Attributional styles and stress-related atherogenic plasma lipid reactivity in essential hypertension

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ABSTRACT

Objective: Hypertension and an atherogenic lipid profile are known risk factors for coronary heart disease (CHD). Hypertensives show greater changes in atherogenic plasma lipids to acute stress than normotensives. In this study, we investigated whether attribution of failure is associated with lipid stress reactivity in hypertensive compared with normotensive men.

Methods: 18 normotensive and 17 hypertensive men (mean ± SEM; 45 ± 2.2 years) underwent an acute standardized psychosocial stress task that can be viewed as a situation of experimentally induced failure. We assessed external stable (ES), external variable (EV), internal stable (IS), and internal variable (IV) attribution of failure and psychological control variables (i.e. extent of depression and neuroticism). Moreover, total cholesterol (TC), low density lipoprotein cholesterol (LDL C), and norepinephrine were measured immediately before and several times after stress.

Results: ES moderated TC and LDL C stress reactivity in hypertensives as compared to normotensives (interaction mean arterial pressure [MAP] by ES for TC: $F = 3.71$, $p = .015$; for LDL C: $F = 3.61$, $p = .016$). TC and LDL C levels were highest in hypertensives with low ES immediately after stress ($p \leq .039$). In contrast, hypertensives with high ES did not differ from normotensives in TC and LDL C immediately after stress ($p's > .28$). Controlling for norepinephrine, depression, and neuroticism in addition to age and BMI did not significantly change results. There were no significant associations between lipid baseline levels or aggregated lipid secretion and IS, IV, or EV ($p's > .23$).

Conclusion: Our data suggest that ES may independently protect from elevated lipid stress reactivity in hypertensive individuals. ES thus might be a protective factor against CHD in hypertension.

Introduction

Essential hypertension ranks among the main risk factors for coronary heart disease (CHD) [1] but the underlying mechanisms are not fully understood. A well known classic risk factor for CHD is an atherogenic lipid profile with increased total cholesterol (TC), low density lipoproteine cholesterol (LDL C), and triglycerides (TG) on the one hand, and decreased high density lipoprotein cholesterol (HDL C) on the other [2,3]. Hypertensives tend to have greater TC, LDL C, and TG resting levels, and lower resting levels of HDL C; moreover the prevalence of hyperlipidemia in hypertension is as high as 40% [4]. Psychological stress has increasingly been implied in CHD development [5,6].

Specifically, studies on short term physiological responses to controlled stress induction serve as a window into complex psychological and physiological processes involved in the development of CHD [7]. Recent studies also suggest that elevated physiological stress reactivity or hyper reactivity is an independent CHD risk indicator per se [8 11]. In particular, stress induced hyper activation of the sympathetic nervous system (SNS) including the cardiovascular system [8], and the hypothalamus pituitary adrenal (HPA) axis [9] have been implicated to in crease CHD risk, either by direct effects and/or by inducing adverse changes in intermediate biological risk factors including blood lipids [10,11]. With respect to hypertension, we recently found greater TC and LDL C changes to acute psychosocial stress in hypertensives compared to normotensives [12]. This suggests that hypertensives are particularly susceptible to stress induced elevations in atherogenic lipids. Given the importance of elevated physiological stress reactivity for CHD, the observed heightened TC/LDL C stress reactivity in essential hypertension may provide one mechanism by which stress might increase CHD risk in hypertension.

