Trait Rumination and Social Anxiety Separately Predict Stress Induced Rumination and Hemodynamic Responses

Hendrik Laicher (hendrik.laicher@med.uni-tuebingen.de)
University Hospital of Tübingen

Isabell Int-Veen
University Hospital of Tübingen

Florian Torka
University of Tübingen

Agnes Kroczek
University Hospital of Tübingen

Isabel Bihlmaier
University Hospital of Tübingen

Helena Storchak
University Hospital of Tübingen

Kerstin Velten-Schurian
University Hospital of Tübingen

Thomas Dresler
University Hospital of Tübingen

Ramona Täglich
University Hospital of Tübingen

Andreas J. Fallgatter
University Hospital of Tübingen

Ann-Christine Ehlis
University Hospital of Tübingen

David Rosenbaum
University Hospital of Tübingen

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Abstract

We aimed to investigate the stress-reactive rumination response to social stress and its association with social anxiety and trait rumination. From previous investigations we know that people with a certain vulnerability to rumination show increased stress-reactive rumination. However, up to date the possible influence of social anxiety to this relationship is still unclear. Therefore, we reanalyzed the data of two of our previous studies assessing healthy low and high trait ruminators and depressed patients performing the Trier Social Stress Test (TSST). We measured cortical oxygenation using functional Near-Infrared Spectroscopy (fNIRS) as well as different behavioral outcome measures (subjective stress levels, negative affect, state rumination). On a behavioral level, we found an influence of both, social anxiety and trait rumination, on state rumination, even when correcting for the other factor, respectively, implying two potentially independent factors of influence. On a neural level, we observed reduced activation in socially anxious subjects in the right inferior frontal gyrus (IFG), as well as time-dependent changes in the left IFG and in the right dorsolateral prefrontal cortex. Results indicate a specific role of social anxiety, at least on a behavioral level, and therefore implicate a crucial factor to be considered in the treatment of depression.

1. Introduction

Comorbid diagnoses are common in mental disorders. For instance, in nationally representative surveys in the United States, Kessler and colleagues found 60% of participants with lifetime Major Depressive Disorder (MDD) to meet criteria of a comorbid anxiety disorder [1], and, more specifically, about one third suffered from comorbid social phobia [2]. Brown and colleagues [3] replicated these findings, which gave rise to future research investigating the potentially similar underlying mechanisms. Repetitive negative thought – such as rumination – seems to be such a transdiagnostic factor, which has been shown to be related to the development of both depression and anxiety disorders [4–6].

Rumination is defined as a perseverative, highly self-referential, pessimistic and abstract thinking style with little or no goal and change-orientation [7]. Furthermore, rumination is conceptualized as a form of repetitive negative thinking, such as worry [8]. Originally investigated by Nolen-Hoeksema under the term “depressive rumination” [9], it was described as “behavior and thoughts that focus one’s attention on one’s depressive symptoms and on the implications of these symptoms” (p. 569, [10]. Since then, different models have been established and broadened the conceptualization of rumination. In the investigation of depressive rumination, experimental designs often use instructions to think a certain way, for instance about negative emotions/negative personality attributes [11–13] or negative life events [14–16] to induce ruminative processes. However, these approaches, even though they assess self-referential thoughts, which are a typical content of depressive rumination, do not capture other aspects of rumination like uncontrollability or repetitiveness. Indirect induction methods using social stress tests like the Trier Social Stress Test (TSST) [17] have been able to successfully provoke increased state rumination [18–24]. In line with longitudinal studies, stress-reactive rumination promises to be a better predictor of depression than

trait rumination [25]. Interestingly, this is not in line with the original definition of rumination by Nolen-Hoeksema [9], which assumed ruminative processes to pose more of a trait rather than a reactive state condition [4].

Social anxiety research has to face similar problems in the investigation of post-event processing, which can be defined “as an individual’s repeated consideration and potential reconstruction of his performance following a social situation” (p. 891, [26], and which is postulated to be a maintaining factor in social anxiety disorders [27]. However, studies in which participants are instructed to imagine hypothetical or recent personal situations [28–30] as well as experimental studies in which impromptu-speech tasks are used [31,32] show highly socially anxious individuals to be more prone to engage in post-event processing. These effects were maintained even one week after experimentally induced confrontations [33], as well as in naturalistic reports of diary-based studies [34]. When stressor-induced ruminative processes are compared in depressed patients and socially anxious individuals, studies found the latter to be more strongly [35] and both uniquely associated with negative post-event rumination [32]. However, it remains unclear in how far momentary ruminative responses represent a construct associated with depressive rumination as defined by Nolen-Hoeksema [9] and/or social anxiety. Potentially, rumination in depression and post-event-processing in social anxiety are to some extent equivalent constructs, which poses the existence of a common underlying mechanism and transdiagnostic phenomenon.

The Trier Social Stress Test (TSST) is a commonly used, highly potent stressor and the gold standard for examining neurocognitive mechanisms of acute stress [36]. Using the TSST in adults with social phobia, Condren, et al. [37] observed significantly higher stress-induced cortisol increases in patients compared to a control group, suggesting that patients with social phobia are hyper-responsive when confronted with psychological stress [38,39]. Concerning rumination in general, it could be demonstrated that in subjects with higher trait rumination the stress response after a TSST was either intensified or prolonged [23,40,41]. However, there are also studies which could not find any differences of socially phobic individuals compared to healthy controls [42], or only subjective but not physiological stress responses to be elevated in the former [43]. Investigating the neural correlates of social anxiety in a public speech task, Tuscan, et al. [44] found elevated frontal cortical oxygenation using fNIRS, but no significant differences between high and low socially anxious individuals. Studies using the TSST in a sample of depressed patients revealed hypoactivity in the prefrontal cortex as well as increased state rumination and negative affect when compared to healthy controls [22,45,46]. Generally, increased activity in regions of the Cognitive Control Network (CCN), comprising the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC) and posterior parietal cortex [47], was observed in fNIRS and fMRI studies as a correlate of social stress induction [48]. Furthermore, in one of our previous studies [22,45] we found decreased activity in the bilateral inferior frontal Gyrus (IFG) as a mediator of post-stress rumination. As the IFG is relevant in inhibition and attention control tasks [48–55], this finding let us conclude that inhibition of the IFG and therefore of these tasks might lead to rumination. However, up to date, neurocognitive studies investigating the association of stress-reactive rumination with social anxiety and trait rumination are scarce. Following the

assumption of a possible common, transdiagnostic factor of rumination in depression and social anxiety, a neurocognitive investigation of stress-reactive rumination in depressed as well as anxious subjects seems to be useful in order unravel a potentially common ground on a neuronal level.

