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ORIGINAL ARTICLE

Social and Material Adversity from Adolescence to Adulthood and Allostatic Load in Middle-Aged Women and Men: Results from the Northern Swedish Cohort

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Abstract
Background Little is known about the theoretically assumed association between adversity exposure over the life course and allostatic load in adulthood.
Purpose This study aims to examine whether social and material adversity over the life course is related to allostatic load in mid-adulthood.
Methods A 27-year prospective Swedish cohort (N=822; 77% response rate) reported exposure to social and material adversities at age 16, 21, 30 and 43 years. At age 43, allostatic load was operationalized based on 12 biological parameters.
Results Social adversity accumulated over the life course was related to allostatic load in both women and men, independently of cumulative socioeconomic disadvantage. Moreover, social adversity in adolescence (in women) and young adulthood (in men) was related to allostatic load, independently of cumulative socioeconomic disadvantage and also of later adversity exposure during adulthood.
Conclusion Exposure to adversities involving relational threats impacts on allostatic load in adulthood and operates according to life course models of cumulative risk and a sensitive period around the transition into adulthood.

Keywords Allostatic load · Life course · Stressors · Prospective study

Introduction

There is plenty of evidence that unfavorable environmental conditions are related to poor physical health, but the mechanisms are not completely understood. One plausible pathway linking environmental conditions to the development of bodily disease is the model of allostatic load [1]. However, although allostatic load is conceptualized within a framework of lifelong development, the life course origins of allostatic load have so far barely been investigated. The present study aims to make a contribution to this task.

Allostatic load represents cumulative dysregulations which eventually develop across multiple interconnected physiological systems as a result of frequently repeated or chronic activation over the life course. Although there is no consensus about the precise operationalization of allostatic load [2, 3], the different formulations used in the literature are hypothesized to reflect a common underlying metafactor of multisystem interrelationships [4]. Allostatic load has been shown to predict various health outcomes in longitudinal studies, such as declines in physical and cognitive functioning, and cardiovascular morbidity and mortality [2, 5, 6]. In support of the hypothesis that allostatic load can arise

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from adverse environmental circumstances, several cross-sectional studies have demonstrated relationships between allostatic load (or similar constructs) and specific kinds of life demands, such as lack of social support/integration [3, 7–9] and work stress [10, 11]. Research suggests that the development of allostatic load might be more influenced by the accumulation of a range of different adversities than by single exposures [12, 13] but also that it might be important to take different types of demands into consideration [14].

Two types of environmental exposures have dominated research on social determinants of health: psychosocial factors and material deprivation. Psychosocial theories focus on interpersonal relationships [15] and include factors of subjective appraisal as well as social exposures of a more "objective" character: concrete manifestations of interpersonal relationships such as the social network, work control, and interpersonal conflict, as mediated by psychological mechanisms [16, 17]. Material deprivation, in contrast, refers to hazardous exposures related to physical or economic circumstances, e.g., inadequate physical living conditions or lack of financial means. So far, allostatic load in adulthood has predominantly been studied in relation to psychosocial factors such as perceived life stress and sense of coherence [14, 18, 19], acute and chronic social stressors such as exposure to life events and social isolation [18, 20], and in relation to structural conditions such as socioeconomic position [21]. Given that interpersonal stressors are powerful activators of physiological stress systems [22], the primary mediators of allostatic load [23], it is conceivable that chronic or frequent exposure to significant social stressors could contribute to allostatic load. Material factors are generally thought to act by nonpsychological mechanisms, but it has also been suggested that both material and social conditions impact on health through the physiological effects of their emotional and social meanings [24], and that the health effects of material conditions act through interpersonal processes [25, 26]. Material exposures such as crowding and low housing quality have been shown to relate to allostatic load in childhood and adolescence [27, 28], but so far little research has been done in adults. Thus, material factors might be of interest as environmental sources of allostatic load in adulthood.

One of the central tenets of the allostatic load model is that allostatic load is a consequence of lifelong insults [1, 3, 29]; "an 'historical' index of prior physiologic toll" [29]. However, the life course origins of allostatic load in adulthood have scarcely been examined [30, 31], and based on retrospective data, the hypothesis that a life course history of stressful conditions is central to the development of allostatic load has been questioned [7]. To the authors' knowledge, only one small-sized study (n=84) has prospectively examined the association between adversity over the life course and allostatic load in adulthood [31].