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In line with such reasoning, it might be of clinical relevance to iden tify conditions that relate to lower TC/LDL C stress reactivity in essential hypertension. We recently found higher social support and beneficial emotional regulation to be related to a reduced stress reactivity of stress hormones in hypertension [13], but studies on this issue are sparse. Pre vious research has suggested links between attributional styles and health outcomes [14 18]. Attributional styles are the habitual manner in which individuals explain positive or negative events in their lives. Seligman's theory of causal attribution distinguishes between an opti mistic and a pessimistic attributional style [19]. The optimistic attribu tional style is characterized by the tendency to explain negative events in terms of external, unstable, and situation specific causes and positive events in terms of internal, stable, and global causes [14,19]. The pessimistic attributional style is defined as the opposite of the opti mistic one. Individuals with an optimistic attributional style are regarded as more optimistic with more favorable expectancies of the fu ture than individuals with a pessimistic attributional style [14]. A variety of studies suggests that optimistic attributional styles or optimism are associated with clinically important benefits in cardiovascular outcomes [18,20 22]. For example, a 10 year large scale longitudinal study dem onstrated a strong association between an optimistic attributional style and lower incidence of CHD [18]. Although the underlying pathways by which an optimistic attributional style or optimism affects cardiovascu lar outcomes are poorly understood, lower physiological stress re sponses are presumed to be involved [23]. The role of attributional styles in the interface between TC/LDL C stress reactivity and hyperten sion has not yet been studied.

The aim of this study was to investigate whether attributional styles might be associated with TC/LDL C stress reactivity in otherwise healthy, middle aged hypertensive men, compared with age matched normotensives. To induce psychosocial stress, we used the Trier Social Stress Test (TSST), a motivated performance task disguised as a job in terview [24]. This standardized stress test combines elements of uncon trollability and social evaluative threat, and creates a context in which participants are unable to get positive feedback despite best effort. Thus, the TSST can be viewed as a situation of experimentally induced failure. We assumed that the habitual manner to attribute failure to ex ternal (e.g. misfortune or task difficulty) but not to internal (e.g. effort or ability) factors might especially be associated with stress preventive ef fects because subjects would not attribute failure as self inflicted. We hypothesized that greater external stable (ES) or external variable (EV) attribution of failure and lower internal stable (IS) or internal variable (IV) attribution of failure would be associated with attenuated increases in atherogenic blood lipids (i.e. TC and LDL C) to acute stress in hypertensives relative to normotensives.

Methods

Participants

The current study is a secondary analysis of a project assessing lipid stress reactivity in essential hypertension [12] and was formally ap proved by the Ethics Committee of the State of Zurich, Switzerland. Due to known gender and menstrual cycle phase related alterations in endocrine stress reactivity [25] we recruited men only. Of a total of 45 participants, 35 men completed our attribution questionnaire. All par ticipants provided written informed consent. With the aid of the Swiss Red Cross of Zurich and through advertisements, we recruited non smoking hypertensive and normotensive men who, apart from hyper tension, were otherwise in good physical and mental health, as confirmed by an extensive health questionnaire and telephone inter view. Specific exclusion criteria, obtained by participants' self report, were as follows: regular strenuous exercise, alcohol and illicit drug abuse, any heart disease, varicosis or thrombotic diseases, elevated blood glucose level and diabetes, elevated cholesterol level, liver and renal diseases, chronic obstructive pulmonary disease, allergies and

atopic diathesis, rheumatic diseases, and current infectious diseases. In addition, participants were included only if they reported no regular or occasional intake of medications. If the personal or medication histo ry was not conclusive, the participants' primary care physician was contacted for clarification.

Assessment of hypertension

After a 15 minute rest, three seated screening blood pressure (BP) measurements were obtained on three separate days by a fully auto mated sphygmomanometry device (Omron 773; Omron Healthcare Europe, Hoofddorp, The Netherlands) and the average BP was comput ed. Participants were categorized into hypertensive and normotensive individuals following the World Health Organization/International Soci ety of Hypertension definition (systolic BP $\geq$ 140 mm Hg and/or diastol ic BP $\geq$ 90 mm Hg) [26]. The screening procedure yielded 17 hypertensive and 18 age matched normotensive men (all with com plete attributional style data) whose characteristics are listed in Table 1. The average mean arterial pressure (MAP) across all individuals according to the formula two thirds diastolic BP + one third systolic BP was used for analysis.

