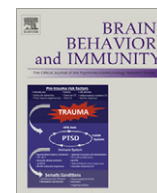




Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Neutrophil function and cortisol:DHEAS ratio in bereaved older adults

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ARTICLE INFO

Article history:

Received 6 January 2011
 Received in revised form 10 March 2011
 Accepted 10 March 2011
 Available online xxxx

Keywords:

Bereavement
 Neutrophil
 Phagocytosis
 Superoxide production

ABSTRACT

Bereavement is a common life event for older adults and is associated with increased risk of morbidity and mortality, though the underlying reasons for this link are poorly understood. Although physical and emotional stressors and ageing are known to suppress immunity, few studies have explored the impact of bereavement upon immunity in the older population. We therefore hypothesised that the emotional stress of bereavement would suppress immune function, specifically neutrophil bactericidal activity, in older adults. A between-subjects design was used to examine the effect of recent bereavement (<2 months) on neutrophil function in elders. Participants were 24 bereaved and 24 age- and sex-matched non-bereaved controls all aged 65+ years. Neutrophil phagocytosis of *Escherichia coli* (*E. coli*) and stimulated superoxide production were assessed. Cortisol and dehydroepiandrosterone-sulphate (DHEAS) levels were determined in serum to assess potential mechanisms. Depressive and anxiety symptoms were measured by questionnaire. Neutrophil superoxide production was significantly reduced among the bereaved when challenged with *E. coli* ($p = 0.05$), or phorbol 12-myristate 13-acetate ($p = 0.009$). Further, the bereaved group had a significantly higher cortisol:DHEAS ratio compared to controls ($p = 0.03$). There was no difference in neutrophil phagocytosis between the two groups. The psychological questionnaire results showed that the bereaved had significantly greater depressive and anxiety symptoms than the non-bereaved. The emotional stress of bereavement is associated with suppressed neutrophil superoxide production and with a raised cortisol:DHEAS ratio. The stress of bereavement exaggerates the age-related decline in HPA axis and combines with immune ageing to further suppress immune function, which may help to explain increased risk of infection in bereaved older adults.

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1. Introduction

Bereavement is considered to be one of the most stressful life events, becoming more frequent as we age, yet the impact upon health is under researched. This is due in large part to the difficulty of accessing this vulnerable group. What is clear is that bereavement, particularly in older adults, is associated with higher risk of morbidity and mortality (Biondi and Picardi, 1996; Clayton, 1990; Manor and Eisenbach, 2003; Stroebe et al., 2007). To try to understand the basis of this association a small number of studies have explored the impact of bereavement upon immunity (Calabrese et al., 1987; Gerra et al., 2003; Goodkin et al., 1996). Bereaved women showed reduced Natural Killer cell activity and increased plasma cortisol levels compared to non-bereaved controls (Irwin et al., 1987). Bereaved parents showed significantly decreased numbers of T-regulatory cells, and significantly increased T-helper cells compared to their matched controls and this effect persisted over 8 months (Spratt and Denney, 1991). More recently, it was found that HIV patients who experienced maladaptive grief

following bereavement showed more rapid losses of CD4 T-cells over time, even when statistically adjusting for age, health status, and use of antiretroviral medications (Goforth et al., 2009).

However, there are very few studies that have examined the impact of bereavement upon immunity in older adults despite the fact that the chances of experiencing a significant bereavement increase with age. This is an important issue as it is now well established that ageing itself results in a decline in immune status, termed immunosenescence (Shaw et al., 2010), with significant consequences for susceptibility to infection. These age-related changes include decreased neutrophil function, with older adults showing a reduction in neutrophil phagocytic ability and superoxide production (Butcher et al., 2001; Hajishengallis, 2010; Lord et al., 2001; Wessels et al., 2010). As stress also suppresses immune function (Segerstrom and Miller, 2004), we propose that stress and ageing combined will have an additive and deleterious effect upon immunity, with significant health consequences for the bereaved older adult.

In support of this notion, we have previously shown that older adults who have suffered bereavement in the past 12 months had a poorer antibody response to the annual influenza vaccination in comparison to non-bereaved older adults (Phillips et al., 2006).

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