day before. Cortisol data was log transformed to correct for positively skewed distributions. Before the log transformation, salivary cortisol values higher than 60 nmol/l were recoded as 61 to minimize the influence of extreme outliers (Dixon & Yuen, 1974). In our sample, only one observation of awakening cortisol level was greater than 60 nmol/l.

For our sample of 82 mothers, we started with an initial data set of 318 days of cortisol data at awakening. Days when mothers woke unusually late or remained awake for more than 20 hours were dropped. We also dropped days when mothers had missing data for the time-varying predictors/covariates. Our final sample consisted of 82 mothers with 279 days of saliva samples.

Daily Stressors—Exposure to (number) and appraisal of (severity) daily stressors were assessed at Time 5 using the Daily Inventory of Stressful Events (DISE; Almeida et al., 2002). The DISE is comprised of a series of seven stem questions that identify whether certain types of stressful events occurred in the past 24 hours (arguments, avoided arguments; home, work, or network stressors; discrimination; and other stressors). Responses to the seven items were summed to create a *total number of stressors* score per day. Scores ranged from 0 (experienced no stressful event) to 7 (experienced all seven stressful events). The most commonly reported daily stressors across the study period were home-related stressors (29.4% of the study days), avoided arguments (24.4%), and arguments (20.7%). When a stressful event was reported on a given day, follow-up question asked the mother to rate the severity of stress (1=not stressful at all to 4=very stressful). To measure *stress severity*, we followed similar stressor severity scoring procedures outlined by Mroczek and Almeida (2004). On days when a stressor was reported, the severity scores for all seven items were summed. Stressor severity scores ranged from 1 (experienced one stressor at a not stressful level) to 28 (experienced all seven events at very stressful levels).

To better able to interpret the directionality of the association of stressors and cortisol levels, we examined the number and severity of stressors from the previous day predicting awakening cortisol level the next morning.

Control Variables—Characteristics of the mother that were controlled included age, education, marital status, medication usage, total number of children in the family, saliva collection time (Keenan, Licinio, & Veldhuis 2001), and length of time between the date of the mother's interview at Time 4 and the date of the beginning of the mother's participation

in the Daily Diary Study at Time 5, which ranged from 21 to 39 months ($M=31.7$, $SD=3.9$). Education level was coded on a 1 to 4 scale (1=less than high school to 4=college graduate). Marital status was coded as 0=not married and 1=married. Studies have shown that certain types of medications may influence cortisol response (Granger, Hibel, Fortunato, & Kapelewski, 2009). To control for potential medication effects, the analyses included a variable that accounted for whether respondents reported taking any medication from a 7 item list (e.g., steroids, anti-depressants or anti-anxiety; 0=no medication, 1=at least one medication). Saliva collection time also was controlled. A saliva collection time log was included in the home saliva collection kit, and respondents were asked to record the exact time that they provided each saliva sample on the log. Mothers, on average, collected their awakening saliva sample at 6:44 AM ($SD=61$ minutes). Based on prior research which showed the effects of behavior problems on maternal well-being and cortisol level (Seltzer et al., 2010), the behavior problems of the individual with ASD at Time 4 also was controlled. The measure of behavior problems was based on the Scales of Independent Behavior-Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1996). Developed for the broad population with developmental disabilities, the SIB-R scales assess the frequency and severity of eight types of behavior problems (e.g., hurtful to self, unusual or repetitive, disruptive). Using standardized algorithm, frequency and severity scores were translated into a summary score.

The average age of the mothers at Time 4 was 51.4 years ($SD=8.4$). Average maternal education level was “some college” ($M=3.1$, $SD=0.8$). Approximately 83% of the mothers were married at Time 4 and nearly 65% reported taking at least one medication during the Daily Diary Study period. The average number of children in the family, including the target child with ASD, was 2.8 ($SD=1.3$). At Time 4, the average age of the individuals with ASD was 22.1 ($SD=7.1$). Fully 79% of the individuals with ASD were males. The average behavior problem score at Time 4 was 110.8 ($SD=10.1$), which fell between the upper end of the cutoff for ‘not clinically significant’ and the lower end of ‘marginally significant’ behavior problems (Bruininks et al., 1996).

Data Analysis Plan

A set of two-level multilevel models (SAS Proc Mixed), where days were nested within persons, assessed the extent to which mothers’ negative life events affect the associations between daily stress and cortisol level on the following morning. For number of daily stressors from the previous day, analyses were carried out in two models—main effects only (model 1) and interaction effect (model 2). The same structure of analyses was conducted for the examination of severity of stressors from the previous day, but only for days when respondents reported experiencing at least one daily stressor. For our analyses of number of daily stressors, the sample consisted of 82 mothers with 279 days of saliva samples. Constrained to days when a stressor was reported, our stressor severity analyses comprised of 80 mothers and 200 days of saliva samples.

