Psychoneuroendocrinology 74 (2016) 24–33

Contents lists available at ScienceDirect

Psychoneuroendocrinology

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

Physiological wear-and-tear and later subjective health in mid-life: Findings from the 1958 British birth cohort

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ARTICLE INFO

Article history:
Received 16 March 2016
Received in revised form 1 July 2016
Accepted 2 August 2016

Keywords:
Allostatic load
Subjective health
Embodiment
Biomarkers
Social gradient
Birth cohort

ABSTRACT

Objective: Our body adapts continuously to environmental challenges and stressful conditions. Allostatic load (AL) is a concept that aims to capture the overall physiological wear-and-tear of the body triggered by the repeated activation of compensatory physiological mechanisms as a response to chronic stress. Growing evidence has shown a link between AL and later health decline, morbidity and mortality. However, due to the global physiological effect captured by the AL concept, it is particularly pertinent to examine its association with subsequent health by taking a broad definition of the latter. We examined the association between AL at 44 years and general health as measured by a latent multidimensional measure of subjective health at 50 years integrating sleep patterns, physical and mental health.
Methods: AL was constructed using 14 biomarkers representing four physiological systems on 7573 members of the 1958 British birth cohort. Health status was captured using self-reported information about subjective health and summarized using a principal component analysis including: seven dimensions of the SF-36 questionnaire of health-related quality of life, the sleep subscale of the Medical Outcomes Study characterizing quality of sleep patterns, and a malaise inventory score detecting depressive symptoms.
Results: Higher AL score was gradually associated with worse subjective health, after taking into account classic confounders.
Conclusions: Using a physiological index to grasp how the environment can "get under the skin" leading to poor health is of great interest, permitting a better understanding of life course origins of disease and social gradients in health.

1. Introduction

Krieger et al. defined the concept of embodiment as "how we, like any living organism, literally incorporate, biologically, the world in which we live, including our societal and ecological circumstances" (Krieger, 2005). Growing evidence supports the idea that exposure to chronic stress over the life course contributes to physiological dysregulation, subsequently translated into disease (McEwen and Seeman, 1999; McEwen and Stellar, 1993; Seeman et al., 2001). Allostasis is the active process of adaptation where our body tries to maintain physiological stability in response to environmental challenges (Sterling, 2004, 2012). The repeated activation of compensatory physiological mechanisms as a result of chronic exposure to stress can lead to a physiological wear-and-tear, known as allostatic load (AL) (Juster et al., 2010; McEwen and Stellar, 1993; McEwen and Wingfield, 2003). AL may be a useful conceptual tool in measuring the biological effect of embodiment.

Based on prospective data, used to capture the history of prior environmental insults (Seeman et al., 2010) researchers have studied the life course origins of AL development. They highlighted the role of social adversity (Gustafsson et al., 2012), and socioeconomic position (SEP) (Gustafsson et al., 2011) as predictors of AL, also identifying the mediating role of material, behavioural and psychosocial factors between SEP and later AL (Barboza Solis et al., 2015; Robertson et al., 2015, 2014). These findings suggest that (a) AL is socially patterned (Dowd et al., 2009; Robertson et al., 2014; Seeman et al., 2010; Szanton et al., 2005), determined by socioeconomic position, material, psychosocial and behavioural factors all over the life span (Robertson et al., 2015), (b) AL conceptual framework may contribute to clarify the biological component of the socioeconomic gradient observed in morbidity and mortality (Carlson and Chamberlain, 2005; Gruenewald et al., 2012).

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http://dx.doi.org/10.1016/j.psyneuen.2016.08.018
0306-4530/

Empirical research has investigated the link between AL and later health outcomes (Beckie, 2012; Karlamangla et al., 2006). However, the conceptual framework of AL is constructed on the basis of a global effect of stress on health, via multiple physiological mechanisms and by impacting several systems and brain structures. Therefore, AL is not designed to be specific, but rather to show an overall effect on health. Several studies have shown links between AL and, diverse health outcomes (Juster et al., 2010; Karlamangla et al., 2002, 2006). However, testing the link between AL and one specific aspect of health, for instance, cardiovascular disease, fragments the notion of overall physiological wear-and-tear. Therefore, due to the global physiological effect captured by the AL concept, it is particularly pertinent to examine its association with subsequent health by taking a broad definition of the latter, not only measured by the absence or presence of diseases.

Health status is indeed a multidimensional and integrative attribute, a latent concept, capturing subjective (e.g. self-rated health, well-being, quality of life, health related quality of life, happiness, life satisfaction), clinical (e.g. morbidity, functional decline) and biological (e.g. biomarkers) dimensions (Hyland et al., 2014). Self-rated health and health-related quality of life (HRQoL) – defined as the perception of the impact of health problems on different spheres of life, including physical, mental, and social aspects (Testa and Simonson, 1996)- have been used as measures of health status since they correlate to morbidity and mortality (Power et al., 1998). Subjective health measures are then frequently used as surrogate endpoints of morbidity and mortality, where their main advantage is to define health through its various dimensions. In this paper we investigate the link between AL and a holistic/integrative latent measure of health using a subjective health variable integrating sleep patterns, physical and mental health at 50 years. We aimed to address this question studying the impact of AL measured at 44 years of age on a latent variable of subsequent subjective health measured at 50. We hypothesised that AL could influence health status in the long term, independently of social determinants and health behaviours.