To shed light on this issue, conceptual models proposed within life course epidemiology might be useful [32, 33]. The model of allostatic load highlights accumulation of insults as a major cause of allostatic load, which is consistent with a life course model of "cumulative risk". The cumulative risk model postulates that the accumulation of exposures over the life course, irrespective of timing of exposure, is of prime importance for adverse health effect to occur later in life. However, there is also evidence that early adversity in childhood and adolescence might result in enduring physiological dysregulations [34, 35], corresponding to a "sensitive period" (or "critical period") life course model. The sensitive period model states that early exposures (e.g., during fetal period, childhood, or adolescence) act directly by impacting on bodily processes at an early age, independently of later exposures in adulthood, e.g., by tracking of biological parameters over the life course and thereby affecting health status in adulthood. Cumulative adversity seems to be capable of impacting on key regulatory systems as early as in childhood [27, 28], thus corroborating that the sensitive period model is a plausible alternative hypothesis to the cumulative risk model. Conversely, there is evidence that early family conditions relate to metabolic disturbances in adulthood partly through adult social circumstances [36], through the relationship between adversity in childhood and subsequent unfavorable social circumstances in adulthood. This pattern is consistent with a "social chain of risk" or "social pathway" life course model, which hypothesizes that childhood circumstances influence adult health indirectly by setting an individual on an unfavorable life trajectory which eventually will affect adult health. Thus, the cumulative risk, sensitive period, and social pathway models all appear to describe life course processes potentially relevant for the development of allostatic load in adulthood, but these issues have not been examined in previous research. Although empirical disentanglement of life course models is a difficult task [37] and different processes may operate in parallel over the life course, the life course origins conceptually integral to the allostatic load model has to be elucidated.

To address the understudied question of the life course origins of allostatic load, the general aim of the present report was to investigate whether exposure to social and/or material adversity over the life course is related to allostatic load in mid-adulthood. Specifically, we aimed to examine to what degree associations between social and material adversity and allostatic load are explained by (1) the accumulation of adversity (the cumulative risk model), and if adversity during specific life course periods are of

particular importance; (2) independently of (sensitive period model); or (3) explained by (social pathway model) subsequent life course adversity.

Methods

Participants and Procedures

The sample was based on the Northern Swedish Cohort, a 27-year prospective cohort study comprising all pupils who entered or who should have entered the ninth grade of the Swedish compulsory school in the town of Luleå in 1981, at 16 years of age (N=1,083; 506 girls and 577 boys). Follow-up surveys were conducted when the participants were 18 (1983), 21 (1986), 30 (1995), and 43 (2008)years of age. The cohort has in various comparisons been found to be representative of the Swedish population [38]. To represent different life course periods, the present report is based on data from the 1981, 1986, 1995, and 2008 surveys. Of the original cohort, there were 1,071 subjects still alive in 2008, of which 1,010 (94%) agreed to participate in the survey at age 43. The high retention rate was accomplished by considerable work directed at tracing all participants across the years, a task facilitated by the Swedish personal identity numbers, and by conveying the results to the participants after each data collection to maintain their willingness to participate.

At each survey, participants completed a comprehensive questionnaire on social, working and financial conditions, health, medication, and leisure activities. In 2008, a health examination was performed by trained medical personnel, comprising measurements of blood pressure, height, weight, and waist circumference according to the World Health Organization MONICA manual [39], and blood samples were drawn after an overnight fast. Participants also performed salivary cortisol sampling with Salivettes during one weekday (at awakening, 15 min post-awakening, pre-lunch, and at bedtime; for details, see [34]). The blood and saliva samples were handled, stored, and analyzed according to the laboratory routines at the Dept of Clinical Chemistry, Umeå University Hospital (see Electronic Supplementary Material: Assay Description for information on the assays). The study was approved by the Regional Ethical Review Board in Umeå and informed consent was provided by all participants at all surveys.

The effective sample size for the main analyses of the present report is N=822 (77%, 394 women and 428 men). The main dropout was due to incomplete biological data at age 43 (n=148), with additional dropout due to item nonresponse in questionnaires (n=40).

Measures

Social and Material Adversity over the Life Course

Adversity was conceptualized as objective environmental exposures which, on theoretical and empirical grounds, might be related to health or child development. The operationalization of adversity was based on the questionnaires completed by the participants at age 16, 21, 30, and 43 years. The majority of items originated from the Swedish Survey of Living Conditions [40] and the Level of Living Surveys [41]. As different versions of the questionnaire were used at different ages (primarily in order to make the questions age relevant), the set of adversities also varied between measurements. The majority of adversity items had binary response options. Accordingly, the remaining items, which for the most part were markedly skewed, were dichotomized as close as possible to the sample 80th percentile to yield comparable frequencies across all adversities. The number of material and social adversities, respectively, was added up for each age (i.e., at age 16, 21, 30, and 43 years) to form age-specific adversity scores, and across all ages to form a cumulative adversity score over the life course. Thus, eight age-specific and two life course adversity scores were constructed: social adversity at age 16 (theoretical range 0–3), 21 (0–3), 30 (0–6), 43 (0–6), and accumulated over the life course (0–18); and material adversity at age 16 (0–3), 21, (0–3), 30 (0–4), 43 (0–4), and accumulated over the life course (0–14). See Electronic Supplementary Material: Supplementary Table 1 for the operationalization of each adversity, and Table 1 for descriptive statistics of the final adversity indices used in the analysis.