Awakening cortisol level was the primary dependent variable. Preliminary analyses were conducted, and the control variables of marital status and number of children in the family were dropped in the final models because they had no significant effects on awakening cortisol level and did not change any of the estimates. The final set of control variables included maternal age, education, medication usage, saliva collection time, the length of time between Times 4 and 5, and the behavior problems of the individual with ASD. Continuous time-invariant predictors/covariates were centered at the sample mean. Because daily stressors (number and severity) and awakening saliva collection time were assessed repeatedly, we included both within- and between-person effects using the person-mean center approach outlined by Hoffman and Stawski (2009). Preliminary analyses indicated that a random intercept only model had acceptable fit, and that the random effect of daily

stress (number as well as severity) did not improve the model fit. Similarly, we examined whether to include a random effect of awakening saliva collection time, and maximum likelihood deviance comparison showed that the random effect of awakening saliva collection time did not improve the model fit.

Results

Table 1 presents the descriptive statistics of negative life events, stressors, and cortisol. The average number of negative life events for this sample was 1.5 ($SD=1.2$). The average number and severity of daily stressors from the previous day were 1.3 ($SD=1.2$) and 5.4 ($SD=3.3$), respectively. The average log cortisol level for awakening was 2.4 nmol/l ($SD=0.5$).

Number of Daily Stressors, Number of Negative Life Events, and Cortisol Level

The first set of analyses examined the effects of number of daily stressors, number of negative life events, and the interaction between number of daily stressors and number of negative life events on cortisol level at awakening the following day. Pearson correlation of life events and number of daily stressors from the previous day ($r=0.02$, $p=0.72$) indicated that these are different types of stressors.

Results from the main effect model (Table 2, Model 1) showed that neither the number of stressors from the previous day nor the number of negative life events in the previous period was a significant predictor of maternal awakening cortisol level. However, there was a significant interaction effect of within-person number of daily stressors and between-person number of negative life events for awakening cortisol level the next day, suggesting that the effects of daily stressors on awakening cortisol level vary with exposure to negative life events (Table 2, Model 2 and Figure 1). To explore the interaction effect, the slopes of daily stressors on the awakening cortisol level the next day were estimated at different levels of negative life event. Results showed that for mothers who experienced no negative life events, there was a positive association between the number of daily stressors-previous day and awakening cortisol level (stressor slope estimated at zero negative life events: $b = 0.097$, $SE = 0.048$, $p < 0.05$). In contrast, there was a negative association at a trend level towards significance between the number of daily stressors-previous day and awakening cortisol level for mothers who experienced a greater number of negative life events (stressor slope estimated at four negative life events: $b = -0.122$, $SE = 0.065$, $p = 0.06$). These results are consistent with our hypotheses.

Severity of Daily Stressors, Number of Negative Life Events, and Cortisol

Next, we explored the effects of stressor severity from the previous day and number of negative life events previously experienced on maternal cortisol level at awakening for days when respondents reported at least one daily stressor. The correlation of life events and stressor severity from the previous day ($r=0.09$, $p=0.19$) indicated the lack of overlap between the two. Results from the main effect model revealed that neither stressor severity from the previous day nor negative life events in the previous period was a significant predictor of maternal cortisol level at awakening (Table 3, Model 1).

We then examined how appraisal of the within-person stressor severity from the previous day interacted with number of negative life events in predicting awakening cortisol level. Results showed a significant interaction effect of within-person stressor severity from the previous day and number of negative life events previously experienced for awakening cortisol level (Table 3, Model 2 and Figure 2). We also examined how the association between stressor severity-previous day and awakening cortisol level varies with previous

exposure to life events by estimating the simple slopes of stressor severity on awakening cortisol at different levels of negative life events. Results showed that there was no significant association between the stressor severity-previous day and awakening cortisol level for mothers who experienced no negative life events (severity slope estimated at zero negative life events: $b = 0.032$, $SE = 0.022$, $p > 0.10$). In contrast, for mothers who experienced a greater number of negative life events in the previous period, there was a significant negative association between stressor severity-previous day and awakening cortisol level (severity slope estimated at four negative life events: $b = -0.068$, $SE = 0.026$, $p < 0.01$). Again, these patterns are consistent with our hypotheses.

Lastly, we examined the three-way interaction effect of negative life events, number of daily stressors-previous day, and stressor severity-previous day on awakening cortisol level. However, the three-way interaction effect was not significant.