2. Materials and methods

2.1. Participants

The National Child Development Study (NCDS) includes all children born during one week in 1958 (N = 18558) in Great Britain. Data collection was carried out on cohort members between birth and 50y. At age 44–45y a biomedical survey was conducted including a self-reported questionnaire, physical measurements, blood and saliva samples (Power and Elliott, 2006). The sample used for this study is described in Fig. S1.

2.2. Ethics & data

Written informed consent was obtained from parents for childhood measurements and ethical approval for the adult data collection was obtained from the National Research Ethics Advisory Panel. NCDS data are open access datasets available to non-profit research organizations. Ethical approval for the age 45 year survey (Gruenewald et al., 2012; Gustafsson et al., 2011) was given by the South East Multicentre Research Ethics Committee.

2.3. Measurements

2.3.1. Allostatic load at 44y

Among available biomarkers, we selected fourteen parameters representing four physiological systems: the neuroendocrine system (salivary cortisol t1 (nmol/L), salivary cortisol t1-t2 (nmol/L)); the immune & inflammatory system (C-reactive protein (CRP mg/L), fibrinogen (g/L), immunoglobulin E (IgE KU/L), insulin-like growth factor-1 (IGF-1 nmol/L),); the metabolic system (high density lipoprotein (HDL mmol/L), low density lipoprotein (LDL mmol/L), triglycerides (mmol/L), glycosylated hemoglobin (%)); the cardiovascular & respiratory systems: (systolic blood pressure (SBP mmHg), diastolic blood pressure (DBP mmHg), heart rate/pulse (p/min), peak expiratory flow (L/min)). These biomarkers were chosen based on previous measures of AL (Barboza Solis et al., 2015; Karlamangla et al., 2002, 2006; Seeman et al., 1997) and according to evidence of their relationship to stressful conditions over life (Butland et al., 2008; Kumari et al., 2013, 2011, 2008). In accordance with the most classical AL operationalization proposed by Seeman et al. (1997), our score was the sum of the fourteen parameters for which the subject was rated in the highest-risk quartile ('1' vs low risk '0') according to gender specific quartiles. A full description of each parameter is given in Table S1. Individuals with missing data were considered as not at risk for the missing biomarker adopting a conservative approach (maximum bias). Exclusion criteria for the analysis is shown in the flow chart (Fig. S1). We additionally run the multivariate analysis using a different operationalization of AL score, by calculating a 0–1 risk score within each system and the results did not vary.

2.3.2. Subjective health index at 50y

We conceptualize health status following an integrative approach incorporating three different dimensions of health from subjective health measures collected at the 8th sweep of the NCDS 1958 British birth cohort. The *SF-36* is a general questionnaire measuring Health Related Quality of Life (HRQoL) (Ware, 2000) through its physical and mental components (Taft et al., 2001) that captures, for instance, the interference with work or other daily activities due to physical health, emotional problems, interference with normal social activities, symptoms associated with anxiety/depression and measures of positive affect (Supplementary material). Each of the eight dimensions is ranged from 0 to 100 with higher scores related to better HRQoL. The SF-36 has been shown to be predictive of subsequent morbidity and mortality (Kaplan et al., 2007; Otero-Rodriguez et al., 2010; Rodriguez-Artalejo et al., 2005; Tsai et al., 2007).

A subscale of four items from twelve original *Sleep Scale of the Medical Outcomes Study* (MOS) was used in NCDS to collect information about sleep patterns in the last four weeks measuring quality of sleep (Hays and Stewart, 1992). Previous studies have provided evidence on the validity and reliability of the MOS sleep measures (Hays et al., 2005; Viala-Danten et al., 2008) (Supplementary material). The self-completion sleep scale included: usual time taken to fall asleep, average number of hours sleep per night, waking-up during night frequency and trouble falling back to sleep, and whether the respondents had slept enough, based on whether they felt rested upon waking. These four items capture three different dimensions of sleep problems, relating to quantity of sleep/optimal sleep duration, perceived sleep adequacy, and sleep disturbance (Chatzitheochari, 2013). Sleep patterns are known to be related to chronic diseases (diabetes, hypertension, cardiovascular), poor health-related quality of life and self-rated poor health (Chatzitheochari, 2013). In terms of physiological balance, sleep disturbances have an impact on metabolic and endocrine functioning (Spiegel et al., 1999).

Finally, the *malaise Inventory* which measures psychological distress, comprising a nine-item score from the original twenty four (Rutter et al., 1970), was included as a continuous variable, with higher scores relating to worst mental health (Supplementary material). The malaise inventory score has been found to have acceptable internal validity in different socio-economic groups in the NCDS sample (Rodgers et al., 1999). Mental health has been

