Psychoneuroendocrinology 67 (2016) 76–85

Contents lists available at ScienceDirect

Psychoneuroendocrinology

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

Sociodemographic, behavioral and genetic determinants of allostatic load in a Swiss population-based study

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ARTICLE INFO

Article history:
Received 21 October 2015
Received in revised form 3 February 2016
Accepted 3 February 2016

Keywords:
Allostatic load
socioeconomic status
physiological dysregulation
population-based
heritability

ABSTRACT

Allostatic load (AL) is a marker of physiological dysregulation which reflects exposure to chronic stress. High AL has been related to poorer health outcomes including mortality. We examine here the association of socioeconomic and lifestyle factors with AL. Additionally, we investigate the extent to which AL is genetically determined. We included 803 participants (52% women, mean age 48 ± 16 years) from a population and family-based Swiss study. We computed an AL index aggregating 14 markers from cardiovascular, metabolic, lipidic, oxidative, hypothalamus-pituitary-adrenal and inflammatory homeostatic axes. Education and occupational position were used as indicators of socioeconomic status. Marital status, stress, alcohol intake, smoking, dietary patterns and physical activity were considered as lifestyle factors. Heritability of AL was estimated by maximum likelihood. Women with a low occupational position had higher AL (low vs. high OR = 3.99, 95%CI [1.22;13.05]), while the opposite was observed for men (middle vs. high OR = 0.48, 95%CI [0.23;0.99]). Education tended to be inversely associated with AL in both sexes(low vs. high OR = 3.54, 95%CI [1.69;7.4]/OR = 1.59, 95%CI [0.88;2.90] in women/men). Heavy drinking men as well as women abstaining from alcohol had higher AL than moderate drinkers. Physical activity was protective against AL while high salt intake was related to increased AL risk. The heritability of AL was estimated to be 29.5% ±7.9%. Our results suggest that generalized physiological dysregulation, as measured by AL, is determined by both environmental and genetic factors. The genetic contribution to AL remains modest when compared to the environmental component, which explains approximately 70% of the phenotypic variance.

1. Introduction

Allostatic load (AL) is an indicator of biological dysregulation representing the cumulative physiological toll experienced by an organism when it fails to adequately respond to chronic psychosocial or physical challenges from the environment (Dowd et al., 2009; McEwen, 1998). Introduced in the early nineties by McEwen and Stellar (1993), AL is measured through a single index, resulting from a combination of biological markers reflecting the states of several axes including cardiovascular, metabolic, dyslipidemic, neuroendocrine, hypothalamus-pituitary-adrenal (HPA) and inflammatory (Nicod et al., 2014; Seeman et al., 2010). High AL has been related to several adverse health outcomes, including physical and cognitive functioning, symptoms of post traumatic stress disorder, risk of cardiovascular events (Crimmins et al., 2003; Juster et al., 2010; Seeman et al., 2001), and all-cause mortality (Seeman et al., 2004).

The concept of AL was originally introduced to represent the physiological consequences of chronic stress, itself influenced by

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http://dx.doi.org/10.1016/j.psyneuen.2016.02.003
0306-4530/