In two previous studies of our lab [22,45], we investigated stress-induced rumination but did not test whether social anxiety has an influence or explains unique variance. More specifically, we investigated the efficacy of a socially stressful situation (the TSST) under laboratory conditions as well as its effects on post-event processing on a neuronal level to find possible neuronal activation patterns for rumination in different sub-samples (high vs. low trait-ruminators, depressed vs. healthy subjects). Furthermore, we measured the physiological and the affective adaptation to this high-stress situation. Therefore, we assessed behavioral data such as subjective stress, state rumination and mood changes as well as heart rate, salivary cortisol and cortical oxygenation in both studies. In the present analysis, we expected higher subjective stress and increased state rumination and negative mood in socially anxious subjects. On a neural level, we expected that social anxiety would show a negative effect on CCN functioning, as already shown for trait rumination. Furthermore, we hypothesized elevated salivary cortisol levels as well as cortical oxygenation in both, socially anxious subjects as well as high trait ruminators. Generally, in line with research suggesting common underlying mechanisms of social anxiety and ruminative processes, we expected high correlations of the Liebowitz Social Anxiety Scale (LSAS) and the Rumination Response Scale (RRS) but unique variance to be explained by both factors in our corresponding outcome measures.

2. Materials And Methods

2.1 Participants

Participants were recruited at the University Hospital of Tübingen and via ambulant psychotherapists. All procedures were approved by the ethics committee at the University Hospital and University of Tübingen and in line with the Declaration of Helsinki in its latest version. All participants gave their written informed consent prior to data collection. Exclusion criteria comprised: diabetes mellitus, kidney insufficiency, hypertension, dysrhythmia, cushing syndrome, substance abuse, adrenal insufficiency, cortisone medication, pacemaker, craniocerebral trauma as well as any medication except for oral contraceptives. In the first study, only healthy controls without a history of mental or neurological disorder were assessed. In the second study, healthy controls meeting the same criteria were compared to a group of patients with major depressive disorder (MDD), from which any other primary mental disorder except ICD-10 diagnosis F32.x, F34.1 and F33.x, as well as suicidality, extraordinarily severe depressive symptoms (BDI-II > 50), deficient emotional stability according to the currently treating psychologist and decompensation under social stress in the past led to exclusion.

The combined sample consisted of 45 healthy controls, 23 subclinical high trait ruminators and 22 depressed patients (see table 1). The diagnosis in the patient sample included recurrent Major Depressive Disorder (MDD) ($n = 15$) and first episode MDD ($n = 7$). The comorbid diagnoses included somatic

symptom disorder (*n* = 2), anxiety disorders (*n* = 2) and personality disorders (*n* = 2). 60% of the patients were currently receiving psychotherapy and 58% antidepressant medication. The mean age of the total sample was 24.11 years (*SD* = 5.24 years) and 80% of all participants were female.

Differences between the study samples (e.g. the BDI-II-score) only concerned outcome measures irrelevant for our analysis. We did not differentiate between healthy and depressed participants, as we could observe a high correlation of social anxiety and rumination in both subsamples. Therefore, we prioritized a larger rather than a homogenous sample. In addition, as social anxiety and rumination are dimensional rather than categorical constructs and seem to play a role not just in depressed patients but also in healthy controls [56,57], we combined the different subsamples from our previous studies for a dimensional approach.

Table 1 gives an overview of the main outcome measures of our analysis, subdivided into the different study samples.

Table 1 *Demographic variables of the samples*

	Study 1				**Study 2**			
	Low trait ruminators (*n* = 22)		High trait ruminators (*n* = 23)		Depressed patients (*n* = 22)		Healthy controls (*n* = 23)	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Age	22.32	3.88	21.70	2.69	27.14	6.15	25.35	5.75
Percent of female participants	86.4		78.3		77.3		78.3	
BDI-II total score	1.95	2.26	8.57	5.80	24.14	11.85	2.13	1.96
RRS mean	1.54	0.22	2.67	0.17	2.59	0.50	1.73	0.39
LSAS mean	0.47	0.19	0.89	0.50	1.32	0.55	0.51	0.33

Note. BDI-II = Beck Depression Inventory II [58], RRS = Rumination Response Scale [9], LSAS = Liebowitz Social Anxiety Scale [59].

2.2 Procedures

In the following section we will briefly describe the paradigm and the used questionnaires as well as the physiological measures we did in the experiment. Figure 1 gives an overview of the procedure and when which measurement and which questionnaire was done.

TSST. The Trier Social Stress Test (TSST) [17] is a highly reliable paradigm to induce psychological stress consisting of a free speech and a mental arithmetic task. We adapted the TSST according to the fNIRS-setting by performing a 7-min resting-state previous to two non-stressful control tasks and another 7-min resting-state after the TSST. Through this adaptation, the TSST delivered an ecologically valid and fNIRS-conform stress situation, that leads to post-event processing in rumination-vulnerable and/or anxious subjects [22,45]. Due to saliva sampling, participants rested for another 45 min, however fNIRS was not recorded during this part of the post-stress phase. After arriving at the laboratory, participants completed several questionnaires assessing depression symptom severity (BDI-II), trait rumination (RRS), as well as social anxiety symptoms (LSAS). Previous to as well as after the stress induction, we assessed momentary affect (PANAS) and state rumination. Further, at several time points, subjective stress was measured on a Visual Analogue Scale (VAS) ranging from 0–100% as well as samples of salivary cortisol were taken using Salivettes. As this investigation focused on behavioral data assessed by the aforementioned questionnaires and fNIRS data during the post-stress resting-state, in the following we will briefly describe these measures, however more detailed information regarding the stress induction and general procedure is to find in [22,45].