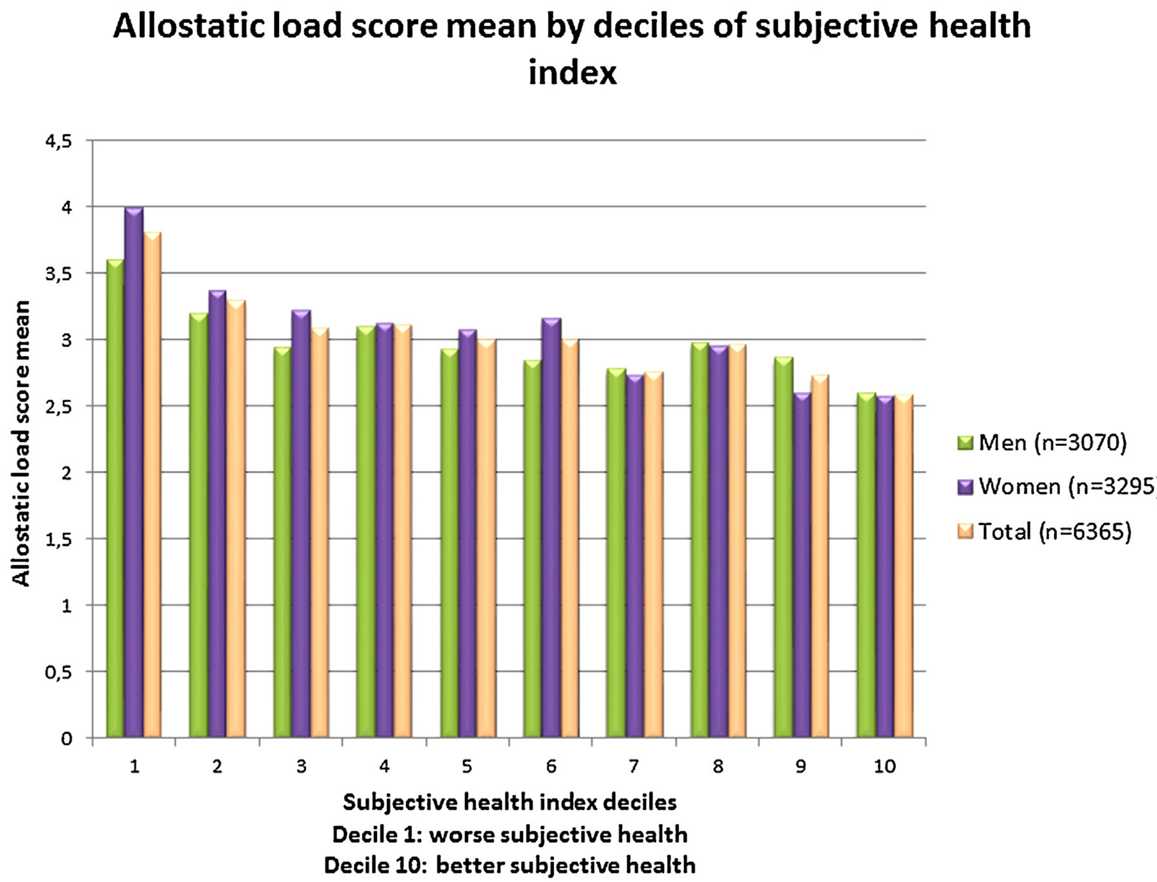

Fig. 1. Allostatic load score mean by deciles of subjective health.

found to correlate to later morbidity and mortality (Vogt et al., 1994).

We ran a Principal Components Analysis (PCA) to sum-up the information of the above self-reported variables using non-imputed data and deriving one single component. The PCA included three groups of variables: (i) the first group was created using seven dimensions of the SF-36 scale of HRQoL questionnaire (physical functioning, role-physical, bodily pain, general health, vitality, role-emotional, mental health). The social functioning subscale was excluded under statistical criteria when running the principal component analysis. (ii) Four items of the *Sleep Scale of the Medical Outcomes Study* included as ordinal continuous variables. (iii) The malaise inventory score ranged between 0 and 9. PCA show an adequate fit to the data (Component 1 eigenvalue = 5.3; Overall Kaiser-Meyer-Olkin measure of sampling adequacy = 0.89; overall α Cronbach = 0.81). Subsequently we standardized the distribution using *Z*scores separately by sex. Fig. S2 shows the distribution of *Z*scores for men and women (Supplementary material). All analyses were performed using STATA V14 taking a statistical significance level of 0.05.

2.3.3. Early life socioeconomic confounders

Information on participant's early life factors was collected via a questionnaire completed at birth by the participant's mother. Maternal education was self-reported (mother left school after legal minimal age/mother left school before legal minimal age). Mother's partner's (or father's if unavailable) occupation was classified in four categories: I-professional occupations & II-intermediate occupations/III-skilled occupations (non-manual)/III-partly skilled occupations (manual)/IV-partly skilled occupations & V-unskilled occupations.

2.3.4. Early adulthood socioeconomic confounders at 23y

The selected variables were: respondent's educational attainment (A level/O level/no qualification) and the equivalent net family income (adjusted for family size and composition with weightings from supplementary-benefit scale) (Power et al., 1998).

2.3.5. Adulthood socioeconomic confounders at 33y

To take the role of material circumstances into account, we investigated firstly household tenure (classified in two categories: owner occupiers/renters, other), whether the participant's or their partner were receiving social security benefits (income support, supplementary, or unemployment benefit), whether the participant declared having mortgage or rent arrears (never been 2 or more month behind/yes, ever been 2 or more moth behind) and occupation (classified in non-manual/manual). To capture social support, marital status was used grouped into the following categories: couple/single/divorced or widowed.

2.3.6. Adult health behaviours at 33y

We investigated the smoking status (non-smoker/former smoker/current smoker), alcohol consumption [moderate (women: between 1 and 14 units in the previous week; men: between 1 and 21 units in the previous week)/abstainers (reported not consuming any alcohol in the previous week)/heavy drinkers (women: >14 units in the previous week; men: >21 units in the previous week)] (2012), and physical activity (physically active/moderately active/inactive). To measure eating habits, we added BMI in the model (normal/underweight/overweight/obese).

