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Salivary cortisol and immunoglobulin A: Responses to stress as predictors of health complaints reported by caregivers of offspring with autistic spectrum disorder

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ABSTRACT

In the caregiving model of chronic stress, few studies have been conducted with young middle-aged samples and no data exists about acute stress response in this population. To extend knowledge in this issue, health complaints and psychological, endocrine, and immunological responses to stress have been assessed in a cross-sectional sample of 41 parents of offspring with autistic spectrum disorder (ASD) in comparison with 37 non-caregiver parents. Salivary cortisol and immunoglobulin A (IgA) levels were measured before, during, and after a mental psychosocial stressor, while mood and state anxiety were evaluated before and after the stress. Health complaints, personality traits, socio-economic status, and characteristics of the care recipient were assessed. Caregivers reported more health complaints showing buffered cortisol and IgA responses and greater increases in fatigue to acute stress than the controls. In terms of predictive power of health complaints, IgA levels, care status, and severity of the care recipient are especially relevant for caregivers. Results strongly suggest a dysregulation in the immune and hormonal stress-induced responses in middle-aged caregivers, with immune component and care characteristics as the main modulators of health complaints. A deficit in the adaptive capability of stress response is plausible in this population, emphasizing the need to consider family approaches when planning protocols for assistance to ASD patients.

Introduction

Caring for a family member who suffers a long-term pathology can be a challenge, which may be experienced as a powerful and persistent stressful situation. In these cases, the demands of the situation overwhelm the individual resources, mainly due to the need for continuous adaptation to changes for which the caregiver may not feel prepared, and this leads to negative health consequences (Chang et al., 2010). Psychologically, some caregivers extract positive feelings by developing their role as a process of resilience (Harmell et al., 2011), but feelings of unpleasantness, stress, physical exhaustion, and personal failure are often reported (Bella et al., 2011). In terms of health, caregiving has been associated with increased risk of mortality and health complaints (Pinquart and Sörensen, 2003; Rabinowitz et al., 2011).

From this viewpoint, informal caregiving can be a reliable and useful model for understanding how the allostatic load of chronic stress can lead to pernicious health consequences (Gallagher et al., 2009). According to the allostatic load model, coping with the challenges of daily life requires an adaptation of neuroendocrine, immunological, and autonomic systems, and there is a cost for the organism. If the adaptation demands are maintained, cumulative wear can result in damaging health consequences. Among other factors, hypothalamic–pituitary–adrenal (HPA) imbalances can mediate these health outcomes (McEwen, 2003). As far as glucocorticoids mediate immunity, chronic disturbances in the HPA axis have also been related to autoimmunity and immune-suppression and a down-regulation in salivary IgA levels, among other immune parameters (Phillips et al., 2006). However, the impact of these disturbances on quality of life and health complaints is heterogeneous, and the specific underlying mechanisms of the neuroendocrine immune network that may explain the stress-related disturbances frequently remain unclear.

Considering the available data regarding caregivers, different factors may obstruct an understanding of the results. The studies of caregivers frequently use mature and elderly caregivers of dementia patients. These caregivers may themselves suffer a compromised immune system and poor health, and these factors may overlap with potential care effects. Younger caregivers provide a more suitable model for the study of chronic stress in caregiving by minimizing the age-related worsening of health and immunosenescence. In addition, caregivers of dementia patients are usually married individuals who care for long-term partners with neurodegenerative pathologies. Attachment feelings have been proposed as a modulator of stress and burden for caregivers (Daire, 2002; Kim and Carver, 2007), and so the effects of care between partners and between parents and offspring may also be relevant. Thus, the results that focused on care-giving

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effects may be slanted by these conditions, and further research is needed with younger subjects and different attachments between the caregiver and care recipient. This would enable a better understanding of the care-giver control model. With regards to the assessed variables, the results are commonly reported separately as endocrine and immunological variables with different samples, thus obstructing the extraction of integrative explanations focused on the neuro-endocrine-immunological network.

Caregiving of offspring is a usual role for parents, but the meaning is different for parents of children with functional limitations, long term dependence, and behavioral problems. The demands of the patients negatively affect the social support and dynamic of the family with consequences on psychological and physical health (Raina et al., 2005; Lach et al., 2009). Moreover, in the case of parents of children with disabilities, caregivers are older than the care recipient. As these offspring are chronically dependent, parents tend to worry intensely about the future of their children when they are unable to continue to care for them. This fact, together with the daily episodes of acute stress that they experience, makes this population of caregivers especially useful as a chronic model of stress.

