Allostatic load and health: a crossed-lagged analysis in the English Longitudinal Study of Ageing (ELSA)

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Introduction

Identifying pathways to poor health and disability has been an intensive area of research in gerontology for example several models of the disablement process have been introduced (Verbrugge & Jette, 1994). Such studies are important because common if the early signs of later disability risks can be identified it may be easier to intervene and slow or halt progression to disability. Additionally, identification of such pathways may provide information relevant to earlier primary prevention. One candidate ‘marker’ of the early signs of bodily dysfunction is allostatic load (McEwen & Stellar, 1993).

Allostatic load has been conceptualised as multisystem physical dysregulation resulting from long-term exposure to stress. The pathway to poor health has been hypothesised to start with early signs in primary mediators, i.e. changes in stress hormones and anti-inflammatory cytokines. The activation of these primary mediators elevates further changes in the metabolic, cardiovascular and immune systems which thus represent secondary outcomes on the pathway from stress reactions to health. Finally, the allostasis-adaptation process may lead to tertiary outcomes: poor health, diseases, such as cardiovascular diseases and diabetes, and eventually death. Allostatic load is a summary way of capturing biomarker measures which may indicate a stage on this process. However, though these pathways have been suggested in the literature, it is not clear whether the association between allostatic load and health outcomes is a recursive one-way or a reciprocal association, or whether some health measures may predict allostatic load.

Very few studies have assessed pathways from allostatic load to poor health in a longitudinal setting. The few studies undertaken generally show that an increase in allostatic load is associated with higher levels of stress and poorer health outcomes (Karlamangla, Singer, & Seeman, 2006) and that the initial level of allostatic load is associated with a number of health outcomes (Goldman, Turra, Glei, Lin, & Weinstein, 2006; Gruenewald, Seeman, Karlamangla, & Sarkisian, 2009; Karlamangla, Singer, McEwen, Rowe, and Seeman, 2002b; Seeman, McEwen, Rowe, and Singer, 2001; Seeman, Singer, Rowe, Horwitz, and McEwen, 1997; Hu, Wagle, Goldman, Weinstein, & Seeman, 2007). However, these earlier studies generally have not tested reciprocal relationships, but treated allostatic load outright as a predictor measured only at baseline.

An effective method for detecting sequences of effects in longitudinal settings is to apply cross-lagged models. These models require the same set of variables repeatedly measured on two or more occasions. Because of the repeated measures for all variables of interest, modeling of the autoregressive stability of each measure over time can be undertaken and the cross-lagged associations between the measures can be estimated. A cross-lagged design makes it possible to investigate the reciprocal predictive relationships: whether the associations are stronger in one way only or whether they go both directions.

Research question

The questions we are concerned with is Does allostatic load predict self-rated health and limiting long-term illness in older age groups? We expected that allostatic load would predict limiting long-term illness. However, because self-rated may also be an early predictor of disability, the association between self-rated health and allostatic load might be reciprocal or, indeed, self-rated health might even precede allostatic load.

Data and Methods
We use data from Waves 2 and 4 of the English Longitudinal Study of Ageing (ELSA), a nationally representative longitudinal study of the older population of England. These waves of the study included a nurse visit to study participants at which biomarker data was collected.

The first wave of ELSA conducted in 2002-2003 included men and women then aged 50 years or more from private households which had participated in any one of the 1998, 1999 or 2001 rounds of the cross sectional Health Survey for England (HSE; an annual government health survey based on a stratified random sample of all households in England). Response rates for the HSE were 69% in 1998, 70% in 1999 and 67% in 2001. This process led to the recruitment of 11,392 core members to the first wave of the ELSA study (response rate 67%). Comparisons with other sources, including the national census, showed that the baseline ELSA survey was nationally representative. 10,770 of Wave 1 respondents were eligible for re-interview at Wave 2 in 2004-5 (excluding those who had died or had moved out of the country) of whom 8,780 (82%) participated. Of these respondents, 6,187 provided enough information on biomarkers in the nurse visit to allow calculation of allostatic load score at wave 2. At wave 4, interview items were available for 4,981 participants, and 4,688 provided enough information for the calculation of allostatic load score.

Measures

Allostatic load was measured using biomarkers obtained during the nurse visits. In the present study, nine biomarkers were used. Five of the biomarkers were derived from blood samples: HDL/total cholesterol ratio (mg/dL) (index of risk for cardiovascular disease), triglycerides (index of lipid metabolism), glycosylated haemoglobin (HbA1c, %) (index of glucose metabolism over the previous 30-90 days), fibrinogen (index of inflammation and cardiovascular disease, mg/dL) and C-reactive protein (index of inflammation and cardiovascular disease, mg/dL). Three of the biomarkers were obtained from anthropometric measures (waist to hip ratio), blood pressure measures (systolic and diastolic blood pressure) and lung function (peak expiratory flow rate). For all nine measures, individuals belonging to the highest 25 percentile indicating the health risk were identified from the sample distribution. Adjustments were made in the analysis to take account of use of medication and inhalers and whether or not blood samples were taken after fasting. Limiting long-term illness (1=one or more, 0=none) was a single item indicating whether or not the respondent reported a diagnosed illnesses which limited their everyday functioning. Self-rated health was a global evaluation of current health on a 5-point scale, ranging from poor to excellent. Covariates were age (in years), gender and a binary indicator distinguishing those with any educational qualification from those with no qualifications measured at wave 2. In addition, being married, current smoking, wealth quintile, and levels of physical activity and social support were measured at both waves.