2.4. Statistical analysis

To control for possible bias due to missing data, twenty imputations were conducted using the multiple imputation program ICE in STATA V14. We took a missing-at-random (MAR) assumption. Each covariable with missing values was imputed including all confounders used in the models as well as variables from other sweeps correlated with the variable to impute but excluding the exposures variable (AL) and the subjective health index (Supplementary material). To observe the unadjusted link and better appreciate the evolution of the link between AL and later subjective health, the first model of the multivariate linear regression took only into account AL. Subsequently, and to mimic life-course experiences, we sequentially adjusted the multivariate linear regression resulting in four models:

1. Model 1: AL
2. Model 2: M1 + Early life socioeconomic confounders at birth,
3. Model 3: M2 + Early adulthood socioeconomic confounders at 23y,
4. Model 4: M3 + Adulthood socioeconomic and health behaviours confounders at 33y,

As some evidence suggests gender-related differences in biological markers (Goldman et al., 2004) and potential sexual dimorphism in AL (Yang and Kozloski, 2011) or other biological measure (e.g. metabolic syndrome) (McMillen and Robinson, 2005), the analyses were stratified by sex (Goldman et al., 2004; Yang and Kozloski, 2011) (Supplementary material).

3. Results

3.1. Sample characteristics

Descriptive statistics of the non-imputed sample are presented in Table 1 for the subsample with complete data for subjective health and AL (n = 3070 for men; n = 3295 for women). Mean of AL for both men and women was equal to 3, ranged from 0 to 12. Table S2 shows the results for the bivariate statistics for both men and women. AL score was associated with subjective health index in men (−0.07 standard deviation (SD); $p < 0.001$) and in women (−0.09SD; $p < 0.001$).

3.2. Allostatic load and subjective health

Fig. 1 shows the AL score mean by deciles of subjective health index. A clear gradient is revealed, individuals in the 1st decile of subjective health index (worse health) had an AL score mean of 3.5 and 4 for men and women respectively. Men and women in the 10th decile of subjective health show an AL score mean of 2.5. Multivariate results are presented in Tables 2 and 3 for men and women respectively. Model 1 showed that AL was significantly associated with later subjective health. Men with higher scores of AL at 44 years had worse subjective health indexes (-0.07SD; $p < 0.001$) at 50 years. The same pattern was observed for women, where higher scores of AL were correlated with worse subjective health index (−0.09SD; $p < 0.001$). In model 2 and model 3 the link was slightly weakened after adjustment for early life and early adulthood socioeconomic circumstances. Model 4 showed that socioeconomic and health behaviours variables reduced the link for both men and women, however it remained significant: a one-point increase of the AL score was associated with a reduction of 0.04SD ($p < 0.001$) and 0.05SD ($p < 0.001$) in the health index for men and women respectively. As sensitivity analyses we constructed an additional AL score by calculating a 0–1 risk score within each system, reflecting the proportion of biomarkers within the system for which the participant's values fell into the highest-risk quartile, allowing an equal weight for each system (Carroll et al., 2015). The results did not vary. We also evaluate which of the biomarkers was having the strongest link with the subjective health index. We run an additional multivariate model fully adjusted for the same confounders, taking each biomarker individually and previously divided into low '0'/high risk '1' in a sample without missing values. For men peak expiratory flow and for women CRP and fibrinogen showed the strongest link (Supplementary material). For men, only four biomarkers were significantly related to the subjective health index, for women only half. This could reinforce the construct of AL, maybe measuring an overall physiological state that better predicts later health than each biomarker separately.

3.3. Life course socioeconomic confounders and later subjective health

From early life, mothers education (only for men) and lower paternal occupational status (skilled manual and semi-unskilled) reduced the subjective health index for both men and women, however these links disappeared after adjustment for socioeconomic variables in adulthood. The fully adjusted model yield additionally interesting findings. For men, having no qualifications at 23y decreased the subjective health index of 0.14SD ($p < 0.001$). Income was found to predict better subjective health only in women (0.23; $p < 0.001$). Worse material and socioeconomic circumstances at 33y were important independent factors associated with lower subjective health index. For both men and women, being a tenant (men: −0.14SD, $p = 0.019$)/women: −0.16SD, $p = 0.004$), receiving social-security benefits (men: −0.30SD, $p = 0.003$/women: −0.21SD, $p = 0.002$) and declaring ever being two or more months behind with mortgage or rent arrears (men: −0.23SD, $p = 0.007$/women: −0.21SD, $p = 0.008$) were significantly associated with a worse subjective health index compared to their counterparts. Model 4 also showed the important role of health behaviours and BMI. Being a current smoker (men: −0.10SD, $p = 0.034$/women: −0.18SD, $p < 0.001$), being classified as a heavy drinker for men (-0.20SD, $p = 0.002$) or an abstainer for women (women: −0.12SD, $p = 0.002$), and being obese (men: −0.15SD, $p = 0.026$/women: −0.29SD, $p < 0.001$), decreased the subjective health index relatively to those classified as non-smokers, moderate drinkers, or having a normal BMI respectively.

4. Discussion

Higher scores of allostatic load at 44 years were found to be associated with worse subjective health six years later in a large prospective cohort, after taking into account classic confounders. This association was independent of socioeconomic variables across the life course, adult health behaviours and BMI. These findings add some evidence to the hypothesis of a plausible biological underlying mechanism between the social environment and later overall health, via stress response systems. We deduce that AL may represent a physiological outcome of embodiment processes, contributing to a better understanding of susceptibility to poorer health and the production of social gradients in health.