Visual Analogue Scale (VAS). Throughout the experiment, participants rated their momentary stress levels on a scale ranging from 0–100%, where steps of 10% were marked at steps of one centimeter. The questionnaire comprised all ratings of the current day of measurement on one page, so participants were able to allow for their last ratings.

Beck Depression Inventory (BDI-II; Hautzinger et al., 2009). In order to screen depression symptom severity, we used the German version of the self-report questionnaire Beck Depression Inventory II. Regarding the previous two weeks, the occurrence of 21 symptoms is rated and symptom severity is assessed as a total score ranging from 0–63. Investigating psychometric properties across different populations and languages, respectively, Wang and Gorenstein [60] could observe overall high internal consistencies (Cronbach's α around 0.9) as well as high retest reliability (mean interval of 2 weeks; r around 0.7–0.9).

Liebowitz Social Anxiety Scale (LSAS; Liebowitz, 1987). The LSAS is a screening measure for social anxiety disorder, comprising 24 social situations that are rated on a 4-point Likert-scale for level of fear (none, mild, moderate, severe) and avoidance (never, occasionally, often, usually) regarding the previous week. The resulting total score (range from 0 to 144) has been shown to have excellent psychometric properties (Cronbach's $\alpha = .95$) [61]. Also, the LSAS was found to be capable of differentiating clinical as well as non-clinical samples [62,63] which is the reason why in the following we will consider LSAS-scores as a measure of levels of social anxiety. Note that we will report LSAS mean scores in order to account for potential missing values.

Ruminative Response Scale (RRS; Noelen-Hoeksema, 1991). Trait rumination was assessed using 22 items which are rated on a 4-point Likert scale ranging from "hardly ever" to "almost always". The total score (range from 22 to 88) has been shown to have high internal consistencies (Cronbach's α = .88–92) [64–66]. Note that we will report RRS mean scores in order to account for potential missing values.

Positive and Negative Affect Schedule (PANAS; [67]. Using the PANAS we assessed momentary positive and negative affect. 20 items are rated using 5-point Likert scales ranging from 1 ("very slightly") to 5 ("extremely"). Both subscales, positive (PA) and negative affecrt (NA) have acceptable internal consistencies in clinical and non-clinical samples [68,69] of = .85-.86 for NA and = .84-.89 for PA.

State rumination

We assessed stress-reactive rumination pre and post stress using adapted items from the RRS [9], ARSQ [70], PTQ [71,72]. The 18 items were answered using a 5-point Likert scale ranging from 1 ("not at all") to 5 ("very often"), totaling to a score between 18 and 90. Note that we will report mean scores in order to account for potential missing values. Subjects were instructed to rate whether the items were in line with their mental state during the last 10 minutes (see supplemental table 1).

fNIRS. During the stress induction as well as both resting-states, an fNIRS measurement was performed to assess cortical activation using a 46-channel continuous wave multichannel fNIRS system (ETG-4000 Optical Topography System; Hitachi Medical Co., Japan) with a sampling rate of 10 Hz. According to our regions of interest, we placed two frontal probesets and one parietal probeset with reference position to Fpz and Cz according to the 10–20 system [73] using an Easycap with sponge rings for additional fixation of the optodes (see table 2 and figure S3). Like this, a fixed inter-optode distance of 3 cm was set for all optodes. Changes in levels of oxygenated (O2Hb) and deoxygenated (HHb) hemoglobin were computed by means of the modified Beer-Lambert Law. Data preprocessing was done in MATLAB [74], using customized scripts, including interpolation of single noisy channels, correction of motion artifacts using Temporal Derivative Distribution Repair (TDDR) in order to remove spikes primarily caused by head movements in our case [75] and Correlation-based signal improvement (CBSI) [76] to combine both signals (O2Hb and HHb) in their merits: High sensibility (O2Hb) and high resilience to arousal artifacts (HHb). We further used bandpass-filtering to remove low-frequency baseline-drifts (below 0.01 Hz) and high-frequency noise (above 0.1 Hz). Then, a second step of channel interpolation followed in case of artifacts due to data correction. Afterwards, a global signal reduction was performed with a spatial gaussian kernel filter with a standard deviation of $\sigma = 40$ [77]. For data analysis, we calculated event-related averages for each trial including a 5 seconds baseline-correction for every region of interest (ROI).

Table 2 *Regions of interest and corresponding probesets and channels, extrapolated based on the Colin 27 template [78]. For probeset placement see also Figure S3*

region of interest	probeset	corresponding channels
left inferior frontal gyrus (lIFG)	left frontal	6 7 9
left dorsolateral prefrontal cortex (lDLPFC)	left frontal	10 11 12
right inferior frontal gyrus (rIFG)	right frontal	18 19 21
right dorsolateral prefrontal cortex (rDLPFC)	right frontal	20 23 24
somatosensory association cortex (SAC)	parietal	25 26 27 28 30 31 32 35 36

Heart rate. We assessed heart rate during both resting-states as well as the stress induction using a 1-channel electrocardiogram in order to monitor heart rate variability as an index of the stress response. After disinfection of the corresponding skin areas, three standard Ag/AgCl ring electrodes were attached using Ten20 conductive paste. Electrodes were placed above the right clavicle, below the left costal arch and on the neck (reference). The signal was recorded using the BrainAmp ExG amplifier with a sampling rate of 1000 Hz and BrainVision Recorder Software (Brain Products, Munich, Germany).