Social adversity Social adversity was defined as acute or chronic exposures which hypothetically would impact on health mainly by directly threatening salient relationships. *Parental loss* (*age 16*) was defined as experience of either parental separation/divorce, or death of either parent, or parents never living together. *Residential instability* (*age 16 and 21*) was based on how many times the participant had moved in their lifetime (at age 16) or during the last 3 years (at age 21), dichotomized at the 80th percentile. *Parental illness* (*age 16*) was defined as one or both parents having a physical illness, mental problems, and/or alcohol or drug problems, as reported by the adolescent. *Illness* and *death* (*age 21*, *30*, *and 43*) were defined as someone close suffering from serious or long-term illness, and if someone close had died, respectively, during the last 3 years (21 years), 12 months (30 years), or 5 years (43 years). *Separation* (*age 30 and 43*) was defined as break-up from a long-term relationship involving cohabituation during the last

Table 1 Descriptive statistics of key variables and differences between women (n=394) and men (n=428)

Variable	Women		Men		Difference
	Sample range	*M* (SD)	Sample range	*M* (SD)	*p* Value
Allostatic load	0–12	5.43 (2.49)	0–12	5.65 (2.42)	0.195[a]
Social adversity					
Age 16	0–3	0.72 (0.81)	0–3	0.71 (0.80)	0.976[b]
Age 21	0–3	0.89 (0.90)	0–3	0.60 (0.78)	<0.001[b]
Age 30	0–6	1.02 (0.98)	0–5	0.89 (0.97)	0.034[b]
Age 43	0–6	1.68 (1.27)	0–6	1.56 (1.24)	0.214[b]
Life course	0–14	4.30 (2.36)	0–11	3.76 (2.24)	<0.001[b]
Material adversity					
Age 16	0–3	0.57 (0.72)	0–3	0.36 (0.60)	<0.001[b]
Age 21	0–3	0.55 (0.70)	0–3	0.51 (0.65)	0.463[b]
Age 30	0–4	0.86 (1.01)	0–4	0.66 (0.82)	0.017[b]
Age 43	0–4	0.53 (0.79)	0–4	0.37 (0.71)	<0.001[b]
Life course	0–13	2.51 (2.09)	0–10	1.90 (1.75)	<0.001[b]
Cumulative socioeconomic status	0–4	1.27 (1.19)	0–4	1.25 (1.16)	0.941[b]

[a] *t* Test

[b] Mann–Whitney *U* test

12 months (at age 30) or since the age of 30 (at age 43). *Social isolation* (*age 30 and 43*) was based on the total score of four items from the Availability of Social Integration scale of the Interview Schedule for Social Interaction [42]. *Low decision latitude* (*30 and 43 years*). Participants responded to six items about decision latitude (four items on skill discretion and two items on decision authority) [43], with responses on a four-level Likert scale. All items were added up and dichotomized at the 20th percentile. *Exposure to threat/violence* (*age 30 and 43*) was, due to low frequencies, defined as a positive response on either of four items: personal persecution at work through mean words and actions from bosses or colleagues, sexual harassment through unwelcome or degrading sexual insinuations, physical violence, threats of violence that were so serious that she or he was scared during the last 12 months.

Material adversity Material adversity was defined as exposure to unfavorable circumstances mainly related to the immediate physical environment or the financial situation. *Parental unemployment* (*age 16*) was defined as one or both parents being unemployed or granted disability pension at the time of the survey. *Poor material standard of living* (*age 16*) was based the presence of on the number of material items in the family's possession, from a list of ten items (e.g., color television and car), dichotomized at the 20th percentile. *Residential crowding* (*age 16*) was defined as the participant not having her/his own room. *Low income* (*age 21*) was defined as a self-reported monthly income <20th percentile. *Unemployment* (*age 21*, *30*, *and 43*) was defined as currently being in unemployment or on disability pension. *Low cash margin (age 21*, *30*, *and 43*) was defined as not being able to raise a certain amount of cash within a week (5,000 SEK at 21 years of age, 13,000 SEK at 30, and 15,000 SEK at 43 years). *Spousal unemployment* (*age 30 and 43*) was defined as the participant's partner being unemployed during the last 5 years (age 30), or currently unemployed or on disability pension (age 43). *Financial strain* (*age 30 and 43*) was based on a question about how often the respondent was forced, due to financial reasons, to abstain from any out of 11 different material needs (e.g., eat a cooked meal, buy clothes, and pay the rent or other invoices). The response options were "often", "seldom", "never", or "not applicable". The number of "often" responses was dichotomized at the 80th percentile.

Allostatic Load at Age 43

Allostatic load was defined according to a previously defined operationalization, described in detail elsewhere [30], from the biological measures collected in 2008. Briefly, allostatic load was based on the following 12 biological parameters: systolic and diastolic blood pressure (mmHg), body mass index (BMI, kg/m^2), waist circumference (cm), fasting glucose, total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (mmol/L), circulating levels of apolipoprotein A1 and B, C-reactive protein (mg/L), and diurnal salivary cortisol area under the curve (AUC, log nmol/L×h) (see Electronic Supplementary Material: Assay Description). Each parameter was divided into tertiles (coded 0, 1, 2) separately for women and men, except for cortisol (coded symmetrically with sextile 1 and