Analysis

Cross-lagged analyses were carried out with Mplus. Maximum likelihood estimation with robust standard errors (MLR) was used. The estimation of the model was carried out under missing data theory using all available data. All three health measures were treated as categorical. The fit of the models was assessed by chi square analysis, Comparative Fit Index (CFI) and Root Mean Square Error of approximation (RMSEA). The equality of the simultaneous paths was tested using the Wald test.

Results

The model for the reciprocal associations between allostatic load, self-rated health and limiting long-term illness fitted the data well ($\chi^2 = 230.23$, $df = 71$, CFI = 0.96, RMSEA = 0.048). The cross-lagged association between the three measures were relatively low, but mostly significant. The estimates
indicated that allostatic load predicted limiting long-term illness, but that the path from limiting long-term illness to allostatic load was not significant. The Wald test showed that these two paths were not equal (Wald test: 4.96 (1), $p = 0.026$). The associations between allostatic load and self-rated health were significant in both directions, although the association was stronger from self-rated health to allostatic load than other way round. The Wald test indicated that these two paths could not be set to equal (Wald test: 11.43 (1), $p < 0.001$). Both allostatic load and self-rated health predicted limiting long term illness, although the strength of the association was somewhat stronger between self-rated health and limiting long-term illness. The association between self-rated health and limiting long term illness was stronger from limiting long-term illness to self-rated health than other way round. The cross-sectional correlations between allostatic load and health were rather low and in some cases even weaker than the cross-lagged effects.

**Discussion**

The results suggest that allostatic load could be considered a predictor of limiting-long term illness, consistent with the formulation of allostatic load theory which defines allostatic load as a chronic stress induced cumulative biological burden predictive of health outcomes (McEwen & Stellar, 1993). Allostatic load may represent the early warning sign of interruption with normal processes and activation of efforts to regain the normal state. From this perspective allostatic load may be parallel with active pathology, the first step in the disenablement process (Verbrugge & Jette, 1994), which leads to impairment, functional limitation and disability, which in the case of the present study is limiting long-term illness. While allostatic load predicted limiting long-term illness, the association with self-rated health was reciprocal. Moreover, the strength of the association indicated that self-rated health was more likely to precede allostatic load than other way round.

The results call for attention to the use of different measures of health and the sequence from stress induced physiological dysregulation to health outcomes. They suggest that self-rated health may be an even earlier indicator of health problems than allostatic load. The finding is in line with previous reports that self-rated health can be useful in predicting a number of health outcomes (Idler, Russell, & Davis, 2000; Lee, 2000; Pietilainen et al., 2011). Interestingly, the cross-sectional correlations between allostatic load and health were rather low and in some cases even weaker than cross-lagged effects, suggesting that the timing between the measures is likely to be sequential rather than simultaneous. A previous study using baseline allostatic load to predict longitudinal health decline also reported strong cross-time effects (Karlamangla et al., 2002a). The modest cross-sectional associations between allostatic load and health also could result from measurement problems. Although allostatic load score is based on objective assessment and the associations with health outcomes tend to be stronger when using a summary score of a number of biomarkers compared to a single biomarker (Karlamangla et al., 2002b), it is not clear what exactly allostatic load score measures. Both limiting long-term illness and self-rated health although widely used, are based on single items and self assessment that can be biased by a number of factors. On the other hand the strength of these measures is the simplicity of using them. They are quick and easy to fill in and convenient to code and analyse. They are less likely to be affected by refusal and missing data. This may be a great advantage compared to some more complicated data collection methods, such as biomarkers for calculating allostatic load score.

In interpreting the results it is important to note that allostatic load score was constructed using secondary outcomes of stress mediation. Consequently, allostatic load as defined in the present study may be closer to health outcomes in the temporal pathway, and less likely to detect early stress-related physiological changes (such as cortisol, epinephrine and norepinephrine) (Clark, Bond, & Hecker, 2007). Previous studies indicate that primary stress mediators and secondary stress outcomes are equally
effective in predicting physical health outcomes (Karlamangla et al., 2002b; Seeman et al., 2001). However, as discussed previously, these studies have not applied longitudinal testing of reciprocal associations between allostatic load and health outcomes. In the light of the present study, allostatic load preceded limiting long-term illness and limiting long-term illness in turn preceded self-rated health suggesting that allostatic load may be useful in detecting predictors of health problems. Poor self-rated health was however also useful in predicting low allostatic load score. Self-rated health includes the positive end of the variation of health which may make it a broader tool to describe health status. This strength, however, may be partly offset by evidence of considerable within and between population variation in responses to self-rated health questions. Further work on pathways to disability is needed.

References