Salivary cortisol. Saliva was collected in salivettes (Sarstedt AG & Co., REF 51.1534.500) and was stored at − 20°C and later thawed and centrifuged for 2 min at 1000g to collect saliva. Further analysis was performed with enzyme immunoassay (IBL International, Cortisol ELISA, REF RE52611) according to the manufacturer's instructions. Average cortisol levels were taken from duplicate runs if intra-assay variation was below 10%. Finally, daytime was regressed out of cortisol coefficients to account for circadian rhythm fluctuations that are not related to the TSST and values were log-transformed. Participants were instructed not to drink alcohol the day before the measurement, to sleep as long as they usually do and to perform no physical activities on the day of the measurement. Also, subjects were told not to drink or eat 30 min before the measurement started.

2.3 Data analysis

After data preprocessing, data analysis was done using R [79] and SPSS [80]. Mixed models were fitted using the R packages lme4 [81] and lmerTest [82] in order to obtain *p*-values using the Satterthwaite approximation. Graphics were plotted using the R package ggplot2 [83] and MATLAB [74]. Using the R-package MuMIn [84], marginal R^2 was computed as a measure of variance explained by the fixed effects in the mixed models. By reporting changes in R^2 we are comparing the more complex with the corresponding less complex model.

In the following, we will analyze subjective stress, negative affect and state rumination. Further, we will analyze heart rate and salivary cortisol, but these analyses are to be found in the supplemental material

as they were not related to our primary hypotheses. We investigated in how far social anxiety (LSAS) and trait rumination (RRS) play a role in each measure and set up mixed models with an increasing number of parameters. Note that we did not include BDI-II as a predictor due to its high correlations with social anxiety and trait rumination (see table 4) and issues of multicollinearity. Fitting mixed models offers the chance to include random effects accounting for non-independence [85], as well as to handle unbalanced data and include continuous predictors [86]. First, we conducted a basic model consisting of the parameters set by the experimental design, such as time (model 1). For the two more complex models, we added z-standardized LSAS (model 2) and z-standardized RRS total scores (model 3) as main effects and interaction effects with time, accounting for social anxiety and trait rumination, respectively. As most complex models, we added the z-standardized RRS (model 4) and LSAS scores (model 5) only as main effects to the previous models. Like that, we controlled for trait rumination and social anxiety and investigated whether there is unique variance explained by the corresponding measure. Note that all predictors were included as fixed effects whereas due to repeated measurements on each subject, intercepts for every participant were modeled as random effects. Table 3 gives an overview over the models conducted for each measure.

For the analysis of cortical oxygenation, we fitted a MANOVA in order to increase statistical power and assess multiple dependent variables simultaneously. For this, we added the same parameters as predictors as in our previous mixed models.

Prior to our analyses, we checked assumptions of the used methods and corrected for potential violations of assumptions. Note that corrections were not applied unless stated otherwise. In case of subjective stress ratings and state rumination, normality assumption was not met but due to insufficient success of common transformations and the robustness of the mixed models [87], we decided to perform the analyses as planned. Furthermore, in case of a detection of outliers, we will report the corrected analyses in detail and summarize results of the uncorrected analyses.

Note that physiological data of heart rate was missing in five subjects, leaving 85 participants, and one participant had to be excluded in the analyses of negative affect for study 1, due to missing data.

Table 3 *Parameters included in the mixed models for each outcome measure*

Name	parameters
Model 1: Basic model	Time
Model 2: Basic model including LSAS	Time + LSAS + Time:LSAS
Model 3: Basic model including RRS	Time + RRS + Time:RRS
Model 4: Basic model including LSAS and correcting for RRS	Time + RRS + LSAS + Time:LSAS
Model 5: Basic model including RRS and correcting for LSAS	Time + LSAS + RRS + Time:RRS
Note. In case of subjective stress and heart rate, time was modelled as linear and quadratic term. Colons symbolize interaction effects. All included parameters except for time were z-standardized.	

Table 4 *Correlation matrix of variables of interest*

	BDI-II	RRS
RRS	.603***	-
LSAS	.600***	.519***
Note. BDI-II = Beck Depression Inventory II [58], RRS = Rumination Response Scale [9], LSAS = Liebowitz Social Anxiety Scale [59]. ***$p < .001$.		

3. Results

3.1 Subjective stress (VAS ratings)

First, we wanted to investigate whether the stress induction was reflected by changes in subjective stress. Calculating mahalanobis distances, we identified seven subjects´ stress ratings as multivariate outliers ($p < .001$) and therefore excluded them from the following analyses. From previous investigations of stress paradigms [45,46] we assumed a quadratic relationship of subjective stress ratings and time and therefore tested a linear model against a quadratic model using a Likelihood-ratio-test. Results revealed a significantly better fit of the quadratic model, $X^2(1) = 244.58$, $p < .001$, which was subsequently used in the analysis. Fitting the basic model, time yielded a significant predictor as a linear $t(664) = 6.607$, $\beta = 13.395$, $p < .001$) as well as a quadratic term ($t(665) = -2.512$, $\beta = -1.538$, $p < .05$) (see table 5) and remained significant even in the more complex models. In model 2, we observed significant interactions of LSAS with both time factors ($t(664) = 2.771$, $\beta = 2.868$, $p < .01$ and $t(664) = -2.719$, $\beta = -0.339$, $p < .01$) and more variance to be explained compared to the basic model (change of $R^2 = .069$). Higher LSAS scores were associated with higher linear increases in the stress response and a stronger quadratic decrease at post stress (see Fig. 2). In model 3, RRS did not explain further variance (change of R^2 compared to the basic model = .021). In model 4, we observed the same pattern as before whereby both interactions of LSAS

and time got significant ($t(664) = 2.771$, $\beta = 2.868$, $p < .01$ and $t(664) = -2.719$, $\beta = -0.338$, $p < .01$) and no change in R^2 was observed compared to model 2. Fitting model 5, only the control variable LSAS yielded a significant predictor ($t(83) = 4.054$, $\beta = 6.416$, $p < .001$). We found the fixed effects of the latter model to explain more variance compared to model 3 (change of $R^2 = .044$). Higher social anxiety was associated with increased subjective stress.