6=2, 2 and 5=1, 3 and 4=0) and HDL cholesterol (coded inversely: 2, 1, 0). Furthermore, because C-reactive protein levels were truncated <3 mg/L and to reduce the influence of ongoing infection, C-reactive protein levels were only coded into two groups: <3 and >10 mg/L=0 (n=554, 67%, of which n=32 >10 mg/L) and 3–10 mg/L=2 (n=268, 33%). To take into account the unbalanced number of parameters measuring similar physiological aspects, mean parameter scores were calculated within six physiological systems usually considered part of the allostatic load concept [2]: cardiovascular regulation (systolic and diastolic blood pressure), body fat deposition (BMI and waist circumference), lipid metabolism (total and HDL cholesterol, triglycerides and Apolipoprotein A1 and B), glucose metabolism (fasting glucose), inflammation (C-reactive protein), and neuroendocrine regulation (cortisol AUC). To consider the fact that the presence of medication might disguise the development of allostatic load, pharmacological treatment was coded as 2 on the affected physiological system categories (antihypertensive medication on cardiovascular regulation; lipid-lowering medication on lipid metabolism; and diabetes medication on glucose metabolism). Because salivary cortisol sampling was incomplete for a large number of respondents (n=123), we imputed those without valid cortisol data to the mean value 1 on the neuroendocrine variable to avoid excluding them from the analysis (the imputation of cortisol was taken into consideration in the coding, i.e., the final neuroendocrine variable had a uniform distribution across the levels 0, 1, and 2). Finally, the scores of the physiological systems were summed up into an index (range 0–12), yielding the (normally distributed) measure of allostatic load.

Cumulative Socioeconomic Disadvantage over the Life Course

We have previously demonstrated that the life course accumulation of low socioeconomic status (SES) relates to allostatic load [30], and because cumulative SES also could be expected to influence adversity exposure it was considered a potential confounder. Participants' own occupational titles at age 21, 30, and 43 were coded according to the socioeconomic classification system of Statistics Sweden [44]. Manual workers were categorized as low socioeconomic status (=1) whereas nonmanual employees and self-employed were categorized as high SES (=0). For participants who were not currently working and for whom information on previous occupation was not available (only at age 21 and 30), highest educational attainment was used as a proxy. Both parents belonging to the manual worker group defined low SES at age 16 (=1), while having at least one parent in higher groups defined high SES (=0). *Cumulative socioeconomic disadvantage* was defined as the number of life course periods with low SES (range 0–4).

Data Analysis

Descriptive sample statistics of all main variables by sex are shown in Table 1. The effective sample did not differ from those excluded due to incomplete data, either on age-specific or accumulated adversity scores, or on cumulative SES (all p values>0.05, Mann–Whitney U test), but material adversity was borderline significantly more frequent at age 16 and accumulated over the life course in excluded women (both p values=0.062), and at age 16 in excluded men (p=0.057), suggesting that individuals with high levels of material adversity at age 16 were slightly under-represented in the analytical sample.

Because social and material circumstances might impact on metabolic parameters differently in women and men, all analyses were stratified by sex. Multiple linear regression analysis was used as the main statistical method. As the adversity indices at different life course stages comprised different sets of adversities and displayed only weak correlations with each other (Table 2), they were treated as independent predictors in the analysis.

The cumulative risk model was examined by regressing allostatic load on cumulative social and material adversity, first separately by simple regression, and then mutually adjusted by multiple regression in order to examine whether accumulated social and material adversity contributed to allostatic load independently of each other. To ascertain that life course SES did not confound any association between adversity and allostatic load, cumulative SES was added in a separate model. To examine whether adversity at specific life course periods was particularly important for allostatic load, and whether this contribution was independent of later adversity exposure (corresponding to a sensitive period life course model), or instead explained by higher risk for adversity exposure later in life (corresponding to a social pathway life course model), allostatic load was regressed on social and material adversity at all life course periods. Bivariate associations were first examined by simple regression analyses, extended to mutual adjustment for social and material adversity, with adversity variables introduced sequentially according to age at exposure, adding cumulative SES in a final model. Independence was assessed by change of standardized regression coefficients after adjustment for later adversity exposure.

Multicollinearity was present only at a moderate level throughout the analyses; in the fully adjusted model, maximum variance inflation factor was <1.42 for women and <1.30 for men, suggesting that jointly explained variance would not greatly interfere with the interpretation

Table 2 Zero-order correlations (Pearson's *r*) between independent variables in women (below diagonal, italics) and men (above diagonal)

