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Long-term effects of early parental loss due to divorce on the HPA axis

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Abstract

We investigated the long-term effects of divorce and early separation from one parent on HPA axis reactivity, in young adults without psychopathology. Participants were 44 young subjects, 22 whose parents divorced before they reached age 10, and 22 controls. Psychiatric symptomatology was measured with the Brief Symptom Inventory (BSI), family perceived stress by the Dyadic Adjustment Scale (DAS), and bonding by the Parental Bonding Instrument (PBI). Assessment of HPA axis function included baseline morning cortisol and ACTH and cortisol response to a CRH stimulation test.

No baseline or stimulated group differences were observed for ACTH. Cortisol levels were consistently but insignificantly lower in the divorce group throughout the CRH stimulation reaching statistical significance only at 5 min ($p<0.03$). Group by time effect reached a trend level ($p<0.06$). A correlation was found between psychiatric symptomatology and PBI scores; however, both parameters did not correlate with HPA axis activity. A significant correlation was found between DAS scores and ACTH. A regression model revealed a contributing effect for both family stress and child–parent bonding to stimulated ACTH levels. These preliminary findings suggest that even in the absence of adult psychopathology, a history of childhood separation from one parent due to divorce may lead to detectable, albeit mild, long-term alterations in HPA axis activity. Furthermore, they suggest that level of stress at home and parental bonding are important determinants of this effect. It is likely that divorce has significant and sustained effects on children's HPA axis only in the context of a traumatic separation.

Keywords: Cortisol; Corticotropin releasing hormone; Divorce; HPA axis; Separation; Psychopathology

Introduction

The significance of early negative life events and especially the loss of a significant figure as possible etiological factors in the development of subsequent adult psychopathology has been subject of much speculation and theory for years (Bowlby, 1963). In many studies, an association was reported between EPL due to death (Perris et al., 1986), or other reasons (Dennehy, 1966; Faravelli et al., 1986; Tennant et al., 1982) and the development of affective disorders. Early work suggested a higher incidence of parental death in the history of depressed individuals while later work on this issue was less conclusive (Lloyd, 1980) yet suggested that the loss of the mother either but death or separation may be more significant then the loss of the father (Brown et al., 1997; Kendler et al., 1992; Roy, 1985). These studies are also inconclusive about the significance of the age of loss. Degree of coping with EPL is an important moderator of future psychopathology as demonstrated by Breier et al. (1988) who reported that psychological suffering and the success or lack of coping with the loss of a parent was predictive of future psychopathology.

A large case control study found the incidence of EPL before the age of 17 due to death or separation to be almost 4-fold greater in hospitalized patients suffering from major depression compared to a control group. Moreover, this difference increased to 11-fold when EPL occurred at an age of under 9, and divorce as a cause for separation was found to be more significant than separation due to death of a parent (Agid et al., 1999). The number of studies looking at divorce as the cause for child–parent separation is small. In cases of divorce, compounded onto the need to cope with a "loss" of a parent, research has shown

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that divorce and life in a single parent family make the child more prone to exposure to stressful life events (Amato and Keith, 1991; Hetherington et al., 1985) and that inadequate parenthood may increase the incidence of depressive illness in adulthood (Parker, 1983). A study in Israeli adolescents whose parents have divorced demonstrated higher levels of psychopathology, and a correlation was found between the attachment pattern with their parents and psychiatric symptoms (Canetti et al., 2000). In fact, there is a growing body of literature showing that there may be a considerable difference between long-term effects of bereavement and divorce, and that the impact of divorce is potentially more complicated to adequately assess due to a multitude of potential environmental moderating factors involved in the process (Luecken and Appelhans, 2005; Mack, 2001).