3.2 Negative affect (PANAS)

To investigate changes in negative affect due to the stress induction, we performed a repeated measurements ANOVA with the factor time (pre stress, post stress, post rest2). Note that the third PANAS assessment (post rest2) was different in study 1 (15 min after the stress induction) and study 2 (60 min after the stress induction), which is why we only analyzed the first two time points. One subject from study 1 was excluded from further analyses due to missing values for negative affect. After identifying another three subjects in study 2 as multivariate outliers, we observed a significant main effect of time for both studies, *Fstudy1*$(1, 43) = 50.1$, $p < .001$, $\eta_G^2 = .207$; *Fstudy2*$(1, 41) = 41.322$, $p < .001$, $\eta_G^2 = .088$, indicating an increase in negative affect due to the stress inductions.

These results led us to combine the data of both studies in the following analyses. Fitting mixed models for negative affect, the basic model including only time as a predictor significantly predicted changes in negative mood ($t(89.00) = 9.111$, $\beta = 6.663$, $p < .001$). In model 2, LSAS predicted the outcome significantly as a main effect ($t(126.10) = 1.295$, $\beta = 3.449$, $p < .001$). This model explained more variance than model 1 (change of $R^2 = .169$). In model 3, RRS yielded a significant predictor ($t(133.24) = 5.589$, $\beta = 4.347$, $p < .001$) as well as an interaction with time ($t(89.00) = 2.446$, $\beta = 1.744$, $p < .05$). Again, this model did explain more variance than model 1 (change of $R^2 = .301$). This pattern remained the same when we corrected for the corresponding other questionnaire: In model 4, LSAS no longer yielded a significant predictor but RRS got significant ($t(89.00) = 5.543$, $\beta = 4.345$, $p < .001$). Like that, this model explained further variance regarding the fixed effects when compared with model 2 (change of $R^2 = .149$). When fitting model 5, RRS significantly predicted the outcome ($t(124.22) = 4.027$, $\beta = 3.473$, $p < .001$), as well as LSAS ($t(89.00) = 2.168$, $\beta = 1.696$, $p < .05$), as well as the interaction of RRS with time ($t(89.00) = 2.446$, $\beta = 1.744$, $p < .05$). Compared to model 3, model 5 explained only little further variance (change of $R^2 = .023$) (see table 5). Rerunning our analyses with inclusion of multivariate outliers, we found the same as the aforementioned results.

3.3 State rumination

After exclusion of one subject which yielded a multivariate outlier ($p < .001$), we fitted a basic model including the factor time, which predicted the outcome significantly ($t(89.00) = 6.63$, $\beta = .470$, $p < .001$) and remained significant even in the more complex models (see table 5). Adding LSAS to the model increased the explained variance by 35%. In model 2, the main effect of LSAS ($t(138.72) = 5.175$, $\beta = 0.358$, $p < .001$) as well as the interaction of LSAS and time ($t(89.00) = 3.986$, $\beta = 0.267$, $p < .001$) significantly predicted state rumination (change in $R^2 = .35$) (see Fig. 3). By fitting model 3, we observed the same effect: RRS ($t(137.33) = 4.954$, $\beta = .340$, $p < .001$) as well as the interaction of RRS and time

significantly predicted the outcome ($t(89.00) = 4.048$, $\beta = .266$, $p < .001$) with additional 33.8% of variance explained (see Fig. 3). Correcting with the corresponding other factor, all predictors of the model significantly predicted the outcome: In case of model 4, time ($t(89.00) = 7.289$, $\beta = .476$, $p < .001$), LSAS ($t(136.78) = 2.828$, $\beta = .199$, $p < .01$) and RRS ($t(89.00) = 5.040$, $\beta = .307$, $p < .001$), as well as the interaction of LSAS and time ($t(89.00) = 3.986$, $\beta = .267$, $p < .001$) significantly predicted the outcome. Fixed effects of this model also explained further variance compared to the model only including LSAS (change of $R^2 = .098$). In the case of model 5, also, time ($t(89.00) = 7.266$, $\beta = .473$, $p < .001$), RRS ($t(136.59) = 2.519$, $\beta = .174$, $p < .05$), LSAS ($t(89.00) = 5.365$, $\beta = .332$, $p < .001$) and the interaction of RRS and time ($t(89.00) = 4.048$, $\beta = .266$, $p < .001$) significantly predicted the outcome. When comparing the variance explained by the fixed effects of model 3 and model 5, the latter model did explain further variance (change in $R^2 = .11$). Generally, we observed increased state rumination following the TSST in socially anxious individuals as well as individuals with higher trait rumination. Both, trait rumination and social anxiety were uniquely associated with increased state-rumination following the TSST. Note that our analyses with inclusion of multivariate outliers yielded the exact same results.