Discussion

This study took a biopsychosocial approach to the study of how parenting a child with a lifelong disability affects the physiological functioning of midlife and older parents. It adds to recent findings that have shown that the stress of parenting a son or daughter with developmental disabilities is more likely to result in chronic state of low hormone release (Seltzer et al., 2010). These previous studies focused on stressors directly related to the symptoms (e.g., behavior problems) of the grown child with developmental disabilities. Less attention has been directed towards the impact of “normative” and everyday stressors on physiological functioning. The current study extends prior conclusions by investigating the extended effect of negative life events and daily stressors on the awakening cortisol level found the next morning in mothers of individuals with ASD.

Findings from this study resonate with the cumulative advantage/disadvantage framework and the stress proliferation literature (see O'Rand, 2009 for a review) by highlighting the importance of historical context to later events and conditions, as related to the pathways of health and well-being. In this study, the physiological toll on maternal caregivers was evident only when both the effects of negative life events experienced in a previous period and daily stressors yesterday were considered together. Among mothers who did not experience any negative life events in the previous period, those exposed to daily stressors responded with increased level of cortisol on the following morning, consistent with typical cortisol reactions to acute stress (e.g., Dickerson & Kemeny, 2004). At a trend level towards significance, we observed a flatter cortisol level in mothers who were exposed to daily stressors provided that they also experienced at least four negative life events in the previous period. In this study, the severity of the stressor was less of an influence on the next day's awakening cortisol level for mothers who did not experience any negative life events in the previous period than for mothers who reported a greater number of negative life events. Together, the results showed that daily stress has differential implications for physiological functioning, depending on personal contextual factors (e.g., prior experience of negative life events).

The observed diminished cortisol level in this study is in line with past findings that showed a pattern of blunted or flattening cortisol response in individuals with PTSD (Yehuda, 2000) and those with stress-related disorders (e.g., burnout, fatigue; Heim et al., 2000; Neeck et al., 1990). Most importantly, the low cortisol level contributes to the growing number of studies demonstrating that blunted or flattening cortisol response appears to be a distinct characteristic of parents of adolescents and adults with DD (Seltzer et al., 2009; Seltzer et al., 2010) across different types of stressors (e.g., general vs. child specific stressors). As elucidated by Fries and colleagues (2005), one pathway in which blunted or flattening

cortisol response develops is from exposure to prolonged periods of stress as well as from the body's difficulty to self-adjusting. In our study, midlife mothers of grown children with ASD who experienced high levels of negative life events may not have the resources to handle the severe stress in their everyday lives. In this challenging and taxing context, daily stressors may represent the proverbial "straw that broke the camel's back".

One implication of our findings is the pressing need for services to support midlife and aging mothers of individuals with ASD. Currently, much of the services and supports are targeted to families of children with ASD, and less has been directed towards parents of adults with ASD. More services are needed to help these midlife and older mothers improve their coping strategies to better handle the complex, multifaceted demands that go beyond their son or daughter's ASD symptoms. Additionally, appropriate intervention is needed to help reduce distress in families raising adult children with disabilities. Much of the current autism intervention research is aimed at parents of young children and early adolescents with ASD, the children themselves, or a combination (e.g., Keen, Couzens, Muspratt, & Rodger, 2010; Landa, Holman, O'Neill, & Stuart, 2011; Strauss et al., 2012). It is important, therefore, that researchers develop empirically based interventions to help midlife and aging parents as they navigate the challenges, as well as the opportunities, associated with their child's transition into adulthood and midlife.

A study limitation is that we did not have a comparison group of mothers with typically developing children. Therefore, we cannot rule out whether the observed effects are specific to caregivers of adolescents and adults with ASD or more general to the population. Another limitation is the time lapse between the assessments of negative life events and daily stressors. Although we controlled for the length of time between the assessments of life events and daily stressors, we cannot rule out whether additional negative life events occurred between the two time points. While the time frame between the two measures is imperfect, the Life Events Checklist offered the opportunity to examine how chronic stressors affect the relation of daily stressors to physiological functioning. We also did not have information on the duration or timing of the reported negative life events (Wheaton, 1990). This study solely focused on mothers who resided with their adolescent and adult children, and did not include mothers of adults in other types of living arrangements. Prior literature has shown that the stress of caring for an adult child with a developmental disability typically decreases after the adult child moves out of the home (Krauss, Seltzer, & Jacobson, 2005). It is possible that other living arrangements would decrease stressor exposure for the maternal caregivers. We focused on midlife and aging mothers of adolescents and adults with ASD. Now that a pattern of blunted or flattening cortisol response is well established for this population by this and other research, it would be important to evaluate the physiological functioning of both younger and older mothers of children with ASD and other types of developmental disabilities to determine the life course onset and development of atypical cortisol responses to daily and global stress, and its effects on aging. Furthermore, it would be worthwhile for future studies to examine whether protective factors, such as availability and effectiveness of support systems, may help to buffer the wear-and-tear toll on the neuroendocrine axis of these caregivers.