There are several limitations in this study. First, since these analyses were performed using a birth cohort, an important weakness is related to attrition and selection bias. However, the surviving cohort remains broadly representative of the initial cohort key childhood and adult characteristics (Atherton et al., 2008). We additionally imputed the data for confounding variables taking the missing at random assumption to preserve important aspects of the distribution, variability, and relationships between variables.

Table 1
Descriptive statistics on the subsample for men (n = 3070) and women (n = 3295).

Variables	Men	Women	Total
Subjective health Z score at 50			
n (min–max)	3070 (−5.0 to 1.6)	3295 (−4.2 to 1.7)	6365 (−5.0 to 1.7)
mean (SD)	0 (1.0)	0 (1.0)	0 (1.0)
Allostatic load score at 44			
0	244 (7.9%)	277 (8.4%)	521 (8.2%)
1	505 (16.5%)	578 (17.5%)	1083 (17.0%)
2	649 (21.1%)	656 (19.9%)	1305 (20.5%)
3	574 (18.7%)	560 (17.0%)	1134 (17.8%)
4	464 (15.1%)	452 (13.7%)	916 (14.4%)
5	280 (9.1%)	313 (9.5%)	593 (9.3%)
6	190 (6.2%)	219 (6.6%)	409 (6.4%)
7	97 (3.2%)	108 (3.3%)	205 (3.2%)
8	56 (1.8%)	83 (2.5%)	139 (2.2%)
9	9 (0.3%)	37 (1.1%)	46 (0.7%)
10	2 (0.1%)	9 (0.3%)	11 (0.2%)
11	0 (0.0%)	1 (0.0%)	1 (0.0%)
12	0 (0.0%)	2 (0.1%)	2 (0.0%)
Maternal education			
Left school at 15 or later	811 (26.4%)	870 (26.4%)	1681 (26.4%)
Left school before 14	2107 (68.6%)	2239 (68.0%)	4346 (68.3%)
Missing	152 (5.0%)	186 (5.6%)	338 (5.3%)
Paternal occupation			
I & II (professional/managerial	624 (20.3%)	612 (18.6%)	1236 (19.4%)
IIINM (skilled nonmanual)	295 (9.6%)	323 (9.8%)	618 (9.7%)
IIIM (skilled manual)	1425 (46.4%)	1557 (47.3%)	2982 (46.9%)
IV & V (semi-unskilled)	568 (18.5%)	610 (18.5%)	1178 (18.5%)
Missing	158 (5.1%)	193 (5.9%)	351 (5.5%)
Education level at 23			
Passed A levels	707 (23.0%)	728 (22.1%)	1435 (22.5%)
Passed O levels	1021 (33.3%)	1 319 (40.0%)	2340 (36.8%)
No qualifications	925 (30.1%)	860 (26.1%)	1785 (28.0%)
Missing	417 (13.6%)	388 (11.8%)	805 (12.6%)
Income at 23			
Q1 – Low income	462 (15.0%)	805 (24.4%)	1267 (19.9%)
2	550 (17.9%)	794 (24.1%)	1344 (21.1%)
3	709 (23.1%)	657 (19.9%)	1366 (21.5%)
Q4 – High income	777 (25.3%)	563 (17.1%)	1340 (21.1%)
Missing	572 (18.6%)	476 (14.4%)	1048 (16.5%)
Household tenure at 33			
Owner	2130 (69.4%)	2361 (71.7%)	4491 (70.6%)
Renter	341 (11.1%)	463 (14.1%)	804 (12.6%)
Rent free, goes with job, equity sharer	23 (0.7%)	37 (1.1%)	60 (0.9%)
Missing	576 (18.8%)	434 (13.2%)	1010 (15.9%)
Social-security benefits at 33			
No	2594 (84.5%)	2766 (83.9%)	5360 (84.2%)
Yes	137 (4.5%)	245 (7.4%)	382 (6.0%)
Missing	339 (11.0%)	284 (8.6%)	623 (9.8%)
Mortgage or rent arrears at 33			
Never been 2/+ month behind	2579 (84.0%)	2818 (85.5%)	5397 (84.8%)
Yes ever been 2/+ month behind	143 (4.7%)	189 (5.7%)	332 (5.2%)
Missing	348 (11.3%)	288 (8.7%)	636 (10.0%)
Occupation at 33			
Non-manual	1453 (47.3%)	2060 (62.5%)	3513 (55.2%)
Manual	1152 (37.5%)	759 (23.0%)	1911 (30.0%)
Missing	465 (15.1%)	476 (14.4%)	941 (14.8%)
In couple at 33			
Couple	2204 (71.8%)	2474 (75.1%)	4678 (73.5%)
Single	376 (12.2%)	273 (8.3%)	649 (10.2%)
Divorced or widowed	140 (4.6%)	250 (7.6%)	390 (6.1%)
Missing	350 (11.4%)	298 (9.0%)	648 (10.2%)
Smoking status at 33			
Non smoker	1388 (45.2%)	1562 (47.4%)	2950 (46.3%)
Former smoker	550 (17.9%)	595 (18.1%)	1145 (18.0%)
Current smoker	791 (25.8%)	859 (26.1%)	1650 (25.9%)
Missing	341 (11.1%)	279 (8.5%)	620 (9.7%)
Alcohol consumption at 33			
Moderate	1984 (64.6%)	1758 (53.4%)	3742 (58.8%)
Abstainers	476 (15.5%)	1105 (33.5%)	1581 (24.8%)
Heavy drinkers	286 (9.3%)	164 (5.0%)	450 (7.1%)