Table 5 *Results of the Mixed Models exploring the association between subjective stress, negative affect, state rumination and social anxiety (LSAS) and trait rumination (RRS) (AIC = Akaike Information Criterion; BIC = Bayesian-Information-Criterion; R^2 = variance explained by the fixed effects) *p < .05, **p < .01, ***p < .001*

	Dependent variables	VAS	Negative affect	state rumination
Model 1: Basic Model	Intercept	5.692** (2.132)	16.045*** (0.952)	1.574*** (0.086)
	Time	13.395*** (2.027)	6.663*** (0.731)	0.470*** (0.070)
	$Time^2$	-1.538* (0.612)		
	$Time*Time^2$	-0.027 (0.05)		
	AIC	6516.1	1233.40	386.79
	BIC	6543.8	1246.13	399.52
	R^2	.223	0.122	.078
Model 2: Basic Model + LSAS	Intercept	6.082** (2.044)	16.013*** (0.856)	1.582*** (0.068)
	Time	13.769*** (2.02)	6.654*** (0.725)	0.476*** (0.065)
	LSAS	2.987 (2.137)	3.449*** (0.859)	0.358*** (0.069)
	$Time^2$	-1.582** (0.609)		
	Time*LSAS	2.868** (1.035)	0.942 (0.727)	0.267*** (0.067)
	$Time^2$*LSAS	-0.339** (0.125)		
	$Time*Time^2$	-0.027 (0.05)		
	AIC	6493.5	1213.41	326.87
	BIC	6535.1	1232.50	345.96

	Dependent variables	VAS	Negative affect	state rumination
	R^2	.292	0.291	.428
Model 3: Basic Model + RRS	Intercept	5.797** (2.105)	15.989*** (0.772)	1.579*** (0.068)
	Time	3.495*** (2.025)	6.641*** (0.708)	0.473*** (0.065)
	RRS	1.343 (1.974)	4.347*** (0.778)	0.340*** (0.069)
	$Time^2$	-1.549* (0.611)		
	Time*RRS	1.284 (0.921)	1.744* (0.713)	0.266*** (0.066)
	$Time^2$*RRS	-0.136 (0.111)		
	Time*$Time^2$	-0.027 (0.05)		
	AIC	6513.9	1187.55	329.05
	BIC	6555.4	1206.64	348.14
	R^2	.244	0.423	.416
Model 4: Basic Model + LSAS while correcting for RRS	Intercept	6.087** (2.043)	15.978*** (0.761)	1.583*** (0.062)
	Time	13.769*** (2.02)	6.654*** (0.725)	0.476*** (0.065)
	$Time^2$	-1.582** (0.609)		
	LSAS	2.615 (2.265)	1.225 (0.863)	0.199** (0.070)

	Dependent variables	VAS	Negative affect	state rumination
	RRS	0.692	4.345***	0.307***
		(1.401)	(0.785)	(0.061)
	Time*LSAS	2.868**	0.942	0.267***
		(1.035)	(0.727)	(0.069)
	$Time^2$*LSAS	-0.338**		
		(0.125)		
	Time*$Time^2$	-0.027		
		(0.05)		
	AIC	6495.3	1189.09	306.53
	BIC	6541.5	1211.37	328.80
	R^2	.292	0.44	.526
Model 5: Basic Model + RRS while correcting for LSAS	Intercept	6.423**	15.985***	1.584***
		(2.041)	(0.757)	(0.061)
	Time	13.495***	6.641***	0.473***
		(2.025)	(0.708)	(0.065)
	$Time^2$	–1.549*		
		(0.611)		
	RRS	-1.359	3.472***	0.174*
		(2.01)	(0.862)	(0.069)
	LSAS	6.416***	1.696*	0.332***
		(1.583)	(0.782)	(0.062)
	Time*RRS	1.284	1.744*	0.266***
		(0.921)	(0.713)	(0.066)
	$Time^2$*RRS	-0.136		
		(0.111)		
	Time*$Time^2$	-0.027		
		(0.05)		
	AIC	6500.9	1184.97	306.11

	Dependent variables	VAS	Negative affect	state rumination
	BIC	6547.0	1207.24	328.38
	R^2	.288	0.446	.526

3.4 fNIRS data

As a next step, we investigated the association of cortical activation with social anxiety and trait rumination using a MANOVA by entering O2Hb values of the different ROIs (left and right IFG, left and right DLPFC and SAC) as dependent variables and time, z-standardized LSAS and RRS, both as interaction terms with time, as predictors. Likewise, we found time ($F(10, 516) = 2.73$, $p < .05$) and LSAS ($F(5, 257) = 3.45$, $p < .05$) to yield significant predictors. Post-hoc univariate ANOVAs revealed that both variables significantly predicted activation in the left IFG and right DLPFC while in the right IFG only LSAS and in the left DLPFC and SAC only time reached significance. For an overview over the results of the univariate post-hoc ANOVAs see table 6.

Table 6 *Results of the univariate post-hoc ANOVAs exploring the association of O2Hb cortical activation with social anxiety (LSAS) and trait rumination (RRS) #p < .1, *p < .05, **p < .01, ***p < .001*

	lIFG	rIFG	lDLPFC	rDLPFC	SAC
Time	$F(2, 261)$ = 7.081**	$F(2, 261)$ = 1.408	$F(2, 261)$ = 8.536***	$F(2, 261)$ = 7.504**	$F(2, 261)$ = 8.145***
LSAS	$F(1, 261)$ = 8.740**	$F(1, 261)$ = 6.603*	$F(1, 261)$ = 0.664	$F(1, 261)$ = 3.990*	$F(1, 261)$ = 3.625#
RRS	$F(1, 261)$ = 3.372#	$F(1, 261)$ = 1.640	$F(1, 261)$ = 0.010	$F(1, 261)$ = 0.675	$F(1, 261)$ = 1.941
Time*LSAS	$F(2, 261)$ = 1.328	$F(2, 261)$ = 0.336	$F(2, 261)$ = 0.612	$F(2, 261)$ = 0.168	$F(2, 261)$ = 0.473
Time*RRS	$F(2, 261)$ = 1.412	$F(2, 261)$ = 1.485	$F(2, 261)$ = 2.230	$F(2, 261)$ = 1.407	$F(2, 261)$ = 1.111

4. Discussion

This study investigated the association of social anxiety and trait rumination with the stress response as induced via the Trier Social Stress Test (TSST). This is crucial as the TSST has recently been used to elicit state ruminative responses as life stress has been shown to be one trigger of rumination and the latter to be a mediating factor of stress and psychopathology [88,89]. In addition, previous findings suggest that social anxiety and depression appear to be uniquely associated with stress induced ruminative processes, although the underlying mechanisms seem to be of a similar manner [32,35]. We analyzed

behavioral, neurobiological and autonomous correlates of trait rumination and social anxiety as predictors of the stress response.