Psychosocial stress procedure

All experimental sessions commenced between 2 pm and 4 pm and lasted for approximately 2 h. Participants abstained from food and drinks (other than water) for 2 h before the experiment, and from phys ical exercise, alcohol, and caffeinated beverages starting the evening be fore the test day. To inflict psychosocial stress, we used the Trier Social Stress Test (TSST). The TSST combines a 5 minute preparation phase followed by a 5 minute mock job interview, and a 5 minute mental ar ithmetic task in front of an audience [24]. The TSST can be viewed as a situation of experimentally induced failure [27] that reliably provokes profound endocrine and cardiovascular responses [24,28]. During the 45 min before introduction to the TSST and for another 60 min after task completion, participants remained seated in a quiet room.

Blood for lipid and norepinephrine (NE) measures was obtained im mediately before stress, immediately after stress, and at 20 min, and 60 min after stress. At the end of blood sampling, participants were debriefed and participation was remunerated with 80 Swiss francs.

Measurements

External and internal attribution of failure

External and internal attribution of failure was measured by the Ger man questionnaire for the assessment of causal attributions (IE SV F; questionnaire for the assessment of internal/external and stable/instable attributions depending on success and failure [Fragebogen zur Erfassung der internalen/externalen und stabilen/variablen Attributionen in Abhängigkeit von Erfolg und Misserfolg] [29]). Using a 5 point rating scale ranging from 1 (not at all) to 5 (absolutely), subjects were asked to rate the extent to which the statements for the given situations of fail ure applied to themselves (e.g. to be more criticized at work is just a co incidence and is independent of my work performance). The subscales external *stable* attribution of failure (consisting of 10 items) and external *variable* attribution of failure (consisting of 9 items) assess the habitual tendency to explain negative events by external stable causes (e.g. task difficulty) or external variable causes (e.g. bad luck), re spectively. The subscales internal *stable* attribution of failure (consisting of 10 items) and internal *variable* attribution (consisting of 11 items) as sess the habitual tendency to explain negative events by internal stable causes (e.g. low ability) or internal variable causes (e.g. lack of effort), respectively. Higher scores reflect a higher tendency to attribute failure to external stable, external variable, internal stable, or internal variable causes. Cronbach's alpha (n = 174) was 0.68 (external stable), 0.69

Table 1
Characteristics of the 35 subjects with complete attributional style assessment

	Hypertensives ($n = 17$)	Normotensives ($n = 18$)	P-ANOVA
Age (years)	45.2 ± 3.6 (22.0–64.0)	46.4 ± 2.7 (28.0–65.0)	.79
BMI (kg/m²)	26.8 ± 0.7 (22.6–33.9)	25.1 ± 0.6 (22.2–32.1)	.07
MAP (mm Hg)	111.5 ± 1.7 (97.8–121.4)	92.1 ± 1.5 (82.8–104.9)	<.001
Cholesterol (mg/dL)	221.8 ± 9.8 (154.0–302.0)	208.7 ± 8.9 (110.0–274.0)	.33
LDL-C (mg/dL)	138.7 ± 5.6 (103.0–181.0)	129.3 ± 6.7 (43.0–167.0)	.30
Norepinephrine (pg/mL)	429.0 ± 28.0 (244.3–650.7)	343.6 ± 27.1 (171.4–533.2)	.035
ES	26.4 ± 1.4 (18–38)	27.7 ± 1.3 (16–38)	.51
EV	23.7 ± 1.4 (14–36)	25.3 ± 1.0 (19–35)	.37
IS	23.2 ± 1.3 (15–39)	21.9 ± 1.0 (13–28)	.41
IV	34.9 ± 2.2 (18–49)	35.9 ± 1.8 (19–45)	.72
Neuroticism	16.0 ± 1.2 (7–24)	15.8 ± 1.0 (9–25)	.91
Extent of depression	12.5 ± 0.8 (9–21)	10.8 ± 0.7 (6–21)	.11

Note: Values given are mean ± SEM and range. Plasma lipid and norepinephrine measures reflect plasma levels at baseline (i.e. immediately before the stressor). BMI, body mass index; MAP, mean arterial pressure; LDL-C, low-density-lipoprotein cholesterol; ES, external-stable attribution of failure; EV, external-variable attribution of failure; IS, internal-stable attribution of failure; IV, internal-variable attribution of failure.

