Psychoneuroendocrinology (2013) 38, 2737—2745

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Social isolation and diurnal cortisol patterns in an ageing cohort☆

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Received 1 February 2013; received in revised form 1 July 2013; accepted 10 July 2013

KEYWORDS
NSHD;
Psychosocial;
HPA axis;
Bereavement;
Social isolation

Summary
Background: Social isolation may operate as a psychosocial stressor which disrupts functioning of the hypothalamic—pituitary—adrenocortical axis.
Methods: Using data from the MRC National Survey of Health and Development, we tested whether living alone, not being married and social network size were associated with diurnal cortisol patterns at 60—64 years. We hypothesised that recent onset compared with long-term isolation would be more strongly associated with cortisol awakening response, cortisol decline over the day and evening cortisol. Models were adjusted for sex, smoking, body mass index, alcohol intake, psychological distress and financial difficulties.
Results: Those widowed within the last three years had a 36% (95%CI 6%, 73%) higher night time cortisol than those who were currently married. Those newly living alone also had a higher night time cortisol and flatter diurnal slope than those living with others.
Conclusion: Independently of multiple behavioural and psychosocial correlates, recent onset of social isolation is related to diurnal cortisol patterns that increase the risk of morbidity and mortality.

1. Introduction

Social isolation is associated with coronary heart disease mortality and morbidity (Lett et al., 2005; Ramsay et al., 2008; Holt-Lunstad et al., 2010; Udell et al., 2012). It has been proposed that social isolation may operate as a psychosocial stressor which affects coronary heart disease risk through disrupted functioning of the hypothalamic—pituitary—adrenocortical (HPA) axis (Cacioppo et al., 2002; Hackett et al., 2012). Activation of the HPA axis causes

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0306-4530/$ — see front matter
http://dx.doi.org/10.1016/j.psyneuen.2013.07.002

an increase in cortisol, which can induce physiological changes in response to the stressor. In healthy individuals cortisol is high on waking, peaks at around 30—45 min post-waking and then falls gradually to reach its lowest point at around midnight (Kumari et al., 2010a). However, repeated or chronic activation of the HPA axis is associated with negative health outcomes including coronary heart disease (Davey Smith et al., 2005; Kumari et al., 2011). Disrupted HPA-axis functioning may be indicated by a flatter than average slope between morning and night time, and a high night time cortisol level (Adam and Kumari, 2009). Both high and low morning cortisol and high or blunted cortisol awakening response (that is, the difference between the waking and peak cortisol) have been associated with poorer health (Adam and Kumari, 2009; Gardner et al., 2011, 2013). In large-scale epidemiological studies, diurnal cortisol has typically been measured in saliva samples as cortisol in saliva accurately reflects levels of free, biologically active cortisol in blood, often with the aim of examining its relationship to social environmental exposures, such as social isolation.

Social isolation may be measured objectively by its structural form (captured by various indicators including living alone, having a small network size and not being married) and as perceived isolation (typically captured by reported feelings of loneliness). Objective isolation is a risk factor for perceived isolation though correlations are moderate in size in older adults and the two forms of isolation appear to relate independently to physical health (Cornwell and Waite, 2009). Individuals may not feel isolated despite lacking structural social connections. Earlier studies provide some support for an association between objective social isolation and cortisol patterns. Concurrently, socially isolated study members of an occupational cohort study, that is having infrequent or no contact with friends and relatives or living alone, were found to have a higher cortisol awakening response (CAR), independently of perceived social isolation (Grant et al., 2009). Based on measurements collected over four days, female students who took part in a greater number of activities with others had a steeper decline in cortisol throughout the day (Stetler et al., 2004). A flatter slope was seen for women who were divorced or widowed compared with those currently married in a small study of cancer patients (Sephton et al., 2000). Others have failed to find an association between objective indicators of social isolation and cortisol response (Turner-Cobb et al., 2000; Lai et al., 2012). To date, although social isolation is more prevalent among older compared with younger people, its association with cortisol patterns has not been established in large, general population samples. In addition, studies have predominantly focused on concurrent social isolation whereas the timing of the onset of isolation may moderate its association with cortisol output. Meta-analysis demonstrated that morning cortisol was lower and daily cortisol output higher for chronically stressed compared with control groups but that the magnitude of these differences reduced with increasing time since stressor onset (Miller et al., 2007). Included studies were based on people who had experienced war, abuse, bereavement, job loss, caregiving and disaster though the impact of recent onset versus long term social isolation was not examined.

Cortisol patterns differ by sex (Kumari et al., 2010a) and a number of behavioural and psychosocial factors that may covary with social isolation including smoking (Kumari et al., 2010a), obesity (Kumari et al., 2010b), alcohol intake (Badrick et al., 2008), psychological distress (Miller et al., 2007) and socioeconomic disadvantage (Kumari et al., 2010c; Agbedia et al., 2011), which are important to take into account in any observational study. The current study addresses two questions: (i) is there a cross-sectional association between multiple indicators of social isolation and diurnal cortisol, and (ii) does time since onset of isolation moderate the association between isolation and cortisol? It extends existing literature by examining these associations in a large, general population sample of older people and by considering the role of recent versus longer-term social isolation. On the basis of previous studies of social isolation and of other indicators of psychosocial stress, we hypothesised that greater isolation would be associated with a blunted cortisol pattern. Since objective isolation may, to some extent, be a matter of individual choice and because individuals adapt psychologically to life events that may increase the risk of isolation including bereavement and divorce (Luhmann et al., 2012), we further hypothesised that recent onset isolation would be more strongly associated with a blunted cortisol pattern than long-term isolation.

2. Methods

The oldest British birth cohort, the MRC National Survey of Health and Development (NSHD), completed its 23rd follow-up between 2006 and 2011 when study members were aged 60—64 years (Kuh et al., 2011). The NSHD is based on a social class stratified sample of 5362 births of all singleton births that occurred within marriage in a week in March 1946 in England, Scotland and Wales. Study members are white Caucasian; recruitment to the study pre-dated major immigration into Britain. The previous main data collection was at 53 years. The 60—64 year data collection consisted of a postal questionnaire followed by clinical assessment by research nurses in one of six clinical research facilities across the UK or at home, during which consent for salivary cortisol sample collection was obtained. A total of 2229 out of 2856 (78%) eligible study members (those known to be alive and with a known address in England, Scotland or Wales) took part in a clinic ($n = 1690$) or home visit ($n = 539$). Those opting for a home visit were more likely to be obese, a lifelong smoker, with lower educational attainment, and occupying a lower socioeconomic position compared with those attending the clinic (Stafford et al., 2013). Invitations were not sent to those who had died ($n = 778$), who were living abroad ($n = 570$), had previously withdrawn from the study ($n = 594$) or had been lost to follow-up ($n = 564$). Ethical approval for the study was obtained from the Greater Manchester Local Research Ethics Committee and the Scotland A Research Ethics Committee. Written, informed consent was obtained from the study member for each component of data collection.

Study members were asked to provide three saliva samples in salivettes at 9—9.30 pm on the evening of the clinic or home visit and at usual waking time and waking +30 min the following day. They were trained in the protocol for cortisol collection by the research nurse and requested not to drink for 30 min before taking the sample and not to smoke, eat or