



A systematic review of the psychobiological burden of informal caregiving for patients with dementia: Focus on cognitive and biological markers of chronic stress



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ABSTRACT

As the physiological impact of chronic stress is difficult to study in humans, naturalistic stressors are invaluable sources of information in this area. This review systematically evaluates the research literature examining biomarkers of chronic stress, including neurocognition, in informal dementia caregivers.

We identified 151 papers for inclusion in the final review, including papers examining differences between caregivers and controls as well as interventions aimed at counteracting the biological burden of chronic caregiving stress.

Results indicate that cortisol was increased in caregivers in a majority of studies examining this biomarker. There was mixed evidence for differences in epinephrine, norepinephrine and other cardiovascular markers. There was a high level of heterogeneity in immune system measures. Caregivers performed more poorly on attention and executive functioning tests. There was mixed evidence for memory performance. Interventions to reduce stress improved cognition but had mixed effects on cortisol. Risk of bias was generally low to moderate. Given the rising need for family caregivers worldwide, the implications of these findings can no longer be neglected.

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1. Introduction

The role of an informal dementia caregiver (i.e. a person providing care to a person with dementia, who is not providing this care in a professional capacity) is a potential source of substantial psychosocial stress. Patients with dementia may depend increasingly upon informal caregivers, typically close family members, to help them with activities of daily living, as well as displaying challenging behaviours and facing safety issues. In addition to heightened stress, family dementia caregivers show increased levels of anxiety and depression (Baumgarten et al., 1994; Mahoney et al., 2005). Although many informal family caregivers display resilience in the face of their relatives' illness, there is a clear mental health risk within this group. The social impact of this care should not be underestimated; the worldwide economic cost of dementia has been estimated at US\$818 billion, and it is predicted that this figure will increase to \$2 trillion by 2030 (Prince et al., 2015). Within this context, family caregiving saves the exchequer spending on care provision. The results of research on the chronic stress of caring for people with dementia can be used to provide targeted interventions for attenuating the impact of stress in this group, and potentially in other groups exposed to chronic stressors.

Although there has been much research on the biological and psychological markers that accompany the acute stress response (Allen et al., 2014; Dickerson and Kemeny, 2004), it is unethical to experimentally expose humans to chronic stress. As a result, naturalistic chronic stressors such as dementia caregiving are a useful means for examining the impact of chronic stress on human physiology. A number of such models have been examined, such as unemployment (Dettenborn et al., 2010; Gallagher et al., 2016; Ockenfels et al., 1995), or the ongoing effects of childhood abuse (Carpenter et al., 2009; Penza et al., 2003). Compared to other forms of caregiving, caregiving for a family member with dementia may be a particularly stressful experience (Clipp and George, 1993; Kim and Schulz, 2008). Estimates of median survival time for dementia patients vary between 3.3 years and 11.7 years (Todd et al., 2013), and so dementia caregiving represents a chronic source of stress.

Biomarker research may provide us with a greater understanding of mechanisms through which psychological stress may impact upon long-term health outcomes. For instance, increases in blood pressure may act to increase the risk of cardiovascular illness (MacMahon et al., 1990) and compromised immune system functioning can impair resistance or response to infectious diseases such as influenza (Godbout and Glaser, 2006). Given that ageing and chronic stress can have similar effects on the brain (Prenderville et al., 2015), the impact of caregiving stress may be compounded where caregivers for elderly relatives are themselves senior citizens. However, this also raises the methodological caveat that the search for biomarkers of caregiver stress should take into account

the age of the caregiver, as well the nature of impairment and changes in caregiving intensity (Lovell and Wetherell, 2011).

The key aim of this paper is to describe the results of a systematic review of the literature examining the biological and psychological burden of the chronic stress of dementia caregiving. We also review research looking at interventions to reduce the impact of chronic stress in caregivers, where biomarkers are examined as an outcome. We appraise the research quality of relevant research and identify potential future directions for research in this area.

2. Methods

This systematic review was pre-registered at PROSPERO. ID: PROSPERO 2015:CRD42015020828. The date of registration was 28th May 2015. This is available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015020828.

2.1. Literature search

The databases Cinahl, PsycINFO, Pubmed, ScienceDirect, Scopus and Web of Knowledge were used as electronic search engines for the systematic review.

The search terms included were: “caregiver” AND “dementia” AND “stress” OR “allostatic load” OR “biomarkers” OR “biological marker” OR “cortisol” OR “cytokine” OR “heart rate” OR “gastrointestinal” OR “interleukin” OR “c-reactive protein” OR “catecholamines” OR “adrenaline” OR “noradrenaline” OR “epinephrine” OR “norepinephrine” OR “pH” OR “amylase” OR “vasopressin” OR “DHEA” OR “DHEA-S” OR “lymphocyte” OR “T-cell” OR “B-cell” OR “monocyte” OR “neutrophil” OR “basophil” OR “granulocyte” OR “macrophage” OR “nuclear factor kappa B” OR “immunoglobulin” OR “heart rate variability” OR “BDNF” OR “d-dimer” OR “tryptophan” OR “kynurenine” OR “blood pressure”.

2.2. Exclusion criteria

Studies were excluded if they were not written in English (and a translation was not available), if they did not report original research, if they did not employ a quantitative design, if they did not assess any biomarkers or if they did not assess informal caregivers (i.e. those caring in a non-professional capacity) for patients with dementia. Study review and selection was completed by two reviewers. See Fig. 1 for flowchart of study exclusion/inclusion.

2.3. Data extraction

Two reviewers extracted data on study design, control group, length of follow up, region and time period of study, outcome definitions, interventions, compliance with the intervention, data source, sample size, attrition rate, treatment of missing

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