(external variable), 0.79 (internal stable), and 0.66 (internal variable) for the respective IE SV F subscale [29].

Psychological control variables

We assessed the extent of depression and neuroticism based on previous findings suggesting associations with attributional styles and/or optimism [30,31].

Extent of depression. We assessed the extent of depression by means of the short version (15 items) of the "Allgemeine Depressionsskala" (ADS K) [32]. The ADS K is the German version of the "Center of Epidemiological Studies Depression Scale" (CES D) [33]. Using a 4 point rating scale ranging from 0 (rare) to 3 (mostly), participants were asked to rate how often they perceived a variety of depressive symptoms within the last few weeks. Higher scores mean higher extent of depression. Cronbach's alpha (calculated in different samples) is between 0.88 and 0.95 for the ADS K [32].

Neuroticism. Neuroticism was measured by the 6 item subscale of the shortened German version of the NEO Five Factor Inventory (NEO FFI) [34,35]. Answers were given on a 6 point rating scale ranging from 1 (strongly disagree) to 6 (strongly agree). Higher scores mean higher neuroticism. Cronbach's alpha (n = 1908) is 0.81 for the neuroticism subscale [35].

Biochemical measures

Blood lipids. Blood lipids (TC, HDL C, and TG) were measured in plasma (mg/dL) with a calorimetric system (AU, Olympus, Hamburg, Germany) following standard laboratory procedures (Synlab, Augsburg, Germany). LDL C was calculated using the Friedewald formula: LDL C = TC − HDL C − (TG/2.19). Hemoglobin (g/dL) and hematocrit (%) were obtained by processing whole blood collected in 2.7 mL EDTA tubes (Sarstedt, Rommelsdorf, Germany) on an automated hematology system (Advia 120, Bayer Diagnostics, Fernwald, Germany).

Norepinephrine. We previously found that NE stress reactivity predicted higher increases in TC and LDL C in response to acute stress [12]. Therefore, we controlled for NE to account for a potential confounding influence on potential associations between attributional style and lipid stress reactivity. For NE assessment, venous blood was drawn into EDTA coated Monovette tubes (Sarstedt, Numbrecht, Germany) and immediately centrifuged for 10 min at 2000 g. Obtained plasma was stored at −80 °C until analysis. Plasma NE was determined by high pressure liquid chromatography (detection limit, 0.25 pg/mL; inter and intra assay coefficients of variation, <5%; Laboratory for Stress Monitoring, Göttingen, Germany). All samples from the same subject were analyzed in the same run.

Statistical analyses

Data were analyzed using SPSS Inc. version 17.0 for Windows (Chicago, IL, USA) and presented as mean ± SEM. All tests were two tailed with the significance level set at $p \leq .05$. G*Power 3.1. analysis suggests that a total sample size of N = 32 is needed to detect an interaction effect between attributional style and plasma lipid stress reactivity in two groups with an expected medium effect size of $f = .20$ in general models with repeated measures with a power of >.80, $\alpha = .05$, given the observed minimum intercorrelation among repeated measures of .63 and $\varepsilon = .79$. Prior to statistical analyses, data were tested for normal distribution and homogeneity of variance using Kolmogorov Smirnov and Levene's tests.

We corrected all plasma lipid levels for stress hemoconcentration following previous methods by computing stress induced changes in plasma volume (i.e., stress hemoconcentration) from hemoglobin and hematocrit measures according to the formula by Dill and Costill [36]. For plasma lipids (i.e. TC and LDL C), areas under the total response curves with respect to increase (AUCs) were calculated using the trapezoid formula [37]. NE stress changes (ΔNE) were calculated as the difference in NE plasma levels immediately after stress and baseline levels.