Table 1 (*Continued*)

Variables	Men	Women	Total
Missing	324 (10.6%)	268 (8.1%)	592 (9.3%)
Physical activity at 33			
Physically active	1932 (62.9%)	2135 (64.8%)	4067 (63.9%)
Moderately active	199 (6.5%)	168 (5.1%)	367 (5.8%)
Inactive	84 (2.7%)	88 (2.7%)	172 (2.7%)
Missing	855 (27.9%)	904 (27.4%)	1759 (27.6%)
BMI at 33			
Normal	1352 (44.0%)	1943 (59.0%)	3295 (51.8%)
Overweight	1047 (34.1%)	695 (21.1%)	1742 (27.4%)
Obese	261 (8.5%)	280 (8.5%)	541 (8.5%)
Missing	410 (13.4%)	377 (11.4%)	787 (12.4%)

Second, we cannot conclude that AL provides an added value for predicting later subjective health, since to answer that question, we would need to adjust the model at baseline for subjective health measures. Unfortunately, our study lacks of the same instruments (SF-36, MOS sleep scale) we used for constructing the subjective health variable at previous sweeps. However, to address this question we decided to run a sensitivity analysis using self-rated health as an outcome at 50y, adjusted for self-rated health at 44y in the same imputed sample. Self-rated heath has the advantage of being available at both baseline and at 50 years; and it is a measure contained within the SF-36 score we used for our subjective health measure. We found that AL was independently associated with self-rated health at 50y after adjusting for self-rated health at 44y. This result reinforces the hypothesis that the association between AL and subjective health at 50y is not due to subjective health status at 44 years.

Third, our score remains limited by pragmatic issues regarding variable availability and operationalization. The biomarkers included in our AL score were derived from available data, as parameters of major regulatory systems with known or hypothesized links with stress responses. For example, our AL score lacks “primary” biomarkers and neuroendocrine biomarkers (e.g. epinephrine and norepinephrine) (Juster et al., 2011). Measures of AL may differ in terms of biomarker choice, variable weight, statistical methods, and risk thresholds. Furthermore, the physiological relationship between biomarkers, and their relative importance in the physiological cascade of stress responses remains unclear (Beckie, 2012). AL operationalization continue to be a central debate around how to better approach physiological wear-and-tear. The operationalization we choose was pragmatic and it does not rigorously corresponds to the dynamic theory and definition of AL, and how it accumulates. In previous work we discussed some of the conceptual and empirical consideration regarding these questions (Delpierre et al., 2016). Several issues remain, for instance, the choice of biomarkers (DNA methylation, telomeres length, markers from -omics technologies; or larger molecules and physiological measures); or the best methodological tool to sum up these biomarkers (weighting, taking into account the dependency of each biomarker) and the measurement models more adapted (canonical correlation, recursive partitioning). Future research requires progress in the collection of biomarkers explicitly designed to assess allostatic load at multiple time points in longitudinal large representative samples (Beckie, 2012). Comparative studies are needed to better comprehend the age-related, sex/gender-related, ethnic-related differences in AL. Further research should propose and explore consistent theoretical explanations of the link between the biological mechanism, the system dynamic and the allostatic load measurement. We have previously attempted to raise and debate some of these issues (Delpierre et al., 2016) but many remain open and deserve further clarification, such as the concept of ‘strain’, ‘cost’, ‘price’ that have never being truly defined and that we could not incorporate in the AL operationalization. At this point, AL is capable of characterizing only a fragment of the causal path between social environment and later health. In our case, adding biomarkers to epidemiological research does not solve the ‘black box’ problem. We can only better ‘trace’ and hypothesize aspects of the biological component of the ‘black box’, by exploring the pathways of associations between the exposures, the biomarkers and the health outcome.

Third, we have a one-time AL measure available, which did not allow for a lifetime health trends analysis. Finally, our subjective health measure remains an ad-hoc index and its reproducibility is limited. Health is a latent variable that can be captured using different psychometric scales, as well as clinical and biological variables. We only integrated standardized and validated measures of subjective health which had already been related to later health and mortality risk. It is worth mentioning that in this study both AL and health measures are confined to a specific social and cultural context. The subjective health measure used here is adapted to a Western population, and the questionnaires used were oriented towards a British population. The notion of well-being and psychological malaise, for instance, are confined to a particular social and cultural context (Ryff et al., 2014). Regarding AL, differences on the perception of stressful conditions may have consequences on the symptoms reported (Lock and Kaufert, 2001), and differences on the biomarkers average levels (Miyamoto et al., 2013). To think in terms of ‘local biologies’ will add some scientific bases when analysing the effects of environmental exposures and health outcomes (Lock and Kaufert, 2001). However, AL is structured to use the distribution of the sample in question, thus it is as local or as global as the sample allows in terms of multi-system wastage. We do believe that common underlying biological mechanisms are plausible, and these biological mechanisms can be captured using different measures according (and more adapted) to the specific social context. The possibility of comparing results from different contexts and to replicate the studies may allow us to observe if the underlying physiological responses, in particular physiological stress responses, are ‘generalizable’.