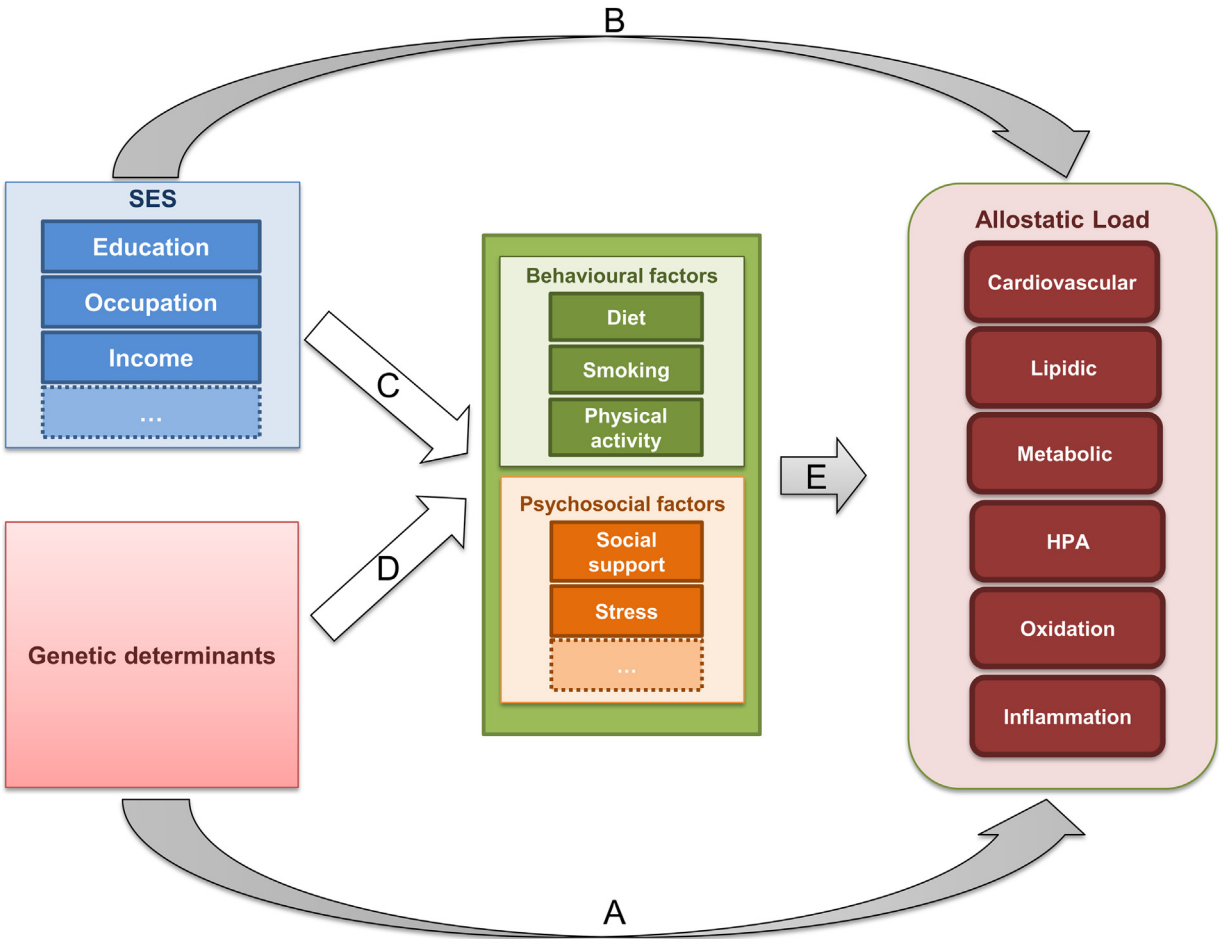

Fig. 1. Simplified conceptual framework for the determinants of allostatic load. AL is represented with its six homeostatic axes. It may be influenced directly by genetic factors (arrow A) and SES (B), or indirectly through behavioural and psychosocial factors (arrows C and D). Behavioural and psychosocial factors may also influence AL directly (E).

socioeconomic status (SES), health behaviors or psychosocial factors. In this context, many studies have found a strong association between low SES, as reflected by low education, adverse financial conditions or receiving social transfers, and high AL (Gruenewald et al., 2012; Nicod et al., 2014). The role of health behaviors in relation to chronic stress and health has also been investigated in previous research, which showed that individuals confronted to stressful daily life (i.e. poverty, crime) are prone to engage themselves into unhealthy behaviors such as smoking or overeating, which may help alleviate symptoms of psychological stress. However, despite these positive, short-term psychological effects, an unhealthy lifestyle has detrimental physiological consequences on the long term and thus results in increased morbidity and mortality (Jackson et al., 2010).

However, the associations between health behaviors and AL have not always been consistent across studies. Gallo et al. (2011) showed, for example, that moderate alcohol consumption was associated with decreased AL, whereas Crimmins et al. (2009) found no association between alcohol intake and AL. Similarly, results for the effect of smoking on AL were inconsistent (Crimmins et al., 2009; Hu et al., 2007). Finally, AL has mainly been studied as a consequence of chronic environmental demands, whereas a limited number of studies have examined the contribution of selected genetic determinants using a candidate gene approach to this phenotype (Brody et al., 2013; Cicchetti et al., 2011). The complex nature of AL suggests that this phenotype is influenced by more than one gene (i.e. a polygenic trait). However, previous studies have mainly focused on the role of specific genetic markers, which are involved in responses to contextual stress, including SES-associated risks, family or personal pressure and the response to physical abuse (Brody et al., 2013; Cicchetti et al., 2011). To date, two markers have been identified, the SLC6A4 serotonin transporter gene, whose shorter variant was associated with high AL, and CRHR1 corticotropin releasing hormone receptor 1 gene, which is involved in HPA axis regulation, and whose TAT variant was associated with high AL. However, to our knowledge, no study has yet investigated nor assessed heritability of AL, which allows the determine the overall genetic contribution to this phenotype, irrespective of the specific function of selected genes.

In this study, we examine the association of socioeconomic (education and occupation) and behavioral factors (marital status, smoking, alcohol consumption, physical activity, dietary patterns, and stress) with AL using data from a Swiss population-based study. Further, we investigate the extent to which AL is genetically determined by assessing narrow sense heritability. We hypothesize that AL is influenced by both environmental (socioeconomic and behavioral) and genetic factors (Fig. 1).

2. Methods

2.1. Study population and design

Data were drawn from the SKIPOGH study (Swiss Kidney Project on Genes in Hypertension), a multicenter family-based population