Univariate analyses of variance (ANOVAs) were calculated to test for differences in hypertensive vs. normotensive subjects with complete attributional style assessment in terms of demographic characteristics, psychological measures, and baseline levels of plasma lipids and NE.

In order to prevent model overfitting in the subsequent main analyses, we first analyzed data without controlling for any potential confounders. In a second step, we controlled for the cardiovascular risk factors age and body mass index (BMI) as covariates. In a third step, we additionally controlled for depression, neuroticism, and ΔNE as a priori defined set of potential confounders [31,38,39].

To address whether associations between attributional style and plasma lipids differ with hypertension status, we used a two step procedure. We first (step 1) correlated attributional styles (i.e. ES, EV, IS, and IV) with baseline levels and the AUCs of plasma lipids. In order to avoid multiple testing in further analyses, we used those attributional styles that were associated with baseline levels or AUCs of plasma lipids at a level of $p < .15$. Next, we calculated moderator analyses as described by Baron and Kenny [40] (step 2). For resting plasma lipid levels, we first calculated linear regression analyses with pre stress measures of plasma lipids as dependent variables and MAP, significantly associated attributional style variables (ES, EV, IS, and/or IV, respectively), and the interaction between MAP and the respective attributional style score as independent variables. For repeated lipid measures, we

calculated general linear models with repeated measures of plasma lipids as dependent variables. As independent variables, we again entered MAP, significantly with AUC associated attributional style variables (ES, EV, IS, and/or IV, respectively), and the interaction between MAP and the respective attributional style score [13]. According to Baron and Kenny [40] statistical moderation holds if the interaction terms significantly relates to the dependent variable while controlling for the variables composing the interaction term. All variables entered in moderation analyses were Z transformed prior to analysis to allow calculation of interaction terms. Significant moderator effects in terms of significant associations between the respective interaction term and lipid measures were further analyzed by performing a median split on the attributional style scale rendering four subgroups of hypertensives and normotensives with either high or low values in the respective at tributional style variable (i.e. hypertensives with high and low ES, EV, IS or IV, and normotensives with high and low ES, EV, IS or IV). Subgroup differences in plasma lipid measurements were tested by ANOVAs. No tably, we used MAP as a continuous variable instead of categorizing hy pertensives and normotensives in a dichotomous variable to increase the statistical power [41].

Effect size parameters (f) were calculated from partial η^2 values and are reported where appropriate (effect size conventions: f: .10 = small, .25 = medium, .40 = large).

Results

Subjects' characteristics

Table 1 provides the characteristics of the 35 hypertensive and normotensive subjects with complete attributional style assessment. MAP and plasma levels of NE at rest were higher in hypertensives as compared to normotensives.

Attributional style variables and blood lipids

Correlation analyses

Lipid baseline levels. ES scores correlated negatively with LDL-C baseline levels ($r = .32$, $p = .065$). In contrast, there were no significant associations between TC or LDL-C baseline levels and IS, IV, or EV, and between TC baseline levels and ES (p's > .23). Further controlling for age and BMI or the full set of confounders (age, BMI, neuroticism, depression, and ΔNE) did not change the results; the associations between ES and LDL-C baseline levels actually got stronger (r's ≥ .37; p's ≤ .036). Moreover, ES scores correlated negatively with TC baseline levels when controlling for the full set of confounders ($r = .35$, $p = .059$).

Lipid AUCs. Whereas there were no significant associations between aggregated TC or LDL-C secretion and IS, IV, or EV (p's > .25), ES scores correlated negatively with aggregated TC secretion ($r = .28$, $p = .105$). Further controlling for age and BMI or the full set of confounders did not change the results; instead the associations between ES und aggregated TC secretion got stronger (r's ≥ .38; p's ≤ .030). Moreover, ES scores correlated negatively with aggregated LDL-C secretion when controlling for age and BMI ($r = .27$, $p = .128$) or the full set of confounders ($r = .36$, $p = .054$).