Despite these limitations, our findings offer several insights with respect to previous studies. There is a growing amount of evidence that supports AL as a better predictor of morbidity and mortality (Gruenewald et al., 2006; Karlamangla et al., 2006; Seeman et al., 2001). However, previous studies have concentrated their analysis on specific dimensions of health mainly using elderly population based studies, and though have a lack of prospective data concerning early life, adolescence and early adulthood circumstances. The main novelty of our study is to focus our analysis on the basis of a global effect of stress on health, using an integrative measure -that is not centered on the dichotomy absence/presence of disease- in middle aged adults that have been followed since birth. This allows us to take into account a variety of material, psychosocial, educational and life styles exposures from early life and across the life course. Here we analyzed health as an integrative measure in middle aged adults using a life course perspective allowing for a better

Table 2
Lifecourse multivariate linear regression between AL and standardized subjective health index Zscores using data from multiple imputation: men (n = 3070).

Variables	Model 1: AL		Model 2: Socioeconomic factors at birth		Model 3: Socioeconomic factors at 23y		Model 4: Socioeconomic and behavioural factors at 33y	
	ß (CI 95%)	p	ß (CI 95%)	p	ß (CI 95%)	p	ß (CI 95%)	p
Allostatic load score at 44	−0.07 (−0.08 to −0.05)	<0.001	−0.06 (−0.08 to −0.04)	<0.001	−0.06 (−0.07 to −0.04)	<0.001	−0.04 (−0.06 to −0.02)	<0.001
Maternal education								
Left school at 15 or later			0		0		0	
Left school before 14			−0.10 (−0.18 to −0.01)	0.034	−0.06 (−0.15 to 0.03)	0.220	−0.05 (−0.14 to 0.04)	0.279
Paternal occupation								
I & II (professional/managerial			0		0		0	
IIINM (skilled nonmanual)			−0.07 (−0.21 to 0.07)	0.306	−0.05 (−0.19 to 0.08)	0.437	−0.05 (−0.19 to 0.09)	0.455
IIIM (skilled manual)			−0.10 (−0.20 to −0.01)	0.039	−0.06 (−0.16 to 0.04)	0.256	−0.06 (−0.16 to 0.05)	0.273
IV & V (semi-unskilled)			−0.12 (−0.24 to 0.00)	0.046	−0.05 (−0.18 to 0.08)	0.450	−0.03 (−0.16 to 0.10)	0.634
Education level at 23								
Passed A levels					0		0	
Passed O levels					−0.08 (−0.18 to 0.02)	0.119	−0.05 (−0.15 to 0.06)	0.369
No qualifications					−0.22 (−0.32 to −0.11)	<0.001	−0.14 (−0.27 to −0.02)	0.025
Income at 23								
Q1 – Low income					0		0	
2					0.11 (−0.01 to 0.23)	0.080	0.05 (−0.07 to 0.17)	0.396
3					0.10 (−0.01 to 0.21)	0.078	0.03 (−0.09 to 0.14)	0.645
Q4 – High income					0.13 (0.02 to 0.24)	0.020	0.06 (−0.06 to 0.17)	0.339
Household tenure at 33								
Owner occupiers							0	
Renters/other							−0.14 (−0.26 to −0.02)	0.019
Social-security benefits at 33								
No							0	
Yes							−0.30 (−0.49 to −0.10)	0.003
Mortgage or rent arrears at 33								
Never been 2/+ month behind							0	
Yes ever been 2/+ month behind							−0.23 (−0.40 to −0.06)	0.007
Occupation at 33								
Non-manual							0	
Manual							−0.01 (−0.10 to 0.09)	0.912
In couple at 33								
Couple							0	
Single							−0.10 (−0.21 to 0.02)	0.092
Divorced or widowed							−0.13 (−0.31 to 0.05)	0.151
Smoking status at 33								
Non smoker							0	
Former smoker							0.00 (−0.10 to 0.10)	0.973
Current smoker							−0.10 (−0.19 to −0.01)	0.034
Alcohol consumption at 33								
Moderate							0	
Abstainers							−0.04 (−0.15 to 0.06)	0.436
Heavy drinkers							−0.20 (−0.32 to −0.08)	0.002
Physical activity at 33								
Physically active							0	
Moderately active							−0.04 (−0.19 to 0.10)	0.549
Inactive							−0.07 (−0.30 to 0.16)	0.562
BMI at 33								
Normal							0	
Overweight							−0.04 (−0.12 to 0.04)	0.275
Obese							−0.15 (−0.29 to −0.02)	0.026

Table 3
Lifecourse multivariate linear regression between AL and standardized subjective health index Zscores using data from multiple imputation: women (n = 3295).