Moreover, the fact that caregiving may be a reliable model of chronic stress leads us to consider measurements such as daily profiles in the home setting, laboratory settings, or procedures with stimulation under more controlled conditions that could add useful data. In studies focused on the daily profiles of HPA activity in caregivers, elevated daytime cortisol levels during the entire day together with greater emotional distress have been reported in elderly caregivers of dementia patients (Vedhara et al., 1999). However, low levels of cortisol together with a lack of variation in anxiety and depression have been found in middle-aged caregivers of multiple sclerosis patients (Vedhara et al., 2002). In younger caregivers, elevated daytime cortisol levels, likely associated with behavioral problems of the care recipient, have been reported (Seltzer et al., 2009, 2010); however, low levels of cortisol have been found in caregivers of children with cerebral palsy (Bella et al., 2011). An interesting aspect of the circadian profile, the cortisol awakening response (CAR) has been reported as a useful index of HPA activity, as a blunted CAR has been correlated with chronic stress (Pruessner et al., 1997). Although the results are far from homogeneous (Lovell et al., in 2012), a blunted CAR has also been observed in the caregivers of patients suffering different pathologies (Gonzalez-Bono et al., 2011; Seltzer et al., 2009), which may be mediated by the symptoms of the care recipient (de Vugt et al., 2005). More recently, Bella et al. (2011) also reported a lower CAR in caregivers along with a worse health status and a higher burden in caregivers of children with cerebral palsy compared with controls. In caregivers of offspring with autistic spectrum disorder (ASD), no significant differences in the cortisol profile and the CAR have been noticed in caregivers of children with autism and attention deficit hyperactivity disorder, despite the evident effect on health status and an elevated concentration of proinflammatory biomarkers (Lovell et al., 2012).

With regards to immunological aspects, caregiving in non-stressful settings is associated with a reduction of immune competence such as a suppression of lymphocyte proliferation, a lower percentage of NK cell cytotoxicity, lower interleukin-2 (IL-2) production, lower immunoglobulin A secretion rates, and blunted response to vaccines (Cacioppo et al., 1998; Gallagher et al., 2008; Segerstrom et al., 2008; Vitaliano et al., 2003). In dementia caregivers, the higher the gravity of patient symptoms, the lower the caregiver IgA levels in daily life (Neri et al., 2007); these results suggest that symptoms or/and autonomy of the patient can be relevant in immuno-competence (Segerstrom et al., 2008). In younger parents, the caregivers of offspring born preterm and developmentally disabled show a blunted immunological efficiency, which in some cases was modulated by the time of caring, the age of the patient, and the behavior of the child (Gennaro et al., 1997; Pariante et al., 1997).

Although hormonal daily profiles provide useful information when examining the effects of caregiving with a high level of ecological validity, other approaches could also be valuable when exploring the interaction between acute and chronic stress in caregivers. This population has to cope with repeatedly acute stressors in their daily lives that are related and unrelated to caregiving demands. This long term situation not only could alter the resting levels of endocrine and immune systems, but may also affect the capability of response to the next acute challenge (Chrousos, 1998) and this, in turn, may modulate health. In fact, increases in cytokine levels have been described in children with high chronic family stress after experiencing an acute event when compared with times when no such event was experienced (Marin et al., 2009). However, studies focused on the interactions between acute and chronic stress in caregivers that employ a standardized stressor in a laboratory are scarce. Data produced in a laboratory approach enables a higher degree of control of variables than in studies performed outside of the laboratory; and so may contribute to a greater understanding of the variables involved in acute-chronic stress interactions in caregivers.

To our knowledge, only two studies have been conducted with brief, acute psychological stressors in caregivers in a laboratory setting, both with caregivers of dementia patients. First, the study by Epel et al. (2010) reported on a group of 22 elderly women caregivers and twenty-two women as controls who were exposed to 20 min of stimuli composed of a speech and an arithmetical task. The results show no differences between the groups despite the fact that caregivers consistently show lower cortisol levels than controls. The second study was conducted by Cacioppo et al. (2000) with a sample of 27 elderly female spouses of progressive dementia patients and 37 women who were non-caregivers. The participants performed a math and speech stressor while immunological, neuroendocrine, and psychological variables were assessed. After the stress, caregivers reported higher scores of negative effects and showed increases in plasma ACTH and a reduced interleukin-1β response compared with the controls (Cacioppo et al., 1998). Other chronically stressed samples, such as depressive patients, have been used to examine the endocrine stress-induced response to psychological acute stressors in laboratory settings, but these data were not conclusive. In this population, suppressed responses of cortisol to acute stress were described (Bagley et al., 2011; McGirr et al., 2010).

With this rationale, the present study examines the effect of an acute episode of stress on psychobiological responses in a long term caregiver population in a laboratory setting. For this, individuals were exposed to a standardized psychosocial stressor. To our knowledge, the present study is a pioneer in examining the psychological, immune, and endocrine responses to acute stress in a sample of caregivers of patients with ASD. The caregiving of offspring with long-term disabilities is especially painful. These patients usually suffer, among other aspects, social difficulties and isolation, limited success in their lives and, in most cases, continuous dependency on their parents (Seltzer et al., 2009). The caregivers witness the fact that their offspring cannot follow the development of other children inside and outside of the family. In addition, these caregivers worry about the future of their offspring when the caregivers will be unable to continue caring for them. Specifically, autism is a complex developmental disability with impairment in communication and reciprocal social interaction and restricted, repetitive, and stereotypical behavior and interests. The impact of this situation on family dynamics can have psychobiological consequences similar to psychological burden and neuroendocrine disturbances (Orsmond and Seltzer, 2007; Seltzer et al., 2009). Several studies have focused on the psychological aspects of ASD, with parents of ASD children reporting feelings of being removed from a common way of life, feeling isolated within the family (Woodgate et al., 2008), having little free time, experiencing greater daily stress (Smith et al., 2010), depressive symptoms, and elevated stress (Abbeduto et al., 2004; Bailey et al., 2007; Singer, 2006). Moreover, these family dynamics can be prolonged (Barker et al., 2011).