At rest

There was no moderation effect of ES with hypertension status in pre-stress plasma lipid levels (p's > .52).

Stress reactivity

Moderation testing revealed a significant MAP-by-ES interaction for TC stress reactivity ($F(2.9/90.1) = 3.71$, $p = .015$, $\eta_{lp}^2 = .107$, $f = .35$; Fig. 1) and LDL-C stress reactivity ($F(3.0/93.0) = 3.61$, $p = .016$, $\eta_{lp}^2 = .104$, $f = .34$, Fig. 2). Post-hoc tests showed that TC levels were highest in hypertensives with low ES immediately after stress (p's ≤ .020). In contrast, hypertensives with high ES did not differ significantly from normotensives in TC immediately after stress (p's > .68). Similarly, in terms of LDL-C, hypertensives with low ES showed highest LDL-C secretion immediately after stress (p's ≤ .039). Moreover, hypertensives with high ES did not significantly differ from normotensives in LDL-C immediately after stress (p's > .28). Further controlling for age and BMI (interaction MAP-by-ES and TC stress reactivity: $F(3.0/87.0) = 3.43$, $p = .022$, $\eta_{lp}^2 = .106$, $f = .34$; interaction MAP-by-ES and LDL-C stress reactivity: $F(3.0/87.0) = 3.34$, $p = .023$, $\eta_{lp}^2 = .103$, $f = .34$) or the full set of confounders (interaction MAP-by-ES and TC stress reactivity: $F(3.0/78.0) = 4.27$, $p = .008$, $\eta_{lp}^2 = .141$, $f = .41$; interaction MAP-by-ES and LDL-C stress reactivity: $F(3.0/78.0) = 4.05$, $p = .010$, $\eta_{lp}^2 = .135$, $f = .40$) did not significantly change results.
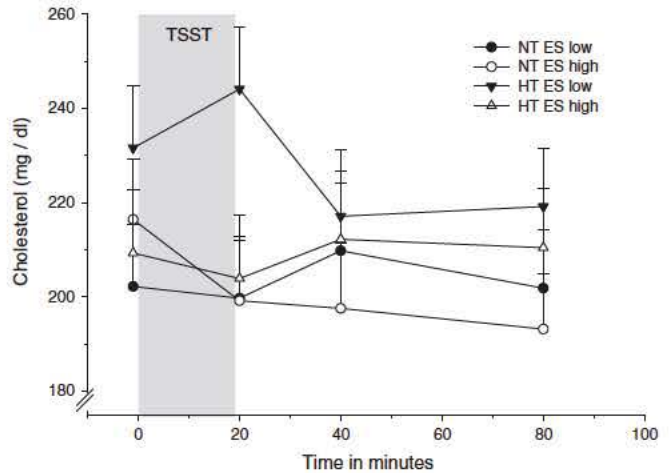

Fig. 1. Total cholesterol reactivity to psychosocial stress in hypertensive (HT) and normotensive (NT) men with high and low external-stable attribution to failure (ES). Values are means and simple error bars for SEM.

Conclusion

This is the first study to investigate associations between attribu tional styles and blood lipid changes to acute psychosocial stress in hy pertensive men, compared with age matched normotensives. The main finding of our study was that in hypertensive men, but not in normoten sives, lower ES scores were associated with higher TC and LDL C chang es to psychosocial stress. Moreover, hypertensives with higher ES scores did not differ significantly from normotensives in their TC and LDL C stress changes. These associations showed large effect sizes and were also independent of a broad set of potential confounders including car diovascular risk factors, NE stress change, and related psychological constructs. In contrast, there were no associations between blood lipids at rest and ES, or blood lipids (at rest as well as aggregated secretion) and EV, IS, and IV.