Our results showed the same effects of the general stress response as in previously published studies. Concerning our hypotheses, we found a significant moderating effect of social anxiety on subjective stress levels. Intuitively, subjective stress was elevated in socially anxious individuals as they were confronted with a social situation. After similar baseline stress, we observed higher ratings in socially anxious individuals prior to and immediately after the stress induction. This is in line with assumed states of social anxiety including anticipatory processing and post-event processing [26,30,33,34,90–92]. In line with the previous analyses of this data [22,45], we did not observe such an interaction for the factor of trait rumination. One possible interpretation of these findings might be that even though the intercorrelation of both, RRS and LSAS, is unsurprisingly very high, trait rumination and social anxiety have different effects on subjective stress. In this regard, rumination does not appear to moderate the subjective stress response as social anxiety does. On the other hand, the link between daily life stress and depression (or depressive symptoms) is mediated by rumination [88,93] and, in the long run, rumination interacts with stressful life events [89,94]. However, the specific types of perceived stress in a social situation and during ruminative processes as well as possible differences between those types need to be further examined. In particular it would be promising to investigate these associations in clinical subsamples, especially in patients with social anxiety disorder (SAD) with and without comorbid MDD.

On a neurophysiological level, we found different impacts of cortical oxygenation for the RRS and LSAS. First of all, we found time-dependent changes in the left dorsolateral prefrontal cortex and the somatosensory association cortex in the whole sample. Concerning different levels of social anxiety, we found time-dependent changes in the left inferior frontal gyrus and in the right dorsolateral prefrontal cortex. Furthermore, we found attenuated cortical oxygenation for high vs. low socially anxious individuals in the SAC. Note that as this latter statistical effect only reached marginal significance, it needs to be interpreted with caution. Nevertheless, these results are in line with a body of research that found the SAC to be relevant in anxiety disorders in general [95,96]. Furthermore, the functional connectivity between the SAC and other brain areas, that seems to be crucial in social anxiety, was found to be increased [97] in subjects with SAD. Regarding trait rumination we only found a marginal significant change in cortical oxygenation in the left IFG in high trait ruminators. This result doesn't replicate the results in our previous studies, where we found significantly lower brain activity in the right IFG in high trait ruminators over the course of the measurement. However, these differential results are due to different statistical analysis. Calculating the same statistical models as in our previous studies, we could replicate the same pattern of frontal hypoactivation and significant changes in cortical oxygenation dependent on time. Nevertheless, over all we constantly found a changed neurophysiological pattern in the bilateral IFG in high trait ruminators in the course of the TSST. This difference in contrast to low trait ruminators could be interpreted as a deficit in cognitive control and inhibition [4], which blends in well with the known functions of the IFG as a central instance in inhibition during cognitive tasks [48–55]. Importantly, the study at hand shows that these neuronal changes are also associated with social

anxiety. However, the latter seems to explain additional variance, which is not covered by ruminative processes alone.

Furthermore, the TSST did successfully induce stress-reactive rumination as well as negative affect. We found both measures to be uniquely associated with social anxiety and trait rumination, even when we controlled for different levels of trait rumination and social anxiety, respectively. This is in line with our hypotheses and recent research investigating ruminative responses to stress [20,21,23,24,88,93] as well as associations of perceived stress in socially anxious individuals [42,98]. As already mentioned, experimental investigations of social stress in socially anxious subjects are scarce. However, it seems to be ostensible that with higher social anxiety there might also be a higher reactivity to socially stressful situations, as indicated by several correlation studies [99–101].

Intuitively, trait rumination and social anxiety did correlate significantly, which is well in line with the high comorbidity of mood disorders, like MDD, with anxiety disorders. However, our results also show that the previously reported effects of trait rumination on stress-induced processing seem to be independent of the potential confounder of social anxiety, at least to a certain degree. This in turn allows us to draw some clinical as well as scientific implications: Once more, we could demonstrate that via the TSST state rumination can be reliably induced. Moreover, this effect seems to be independent from social anxiety and therefore the TSST is a highly efficient tool to induce post-event processing in subjects with and without social anxiety. In a clinical or psychotherapeutic context our results might demonstrate that in the treatment of SAD a training of social skills to handle daily and/or stressful situations will not be sufficient, but it is also important to learn strategies to overcome rumination, for example via emotion regulation strategies [95].

Additionally, social anxiety and state rumination are not interchangeable as they only explain about 25% of common variance. Supporting this, we found trait rumination and social anxiety to independently influence outcome measures of the TSST on a behavioral as well as on a neurophysiological level. Taken together, these results strengthen the hypothesis of an underlying unifying mechanism which is potentially also transdiagnostic regarding other psychopathologies.

However, some limitations of the study have to be considered when interpreting the results. As not primarily socially anxious participants with diagnosed SAD were recruited, the analyzed data does not cover the full range of variance of social anxiety, especially if it is regarded as a dimensional construct. Even though we did find high variations in LSAS scores, investigations with a clinical sample of patients with SAD would potentially extend evidence for the unique effects of social anxiety on responses to the TSST. Further, we did not collect new data, as our hypotheses have not been analyzed with the used data yet, neither separately for each study nor for the merged sample. However, by merging the two datasets of our lab, we were able to increase the power of our statistical investigations and gather more evidence for the presence of our reported effects. Concerning the investigation of the neural correlates, we used fNIRS, which is highly useful in naturalistic investigations due to decreased sensitivity to motor artifacts [102–104], penetration depth is limited to about 1,5 – 2 cm of the cortex [105], which limits our findings to cortical

areas. Nevertheless, fNIRS offers the chance to reliably investigate neurobiological mechanisms in an ecologically valid setting [36].