Variables	Model 1: AL		Model 2: Socioeconomic factors at birth		Model 3: Socioeconomic factors at 23y		Model 4: Socioeconomic factors and behavioural at 33y	
	ß (CI 95%)	p	ß (CI 95%)	p	ß (CI 95%)	p	ß (CI 95%)	p
Allostatic load score at 44	−0.09 (−0.10 to −0.07)	<0.001	−0.08 (−0.10 to −0.07)	<0.001	−0.07 (−0.09 to −0.06)	<0.001	−0.05 (−0.07 to −0.04)	<0.001
Maternal education								
Left school at 15 or later			0		0		0	
Left school before 14			−0.07 (−0.15 to 0.02)	0.118	−0.01 (−0.10 to 0.07)	0.775	−0.02 (−0.10 to 0.07)	0.686
Paternal occupation								
I & II (professional/managerial			0		0		0	
IIINM (skilled nonmanual)			0.09 (−0.05 to 0.22)	0.204	0.10 (−0.03 to 0.23)	0.147	0.11 (−0.03 to 0.24)	0.113
IIIM (skilled manual)			−0.11 (−0.21 to −0.01)	0.026	−0.06 (−0.16 to 0.04)	0.212	−0.03 (−0.13 to 0.07)	0.520
IV & V (semi-unskilled)			−0.20 (−0.31 to −0.08)	0.001	−0.11 (−0.23 to 0.01)	0.072	−0.06 (−0.18 to 0.06)	0.314
Education level at 23								
Passed A levels					0		0	
Passed O levels					−0.05 (−0.14 to 0.05)	0.318	0.00 (−0.09 to 0.09)	0.976
No qualifications					−0.22 (−0.33 to −0.11)	<0.001	−0.08 (−0.20 to 0.03)	0.166
Income at 23								
Q1 – Low income					0		0	
2					0.14 (0.04 to 0.23)	0.005	0.08 (−0.01 to 0.18)	0.091
3					0.16 (0.06 to 0.27)	0.002	0.07 (−0.03 to 0.18)	0.171
Q4 – High income					0.33 (0.22 to 0.44)	<0.001	0.23 (0.12 to 0.33)	<0.001
Household tenure at 33								
Owner occupiers							0	
Renters/other							−0.16 (−0.26 to −0.05)	0.004
Social-security benefits at 33								
No							0	
Yes							−0.21 (−0.35 to −0.08)	0.002
Mortgage or rent arrears at 33								
Never been 2/+ month behind							0	
Yes, ever been 2/+ month behind							−0.21 (−0.36 to −0.06)	0.008
Occupation at 33								
Non-manual							0	
Manual							−0.03 (−0.11 to 0.06)	0.559
In couple at 33								
Couple							0	
Single							−0.11 (−0.24 to 0.02)	0.088
Divorced or widowed							−0.10 (−0.23 to 0.03)	0.141
Smoking status at 33								
Non smoker							0	
Former smoker							−0.03 (−0.12 to 0.06)	0.541
Current smoker							−0.18 (−0.27 to −0.10)	<0.001
Alcohol consumption at 33								
Moderate							0	
Abstainers							−0.12 (−0.19 to −0.04)	0.002
Heavy drinkers							−0.02 (−0.18 to 0.14)	0.802
Physical activity at 33								
Physically active							0	
Moderately active							−0.02 (−0.17 to 0.12)	0.769
Inactive							0.02 (−0.18 to 0.22)	0.823
BMI at 33								
Normal							0	
Overweight							−0.05 (−0.13 to 0.04)	0.293
Obese							−0.29 (−0.41 to −0.17)	<0.001

understanding of the causal sequence of events. We studied the link between a physiological measure and a subjective measure adjusted for a large panel of confounders which reduces the risk of a spurious link. In previous work, we investigated the socioeconomic determinants of AL, trying to disentangle the mediating pathways between early environment and AL (Barboza Solis et al., 2015). We intended to wed two major conceptual frameworks: AL theory – conceptualized in the stress and neuroendocrinology research- and ecosocial theory – conceptualize within the social epidemiology and health inequalities research- (Delpierre et al., 2016). We used a birth cohort study to capture the physiological impact of embodiment over the life course using an AL index. We hypothesised that the exposure to stressful and challenging events may be embodied, leaving a physiological stamp, partially captured by AL. Here we show that AL predicts subsequent health status by conceptualizing health as a measure beyond the classic definition of pathology, taking into account self-reported measures that could capture health capacities and resources, rather than clinically diagnosed categories of pathology or mortality.

These findings may add a conceptual validity to the hypothesis that social challenges become biologically embedded. The results showed the important role of socioeconomic factors across the life course for both men and women, the most important variables affecting subjective health being behaviours and material circumstances at 33y (model 4). Material circumstances have previously been linked via low socioeconomic position, to different measures of health status, through exposures related to bad housing, work conditions, neighborhood characteristics, etc. (toxins, allergens, overcrowding) (Galobardes et al., 2006). In terms of health behaviours, smoking, alcohol and BMI had the strongest effects on subjective health. Concerning BMI our findings are consistent with previous literature were BMI was found to correlate with well-being and health related quality of life (Ford et al., 2001). Obese individuals are more likely to suffer from low self-esteem, depression (Luppino et al., 2010) and discrimination with a well-established link between BMI and metabolic status, morbidity and mortality (Berrington de Gonzalez et al., 2010; Calle et al., 1999; Ferrucci and Alley, 2007).

5. Conclusion

In this study we show evidence of a link between physiological wear-and-tear, as measured by allostatic load, and health status, captured by latent variable of subjective health. These findings add some evidence to the hypothesis of a plausible biological underlying mechanism between the social environment and later overall health, via stress response systems. Allostatic load may represent a physiological outcome of embodiment processes contributing to a better understanding of early disease processes and social gradients in health. Hence, using a physiological index to grasp how the environment in which we live can "get under the skin" leading to poor health is of great interest in public health research.

Conflict of interest

The authors declare no conflict of interest.

Role of the funding source

C.B.S. is supported by the University of Costa Rica and funded by the European Commission (Horizon 2020 grant no. 633666). The present work is part of the Incorporation Biologique et Inégalités Sociales de Santé project supported by funds from Agence Nationale de la Recherche (ANR-12-DSSA-0004).

Acknowledgments

We thank the cohort members who are part of the 1958 National Child Development Study. C.B.S. is supported by the University of Costa Rica and funded by the European Commission (Horizon 2020 grant no. 633666). The present work is part of the Incorporation Biologique et Inégalités Sociales de Santé project supported by funds from Agence Nationale de la Recherche (ANR-12-DSSA-0004).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.psyneuen.2016.08.018.

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