Our data suggest that the habitual manner of hypertensive subjects to attribute failure to external stable causes, such as task difficulty, re lates to the extent to which atherogenic lipid levels increase following stressful events: the higher the ES, the lower the stress induced TC and LDL C increases in individuals with hypertension. Several decades
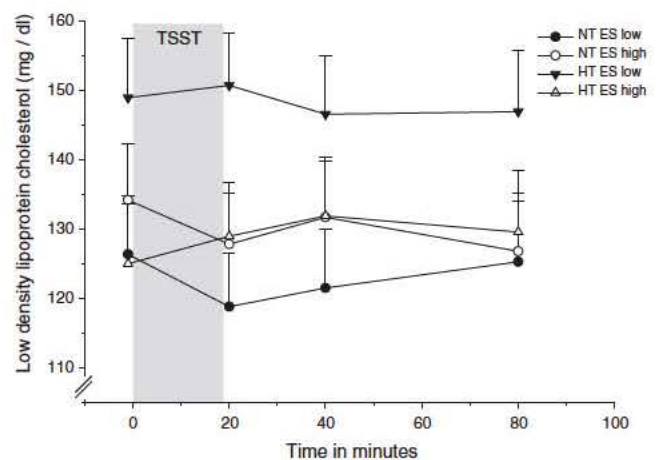

Fig. 2. Low-density-lipoprotein cholesterol reactivity to psychosocial stress in hyperten sive (HT) and normotensive (NT) men with high and low external-stable attribution to failure (ES). Values are means and simple error bars for SEM.

of research have provided strong empirical evidence that elevated TC and LDL C blood levels substantially increase the risk of atherosclerotic cardiovascular disease, especially among hypertensive patients [2,3,42]. However, it is unknown whether, and if so, to what extent acutely increased atherogenic lipids deposit at sites of endothelial lesions, thereby contributing to the initiation of fatty streaks, atherosclerosis progression, and ultimately coronary occlusion. Consequently, the clinical relevance of any dampening effect ES may have on stress reactivity of atherogenic lipids in hypertensive subjects remains to be elucidated. Notwithstanding this, it has been shown that acute lipid stress reactivity predicts higher LDL C levels and TC/HDL C ratios several years later [43]. Thus, over a lifespan, an acutely exaggerated lipid response might contribute to clinically manifest atherosclerosis in hypertensives. Therefore, ES might be a protective factor for stress induced lipid related atherogenesis in essential hypertension. However, further studies are needed to determine the implications of our observations in health, essential hypertension, and CHD.

To the best of our knowledge, no study has yet investigated the effects of attributional styles on lipid responses to acute stress, neither in healthy individuals nor in hypertensive subjects. Our study provides first indications of a possible relationship between ES, stress, and atherogenesis in essential hypertension. The findings described here are in line with research on beneficial effects of optimistic attributional styles or optimism, respectively, on cardiovascular outcomes. For instance, a prospective study found that optimism predicts a lower rate of and longer period before rehospitalization after coronary bypass surgery [44]; moreover, a 3 year longitudinal study found that optimists are less likely to show increases in carotid intima medial thickness (a subclinical marker of atherosclerosis) than pessimists [21]; a recent meta analytic review also demonstrated that heightened levels of optimism are associated with reduced risk of CHD [20]. Individuals who usually explain negative events by causes that are external, unstable, and specific ("it's bad luck but not me"), are said to have an optimistic attributional style; thus, external attribution of failure can be interpreted as an optimistic attributional style.

EV can also be interpreted as an optimistic explanatory style making the dampening effect on lipid stress changes only for ES, but not for EV puzzling. However, our sample size was relatively small and the variance within the EV variable was also smaller than in the ES variable. We therefore cannot rule out methodological causes for the non significant EV effects. The strong positive association between EV and ES in our sample (data not shown) further corroborates this notion. We thus feel the non significant EV effect should be interpreted with caution.