Variable	Social adversity (SA)					Material adversity (MA)					SES[a]
	Age 16	Age 21	Age 30	Age 43	Life course	Age 16	Age 21	Age 30	Age 43	Life course	Life course
SA 16	–	0.17***	0.04	0.10*	0.49***	0.20***	0.05	0.16***	0.14**	0.22***	0.05
SA 21	*0.03*	–	0.01	0.16***	0.51***	0.04	−0.01	0.09	0.10*	0.09	0.01
SA 30	*0.15***	*0.07*	–	0.21***	0.57***	0.02	0.05	0.26***	0.17***	0.22***	0.24***
SA 43	*0.16***	*0.05*	*0.28****	–	0.74***	0.11*	0.11*	0.22***	0.31***	0.31***	0.26***
SA LC	*0.50****	*0.45****	*0.64****	*0.73****	–	0.16**	0.10*	0.32***	0.33***	0.37***	0.27***
MA 16	*0.16***	*−0.03*	*0.20***	*0.14***	*0.21****	–	0.12*	0.18***	0.18***	0.54***	0.14**
MA 21	*0.05*	*0.04*	*0.12**	*0.16***	*0.17****	*0.15***	–	0.10*	0.21***	0.55***	0.00
MA 30	*0.13***	*0.13**	*0.26****	*0.29****	*0.36****	*0.07*	*0.28****	–	0.32***	0.70***	0.16***
MA 43	*0.09*	*0.08*	*0.26****	*0.43****	*0.39****	*0.13***	*0.26****	*0.37****	–	0.69***	0.26***
MA LC	*0.17****	*0.10*	*0.34****	*0.41****	*0.45****	*0.48****	*0.62****	*0.74****	*0.69****	–	0.23***
SES	*0.16***	*0.06*	*0.29****	*0.30****	*0.35****	*0.22****	*0.18****	*0.37****	*0.34****	*0.45****	–

*$p<0.05$, **$p<0.01$, ***$p<0.001$

[a] *SES* cumulative socioeconomic status

of partial beta weights. The main analyses were rerun excluding those with missing cortisol data who had been assigned the middle value 1 ($n=123$). The coefficient estimates in these complementary analyses were comparable to those based on the full sample (data not shown), with the possible exception of social adversity for men in the fully adjusted analysis, which did not reach significance level ($\beta=0.10$, $p=0.071$). To preserve power and avoid selection bias, only results based on the full sample are reported in the "Results" section. As there is some controversy about how to handle high C-reactive protein values, which can indicate infection [45, 46], the analyses were rerun both with exclusion of the cases with C-reactive protein >10 mg/L, and in models where C-reactive protein >10 mg/L were coded as 2 instead of 0. The analyses yielded similar regression estimates and *p* values (data not shown). We also reran the main analyses with an allostatic load formulation in which the 12 individual components rather than the six systems were summed up; these complementary analyses lead to similar results as those presented (data not shown).

Results

As can be seen in Table 1, women reported more social and material adversities over the life course than did men. Table 2 displays zero-order correlations between exposures in women and men. Both social and material adversity at age 16 correlated weakly with the corresponding adversity indices at age 43 in both women and men, indicating that early adversity involved a slightly greater risk for adverse life circumstances later in adulthood. Cumulative SES over the life course was related to both social and material cumulative adversity, numerically slightly more strongly in women ($r=0.35-0.45$) than in men ($r=0.23-27$).

In simple regression analyses (Table 3, model 0), allostatic load was related to both social and material cumulative adversity measures in women but only to social adversity in men, and cumulative SES was related to allostatic load in both women and men. In women, mutual adjustment for social and material adversity (Table 3, model 1) substantially attenuated the standardized regression coefficient (β) for material adversity (below significance), whereas the coefficient for social adversity was only slightly attenuated by adjustment for cumulative SES (model 2). Comparable but less pronounced findings were found in men. Cumulative social and material adversity jointly explained 4.6% of the variance in women and 2.0% in men.

As an examination of the contribution of adversity at specific life course periods (Table 4), simple regression analyses in women showed that allostatic load was related to social adversity at age 16 and 43 ($\beta=0.16$, $p=0.001$), and to material adversity at age 30 ($\beta=0.11$, $p=0.036$) and 43 ($\beta=0.16$, $p=0.002$). Sequential introduction of the adversity measures at each life course period showed that social adversity at age 16 and 43 remained significant after adjustment for adversity at the other life course periods (model 3), suggesting that adolescence was a sensitive period for the physiological impact of social adversity but that contemporaneous social adversity also was important. Coefficients only changed slightly by the addition of cumulative SES (model 4).

In men, social adversity at age 21 and material adversity at age 43 contributed to allostatic load in bivariate analyses

Table 3 Summary of linear regression models in women (n=394) and men (n=428), with allostatic load on cumulative social and material adversity over the life course in simple regressions (model 0), with mutual adjustment for both social and material adversity (model 1), adding cumulative socioeconomic status (SES; model 2)

Estimate	Model 0	Model 1	Model 2
Women			
Predictor estimates, β (p)			
Cumulative social adversity	0.21 (<0.001)	0.20 (<0.001)	0.18 (0.001)
Cumulative material adversity	0.12 (0.014)	0.04 (0.531)	0.01 (0.854)
Cumulative SES	0.14 (0.007)	–	0.07 (0.234)
Model R^2 (shrunken R^2)	–	0.046 (0.041)	0.049 (0.042)
Model p	–	<0.001	<0.001
Men			
Predictor estimates, β (p)			
Cumulative social adversity	0.14 (0.003)	0.14 (0.009)	0.12 (0.022)
Cumulative material adversity	0.07 (0.171)	0.02 (0.768)	0.00 (0.937)
Cumulative SES	0.11 (0.028)	–	0.07 (0.147)
Model R^2 (shrunken R^2)	–	0.020 (0.016)	0.025 (0.018)
Model p	–	0.012	0.012