In spite of some limitations, our study has a number of important strengths. The daily diary approach provides a less biased account of well-being and reactions without decay of recollection over time (Nisbett & Wilson, 1977). The daily diary methodology also enabled us to more accurately capture the temporal order effects of daily stressors on the next day's cortisol activity. Instead of bringing participants into a controlled laboratory setting where they provide saliva samples in response to challenge tasks (e.g., Dickerson & Kemeny, 2004), participants provided saliva samples in their everyday settings. By utilizing a naturalistic field approach, we hoped to gain better insights into the stress-responsive

physiology system of mothers with respect to naturally occurring stressors both acutely and over time.

In conclusion, this study adds to a growing literature examining cortisol responses in midlife and older mothers of adolescents and adults with ASD. Collectively, the findings suggest that the wear-and-tear toll on the neuroendocrine axis is comparable to that of job strains (e.g., Steptoe et al., 1998) and illnesses with chronic symptoms such as fibromyalgia (e.g., Riva, Mork, Westgaard, Rø, & Lundberg, 2010). Further, in our sample of middle-aged and older maternal caregivers of adolescents and adult children with ASD, the impact of severe daily stressors on awakening cortisol level is only evident in the context of negative life events.

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Figure 1.
Log awakening cortisol level by number of daily stressors (previous day) and number of negative life events.

Figure 2.
Log awakening cortisol level by severity of daily stressors (previous day) and number of negative life events.

Table 1

Descriptive Statistics of Life Events, Stressors, and Cortisol

	<i>M</i>	<i>SD</i>
Number of negative life events	1.5	1.2
Number of daily stressors-previous day ^a	1.3	1.2
Severity of stressors-previous day ^a	5.4	3.3
Log awakening cortisol level ^a	2.4	0.5

^aMean value reflects average taken across study days.

Table 2

Multilevel Model of Daily Number of Stressors (Previous Day) and Number of Negative Life Events Predicting Log Awakening Cortisol Level

	Model 1	Model 2
<i>Fixed Effects</i>		
Intercept	2.473 (0.070) ***	2.473 (0.070) ***
Age	0.005 (0.005)	0.005 (0.005)
Education	-0.069 (0.056)	-0.069 (0.056)
Taking at least one medication (yes=1)	-0.101 (0.089)	-0.102 (0.088)
Months between times 4 and 5	-0.022 (0.011) ^t	-0.022 (0.011) ^t
Behavior problems	-0.002 (0.005)	-0.002 (0.005)
Number of negative life events	-0.031 (0.035)	-0.031 (0.035)
Awakening collection time (BP)	0.027 (0.046)	0.027 (0.046)
Awakening collection time (WP)	0.002 (0.031)	0.004 (0.031)
Number of daily stressors-previous day (BP)	-0.059 (0.052)	-0.058 (0.052)
Number of daily stressors-previous day (WP)	0.011 (0.031)	0.013 (0.031)
Negative life events × daily stressors-previous day (WP)		-0.055 (0.023) [*]
<i>Variance Components</i>		
Between-person intercept (level 2)	0.082 *** (d.f.=73)	0.083 *** (d.f.=73)
Within-person (level 1)	0.173	0.168

Note. BP=between person; WP=within person.

** $p < .01$

^t $p < .10$

* $p < .05$

*** $p < .001$.

Table 3

Multilevel Model of Severity of Daily Stressors (Previous Day) and Number of Negative Life Events Predicting Log Awakening Cortisol Level

	Model 1	Model 2
<i>Fixed Effects</i>		
Intercept	2.509 (0.083) ***	2.509 (0.082) ***
Age	0.005 (0.006)	0.005 (0.006)
Education	-0.114 (0.067) ^t	-0.113 (0.067) ^t
Taking at least one medication (yes=1)	-0.133 (0.102)	-0.132 (0.102)
Months between times 4 and 5	-0.024 (0.013) ^t	-0.024 (0.013) ^t
Behavior problems	-0.006 (0.005)	-0.006 (0.005)
Number of negative life events	-0.038 (0.040)	-0.038 (0.040)
Awakening collection time (BP)	0.039 (0.053)	0.040 (0.053)
Awakening collection time (WP)	0.041 (0.040)	0.050 (0.039)
Severity of daily stressors-previous day (BP)	0.002 (0.019)	0.002 (0.019)
Severity of daily stressors-previous day (WP)	-0.012 (0.013)	-0.006 (0.013)
Life events × daily stressors severity-previous day (WP)		-0.025 (0.010) [*]
<i>Variance Components</i>		
Between-person intercept (level 2)	0.091 *** (d.f.=71)	0.094 *** (d.f.=71)
Within-person (level 1)	0.175 ***	0.167 ***

Note. BP=between person; WP=within person.

** $p < .01$

^t $p < .10$

* $p < .05$

*** $p < .001$.