Interestingly, we also failed to find any association between the habitual manner of hypertensive subjects to attribute failure to internal stable causes (such as e.g. ability), or internal variable causes (such as e.g. effort) and stress induced increases in atherogenic lipid levels. Given that IS and IV can be interpreted as a pessimistic attributional style [14,19] our findings suggest effects on atherogenic blood lipid changes to acute psychosocial stress in hypertensive subjects only for optimistic but not for pessimistic explanatory styles. Notably, this is in line with studies suggesting that optimism and pessimism are distinct constructs [45,46].

What are the underlying pathways by which ES impacts lipid stress changes in hypertensives, but not in normotensives? Lipid stress reactivity is thought to be caused by multiple mechanisms, including stress associated alterations in plasma volume and alterations in lipid metabolism during stress [47 50]. It is unlikely that the observed effects of ES on lipid stress changes are a concomitant phenomenon of stress hemoconcentration, as we controlled for stress induced shifts in hemoconcentration before all analyses. We can only speculate that underlying mechanisms may include altered lipid metabolism. We further speculate that an increased tendency to attribute negative events or failure to external stable causes (such as task difficulty) is associated with a reduced perception of stress and, as a result, with a reduction in neuroendocrine stress responses, which in turn relate to lipid stress reactivity [12]. To examine if NE moderates the association between ES and lipid changes in response to stress, we statistically controlled for NE stress changes. However, our findings even became stronger after controlling for NE stress changes, suggesting that although NE stress changes independently related to higher lipid stress responses [12] they did not confound lipid changes to stress in relation to ES. Future studies are needed to examine additional pathways that may mediate ES related lipid stress changes. For example it remains to be tested whether ES relates to alterations in cognitive processes such as stress appraisal or state anxiety that in turn may relate to alterations in endocrine stress reactivity that may affect lipid stress reactivity.

What are the potential therapeutic implications of our study? Since we found in our cross sectional data that hypertensives with higher ES show lower lipid stress reactivity we speculate that it is more likely that ES is a cause rather than a consequence of the lower lipid stress reactivity. Given this, therapeutic interventions in hypertensives may aim at increasing ES e.g. by cognitive restructuring. However, it remains to be studied whether a potential intervention induced increase in ES consequently reduces lipid stress reactivity in hypertensives.

Our study has several strengths, which include recruitment of apparently healthy and unmedicated subjects with reasonable health habits. This is crucial since blood lipid metabolism is affected by several drugs, including antihypertensives, and lifestyle habits [51]. We also controlled for a variety of known and potential confounders to rule out a potential confounding influence on the measured variables. Moreover, we corrected plasma lipid levels for stress induced shifts in hemoconcentration prior to all analyses. Finally, we used a highly standardized and potent stress test that reliably induces neuroendocrine stress responses. The study also has its limitations. First, its cross sectional nature does not allow us to interpret the direction of the ES lipid stress link in hypertensives. However, as our attributional style measure refers to a habitual manner and as we induced lipid stress reactivity acutely, our study design may support the conclusion that it is ES that likely attenuates lipid stress reactivity rather than vice versa. Second, our sample size was relatively small and included only apparently healthy men. Thus, our findings may not be generalized to women and hypertensive patients with overt CHD. Moreover, it remains to be tested whether our findings also apply to hypertensive patients on antihypertensive treatment, particularly if the patient presents with ES. Given that we found NE stress increases to relate to lipid stress reactivity [12] one could speculate that antihypertensive treatment particularly with adrenergic blockers may prevent or reduce stress induced catecholamine increases and consequently catecholamine induced effects such as potential lipid increases. Future studies are needed to determine the implications of our observations in hypertensive patients on antihypertensive treatment.

Taken together, our data suggest a buffering effect of ES on atherogenic blood lipid changes to acute psychosocial stress in men with essential hypertension. Our observations require replication in larger samples, possibly in naturalistic settings, and other populations including patients on antihypertensive treatment. Moreover, the clinical implications of our observations in health, essential hypertension, and CHD need to be demonstrated.

Conflict of interest statement

The authors have no competing interests to report.

Acknowledgments

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