Predictor estimates are standardized regression coefficients (β) and p values

Table 4 Summary of linear regression analyses in women (n=394) and men (n=428): allostatic load on social and material adversity at each age in simple regression (model 0), mutual adjustment for social and material adversity at age 16 (model 1), age 16 and 21 (model 2), age 16, 21, 30, and 43 (model 3), adding cumulative socioeconomic status (SES; model 4)

Estimates	Model 0	Model 1	Model 2	Model 3	Model 4
Women					
Predictor estimates, β (p)					
Social adversity, age 16	0.16 (0.001)	0.16 (0.001)	0.16 (0.002)	0.14 (0.008)	0.13 (0.010)
Material adversity, age 16	0.02 (0.758)	−0.04 (0.829)	−0.04 (0.832)	−0.03 (0.569)	−0.04 (0.460)
Social adversity, age 21	0.07 (0.153)	–	0.07 (0.180)	0.05 (0.282)	0.05 (0.285)
Material adversity, age 21	0.02 (0.648)	–	0.01 (0.794)	−0.03 (0.554)	−0.03 (0.539)
Social adversity, age 30	0.06 (0.211)	–	–	−0.02 (0.724)	−0.03 (0.617)
Material adversity, age 30	0.11 (0.036)	–	–	0.02 (0.674)	0.01 (0.879)
Social adversity, age 43	0.19 (<0.001)	–	–	0.14 (0.015)	0.13 (0.021)
Material adversity, age 43	0.16 (0.002)	–	–	0.09 (0.127)	0.08 (0.183)
Cumulative SES, age 16–43	0.14 (0.007)	–	–	–	0.07 (0.245)
Model R^2 (shrunken R^2)	–	0.026 (0.021)	0.031 (0.021)	0.066 (0.047)	0.069 (0.048)
Model p	–	0.006	0.016	<0.001	0.001
Men					
Predictor estimates, β (p)					
Social adversity, age 16	0.09 (0.077)	0.10 (0.047)	0.08 (0.124)	0.06 (0.204)	0.06 (0.199)
Material adversity, age 16	−0.04 (0.361)	−0.06 (0.199)	−0.07 (0.189)	−0.08 (0.103)	−0.09 (0.075)
Social adversity, age 21	0.13 (0.005)	–	0.12 (0.012)	0.11 (0.020)	0.12 (0.017)
Material adversity, age 21	0.00 (0.968)	–	0.01 (0.881)	−0.02 (0.717)	−0.01 (0.818)
Social adversity, age 30	0.08 (0.109)	–	–	0.06 (0.266)	0.04 (0.410)
Material adversity, age 30	0.06 (0.247)	–	–	0.00 (0.991)	0.00 (0.983)
Social adversity, age 43	0.06 (0.234)	–	–	−0.01 (0.906)	−0.02 (0.712)
Material adversity, age 43	0.13 (0.006)	–	–	0.12 (0.021)	0.11 (0.044)
Cumulative SES, age 16–43	0.11 (0.028)	–	–	–	0.08 (0.118)
Model R^2 (shrunken R^2)	–	0.011 (0.007)	0.026 (0.017)	0.045 (0.027)	0.050 (0.030)
Model p	–	0.092	0.025	0.013	0.009

Predictor estimates are standardized regression coefficients (β) and p values

(model 0), independently of the other adversity measures (model 3) and of cumulative SES (model 4), suggesting young adulthood as a sensitive period for social adversity and also indicating an importance of current material conditions.

The adversity measures at age 16 and 21 comprised only three adversities each and the estimated contribution of social adversity could therefore be particularly sensitive to the presence of some particular adversity. Therefore, analyses were rerun with three reduced formulations of social adversity, excluding one of the three adversities from the adversity index in each analysis. The significant contribution of social adversity at age 16 in women remained in the adjusted model (corresponding to model 4) after excluding residential instability (β=0.13, p=0.009), parental loss (β=0.10, p=0.044) or parental illness (β=0.11, p=0.040), indicating that the demonstrated association was not merely explained by the presence of some particular adversity. Corresponding analyses of social adversity at age 21 in men showed that the contribution of social adversity at age 21 remained significant in the adjusted model after excluding illness of a close one (β=0.15, p=0.002), but dropped below significance after excluding death of a close one (β=0.08, p=0.109) or residential instability (β=0.08, p=0.101), suggesting that death of a close one and residential instability were important for the estimated contribution of social adversity at age 21 in men.

Discussion

The present study is the first prospective community-based study investigating life course exposure to adversity and allostatic load in adulthood. Our results support the hypothesis that allostatic load in mid-adulthood is influenced by the accumulation of unfavorable social exposures over the life course, but also by social adversity measured around the transition into adulthood, independently of later adversity. Thus, we found support for both the cumulative risk and the sensitive period life course models, but little support for a social pathway model. With regard to quality of exposure, the contribution of material adversity seemed to be dependent on social adversity, whereas social adversity was the exposure domain most consistently and independently related to allostatic load.