Abnormal function of the Hypothalamic–Pituitary–Adrenal axis (HPA axis) has been well documented in a number of major psychiatric syndromes such as major depression and posttraumatic stress disorder. Hypercortisolemia, a condition that is associated with stress (Kalin and Takahashi, 1988) has been reported to induce glucocorticoid receptor changes and a reduction in hippocampus volume in animal models (Herman et al., 1995; Lopez et al., 1998; Sapolsky, 1996) and in humans (Heim and Nemeroff, 1999; Sheline et al., 1996). It has been suggested that early negative life events may cause hypercortisolemia, which in turn may cause damage to the developing brain during critical periods of development (Gunnar, 1998). In babies, there is a period of decreased reactivity of the HPA axis (Gunnar et al., 1996; Suchecki et al., 1993), which has been found to be dependent on the quality of the baby-parent relationship (Nachmias et al., 1996). Furthermore, in a number of animal models, states of maternal deprivation caused long-term changes of the HPA axis demonstrating a pattern of hyperstimulation (Ladd et al., 1996; Plotsky and Meaney, 1993). Findings in non-human primates exposed to deprivation have not been consistent, with some showing increased (Coplan et al., 1996; Fahlke et al., 2000) and others showing decreased (Clarke, 1993) basal and stress-induced cortisol levels, or decreased morning cortisol levels in monkeys exposed to maternal separation (Dettling et al., 2002). In humans, while a number of studies have demonstrated long-term effects of childhood maltreatment and sexual abuse on the HPA axis, mainly showing increased stress reactivity (De Bellis et al., 1994; Heim et al., 2000, 2001), only a few studies have focused on the effects of parental loss or separation on the HPA axis. In children, studies have been contradictory, some reporting increased morning cortisol in adopted children (Gunnar et al., 2001) and elevated diurnal cortisol secretion in institutionalized children (Kaufman, 1991), and others showing lower morning cortisol in socially deprived children (Carlson and Earls, 1997). In adults with EPL due to parental death, Luecken reported that increased cortisol responses during a psychological stressor were moderated by the quality of the parent-child relationship (Luecken, 2000; Luecken and Appelhans, 2006). Furthermore, whereas, Breier et al. (1988) have reported elevated afternoon cortisol plasma levels only in adults with EPL who had a history of psychopathology, recently, elevated salivary cortisol levels throughout the day but especially in the morning, were reported in adult men who experienced parental death, regardless of psychopathology (Nicolson, 2004). However, a recent study in healthy young adults with EPL (death or separation), found decreased morning salivary cortisol levels (Meinlschmidt and Heim, 2005), while another study did not find a differential cortisol response in adults exposed to various childhood traumatic events (Otte et al., 2005). In the case of divorce as an early life adverse event, there is no literature regarding the long-term effects of this stressor on the HPA axis, though it has been proposed that HPA axis dysregulations may play an important role in the development of mood and behavioral maladjustment to the consequences of divorce (Troxel and Matthews, 2004).

The design of the current study was based on the hypothesis that if EPL indeed causes permanent alterations in the HPA axis, these alterations will precede and may mediate subsequent psychopathology. If this hypothesis is correct, such alterations in the HPA axis are expected to be present even in the absence of psychiatric symptoms (in contrast to the previously described Breier study). To test this hypothesis we studied the long-term effects of childhood parental separation due to divorce on the HPA axis, using the Corticotropin Releasing Hormone (CRH) test, in a young adult population without DSM-IV axis I psychopathology, whose parents divorced (with one of them leaving home) before the subject turned 10 years of age. These criteria were selected to separate the effect of early stress due to divorce from that of current mental condition on the HPA axis. Our main hypotheses were: (a) divorce in early childhood would have long-term effects on the HPA axis in healthy young adults in the form of lower or normal basal cortisol levels, but an increased HPA axis response to CRH stimulation, (b) the effect of divorce on HPA axis response to CRH stimulation will be moderated by level of stress at home prior to the divorce and by the quality of bonding between the child and each one of the parents during childhood.

Materials and methods

Subjects

The separation group comprised of 22 healthy subjects, aged 21–25 whose parents had divorced (with one parent leaving home permanently) before the subject had turned 10 (mean age at divorce=4.6±2.9), and 22 comparison subjects matched on age and sex, who grew up with two married parents at least until age 18. All subjects were recruited by advertisements posted at two university campuses. Interested subjects were screened by phone to exclude those with significant physical or mental illness including brain trauma and alcohol or drug abuse. Also excluded were night shift workers, those whose families have immigrated to Israel before the age of 10, and those who had a deceased parent. The comparison group consisted of volunteers matched for age and sex who grew up with two married parents at least until age 18. All subjects gave written informed consent after they received a detailed explanation regarding the study, which was approved by the hospital's IRB. All participants went through a structured clinical diagnostic interview for DSM-IV (SCID-Hebrew version) (Shalev et al., 1994) to exclude past and present axis I diagnoses. Participants were interviewed regarding their personal demographic details, past traumatic life events (by the Trauma History Questionnaire), personal and family physical and mental disorders, and menstrual history and contraception methods for the women. Exclusion criteria were any past or present axis I disorder, serious physical illness, a past trauma such as a physical