The earliest adversity exposure was measured at age 16 but can, at least partially, reflect family circumstances from earlier in childhood. It has previously been shown that cumulative stressor exposure is related to allostatic load [27] and to other aspect of stress physiology [47] as early as in childhood, and that parental responsivity can affect the physiological impact of cumulative stressor exposure in childhood [28]. The present study suggests that social stressors around the transition into adulthood might leave enduring physiological traces into mid-adulthood, to a considerable degree independently of the amount of adversity encountered later in the adult life course. The estimated effect sizes were modest; e.g., cumulative adversity and adversity at age 16 explained 4.6% and 2.6%, respectively, of allostatic load variance in women, which would be considered small- to medium-sized effects [48]. Still, it is remarkable that effects were observable despite the fact that in some analyses decades had passed between exposure and outcome, and despite the limited range of measured adversities. Our results highlight adolescence as a sensitive period in women, corresponding to the notion that adolescence may be a developmental period in which stress might confer long-term impact on neuroendocrine circuits involved in the stress response [49]. Adversities such as residential instability and parental separation may lead to disruption of significant social ties, and parental illness might compromise family functioning, which might lead to particular strain for adolescent girls, e.g., due to increased household responsibilities [50]. The observation of adolescent social adversity being significant only in women should not be overstated as similar tendencies were present in men, but is in accordance with studies on a more pronounced effect of childhood socioeconomic status on women's metabolic health in adulthood, e.g., the metabolic syndrome [51]. In men, young adulthood appeared to be the most deleterious period for social adversity exposure to confer long-term physiological dysregulations. The presence of residential instability and death of a close one were essential for a significant effect, perhaps reflecting the importance of social ties at an age when adult relationships are formed.

The cumulative life course effects of adversity reported in the present study corroborate the hypothesis that allostatic load can be a product of repeated adaptations to social challenges over the life course. Our results are consistent with a retrospective study reporting that the accumulation of positive relations in child- and adulthood is related to lower allostatic load [8], but contrary to a retrospective study reporting no association between the life course duration of psychosocial stressors and the neuroendocrine portion of allostatic load [7]. We found that associations were most pronounced in women (e.g., cumulative adversity explaining 4.6% of allostatic load variance in women and 2.0% in men), and women also reported a greater amount of both social and material adversity over the life course. A recent cross-sectional study in middle-aged Mexican–American women by Gallo et al. [14] reports that the subjective appraisal of both

interpersonal (work and caregiving stress) and material (financial strain) stressors were related to allostatic load (explaining 7.1% of variance). Methodological differences preclude any direct comparison, but our results in women are quite similar with adversities over the life course jointly explaining 6.6% of variance and with independent contributions mainly of concurrent social (β=0.14) and material (β=0.09) adversity, but notably also of social adversity at age 16 (β=0.14).

The apparent importance of interpersonal exposures—accumulated over the life course and around the transition into adulthood—is consistent with the observation that social stimuli are powerful activators of physiological stress systems [22]. More specifically, relational aspects of the environment have been put forward as key environmental causes of chronic stress-related physiological adaptations [8, 11, 52, 53]. The weak and nonsignificant impact of material circumstances in adolescence on adult allostatic load might possibly be explained by marital and parent–adolescent relational processes mediating the effects, in contrast to adulthood when material hardship might impact more directly on the individual [26]. Indeed, in both women and men, the contribution of material adversity to allostatic load seemed to be stronger for exposure during later life course periods. Allostatic load is a specific form of physiological disturbance which, although sensitive to a range of exposures [29], is conceptualized within a psychoneuroendocrinological framework. Although early material circumstances might be mediated by physiological effects of their emotional and social meaning, they might also impact on health status more directly [24], such as by increasing the risk for early acquired infections [54], and by exacerbating the influence of early life growth on later hypertension [55]. Our findings of a comparatively weak independent influence of material condition might thus be a result of allostatic systems being particularly sensitive to social demands, but could also indicate that the effect of material hardship is largely mediated by social relationships. It is conceivable, and in accordance with the allostatic load model that the demonstrated associations are mediated by psychological pathways (e.g., distress) at some period(s) during the life course, eventually leading to physiological dysregulations. It is also possible that unhealthy behaviors (e.g., as a way of coping with psychological distress) could mediate the associations, but previous findings suggest that health behaviors do not explain the association between life stress and allostatic load to any substantial degree [14]. More research is needed to identify the key mediational processes.

Cumulative SES did not substantially attenuate the contribution of adversity to allostatic load, suggesting that the observed associations were not simply explained by the higher risk for adversity exposure among those with low SES across the life course. Of interest is also the observation that although cumulative SES was related to allostatic load, a finding that we have reported previously [30], the effect was substantially attenuated by the addition of cumulative adversity. This observation is consistent with the hypothesis that socioeconomic determinants of health are mediated by relational and material pathways [24, 25]. Considering that allostatic load is a decent predictor of clinical morbidity [5, 6], our findings might very well signify pathways by which socioeconomic disadvantage contributes to the development of manifest disease over the life course.

Methodological Considerations

Important methodological strengths of the study include the large community-based sample and the prospective design. Retrospective recall of childhood conditions in adulthood can be subject to recall bias [56], and short-term retrospective and concurrent reports are therefore preferable. Although there was a moderately large drop-out with respect to biological markers at age 43, the low overall attrition rate across the 27 years allowed us to explore potential systematic drop-out. The little evidence of systematic drop-out found and the fact that attrition due to death was minor (n=12) suggests that selection bias is not substantial. For the 123 cases with missing cortisol measurements, neuroendocrine system values were imputed by mean substitution; complete case analyses indicated no major deviations from the estimates found in the full sample, although the coefficient for social adversity at age 21 for men did not quite reach significance. As both hyper- and hypocortisolism indicate dysregulation, other approaches such as multiple imputation might not be suitable. Moreover, the parameterization anyhow involved a substantial loss of variance as a result of component trichotomization, and cortisol only represented 1 out of 12 components, which suggests that the choice of imputation would have no major impact on the estimates.

There is no consensual operational definition of allostatic load. Our operationalization [30] attempts to reflect allostatic load as a continuous concept including subclinical dysregulations across multiple physiological systems [29], while also including information on medication that could conceal the presence of dysregulations. The included parameters tap into the physiological systems usually considered parts of allostatic load [2]. Weighting of parameters was done to reduce the problem of an unbalanced number of parameters within each physiological system, which otherwise would result in particular physiological systems contributing disproportionally to the variation in allostatic load. However, the systems comprising more

parameters would still be expected to be measured with greater reliability, and the individual parameters may also differ with respect to physiological stability and reliability of measurement. For example, even small delays in awakening sampling of salivary cortisol might impact on estimated cortisol levels in the morning, and in this study sampling was done by the participants themselves with self-reported sampling times (see [34] for further details of the saliva sampling), which might contribute to measurement error [57].

The present study focused on the differential impact of classes of exposures based on an a priori distinction of social vs. material exposures, which has received much interest in current research on social determinants of health [24]. Because exposures with similar qualitative characteristics theoretically can be similarly related to an outcome regardless of the presence of clustering of said exposures, i.e., without the existence of a latent construct, factor analysis was not utilized to determine the categorization of individual exposures.

Estimating total exposure to acute and chronic stressors over the life course is a daunting task [3], and our operationalizations, measured at four time points, include only a limited sample of the theoretical total exposure. Although there are theoretical and empirical grounds to suspect that each individual adversity might activate physiological stress systems, some adversities might also act as markers or causally precede other factors, rather than exert a direct causal effect. For example, the adult health impact of childhood residential instability might be explained by the clustering of other childhood adversities [58]. Therefore, the present study cannot ascertain to what degree the estimated relationships represent true causal chains or are a consequence of unmeasured confounders. It is possible that the apparent effect of the simple count of adversities is confounded by the severity of exposures [59] or by qualities not considered, such as stressor domains [14]. Mental illness could also put an individual at risk for adversity exposure and thus act as a confounder rather than a mediator, or bias the reports of adversities, e.g., by over-reporting of adversities in attempts to give meaning and explanation to suffering [60].

Most adversities were measured by binary response options and the adversities measured with ordinal responses were asymmetrically distributed. These circumstances make operations such as converting to z scores dubious, which is why we chose to dichotomize all adversities prior to constructing the adversity indices. The precision of measurement might vary between individual adversities, and such issues could have contributed to the estimated attenuation of cumulative material adversity by social adversity [16]. There were few adversities included at age 16 and 21, but at least for social adversity at age 16 in women, the results remained unchanged when excluding each individual adversity, indicating that the results are not driven by a particular exposure. Similar to other studies measuring exposures at one point during childhood/adolescence, we cannot disentangle to what degree experiences earlier in childhood explain the findings concerning exposures measured in adolescence.

Although most theoretical models of the stress process also encompass moderating and mediating effects, e.g., subjective appraisal, coping, or contextual factors [61], the focus of the present study was to examine if exposure to environmental stressors relate to allostatic load, analogously to what has been described as an environmental stress perspective [61]. Although measurement of subjective appraisal, which assumedly would mediate a large part of the impact of environmental exposures and thus potentially would strengthen the estimated associations [14], the measurement of subjective appraisal is conceptually and empirically difficult from a life course perspective, e.g., to disentangle the effects of appraisal at the time of the stressful exposure from appraisal and distress related to the exposure but experienced a long time after the cessation of the exposure. This issue is made more problematic by the fact that subjective reports of psychological distress in response to stressors might correlate poorly with the physiological response [22], possibly because other than conscious processes are involved in the activation of stress systems. In concert with other approaches, such as those highlighting the subjective appraisal of stressors [14], our "environmental" approach contributes to the understanding of which environmental exposures, and the subjective appraisal of them, affect bodily systems. Nevertheless, we acknowledge that our adversity measures are crude operationalizations of vastly complex exposures.

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