5. Conclusion

Taken together and considering the current state of research [106,107], ruminative responses could be interpreted as a transdiagnostic construct in social anxiety and major depression disorder. However, both factors showed to be uniquely associated with stress-reactive rumination. Going further, previous studies could show that rumination also seems to play a role in other psychopathological syndromes associated with problems in emotion regulation (e.g. eating disorders [108], personality disorders [109] as well as substance abuse [110]). Future research should therefore extend findings of experimentally stress-induced rumination using samples of various mental disorders, as this promises to give support for a transdiagnostic and emotion-reactive understanding of rumination. This, in turn, could help to improve existing and to develop new psychotherapeutic interventions, of which one possible focus should be the treatment of ruminative thinking. For this purpose, fNIRS is a useful tool as it can be assessed easily in an ecologically valid manner (like we did it in the TSST) and it is very helpful to investigate the neurobiological basis of ruminative processes. In the future it could be used in a neurofeedback-design to help patients initially recognizing their ruminative processes and to overcome those. In this context, emotion regulation seems to be a promising strategy, what we are currently examining in a depressive sample.

Declarations

Data availability

The data of this study is available upon request from the first or the last author.

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Authors Contributions

H.L. & I.I. contributed in the analysis and interpretation of the data for the work and did the primary drafting. F.T., A.K., I.B., H.S., K.V.-S., T.D., R.T., A.J.F., A.-C.E. & D.R. contributed in the design and acquisition of the work and revised it critically for important intellectual content.

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Competing interests

No author reported conflicts of interest.

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Figures

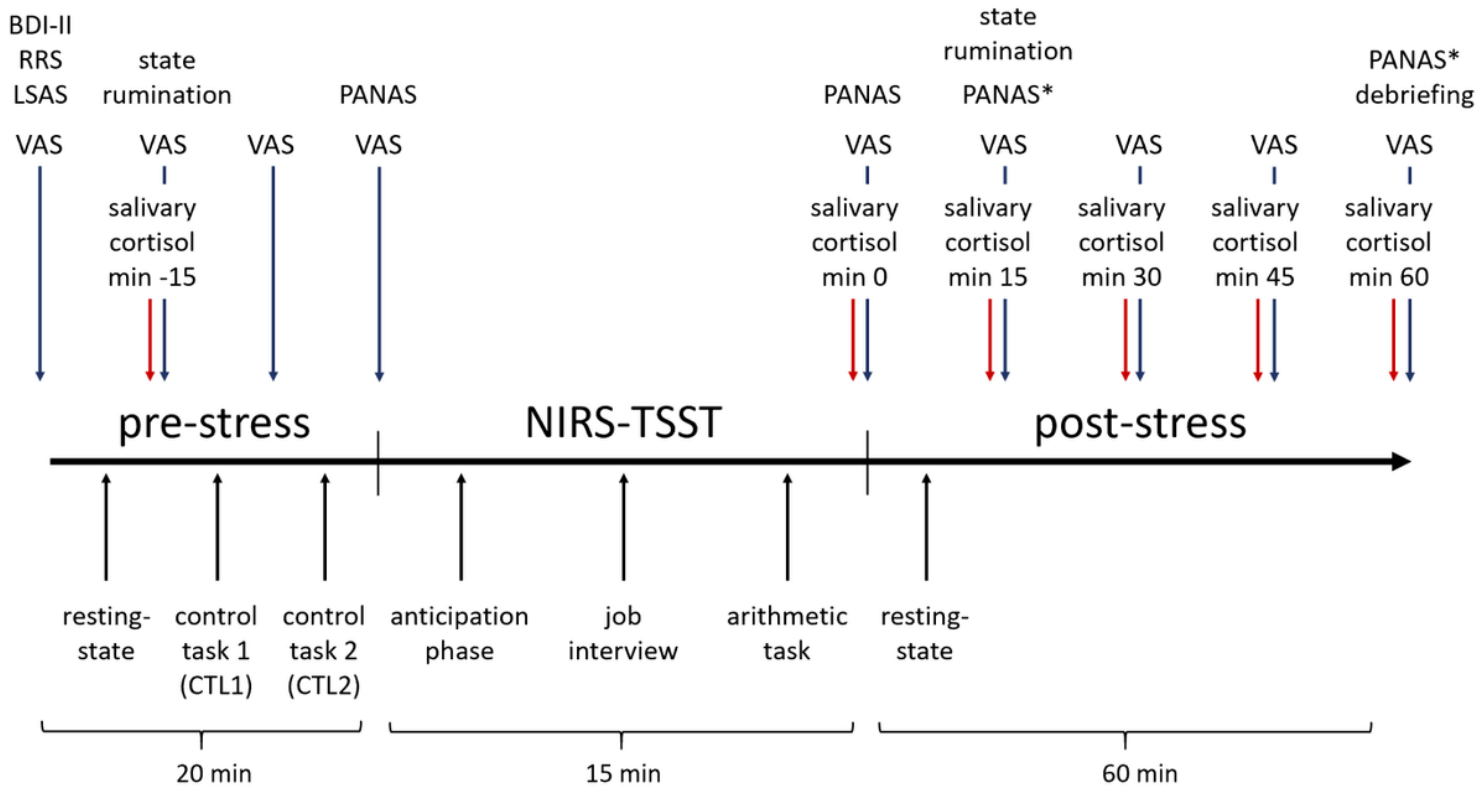

Figure 1

Time course of the TSST. VAS = Visual Analogue Scale assessing the subjective stress ratings, BDI-II = Beck Depression Inventory II 58, RRS = Rumination Response Scale 9, LSAS = Liebowitz Social Anxiety Scale 59, PANAS = Positive and Negative Affect Scale 67. *The third PANAS was differently assessed in study 1 (post 15 min) and 2 (post 60 min).

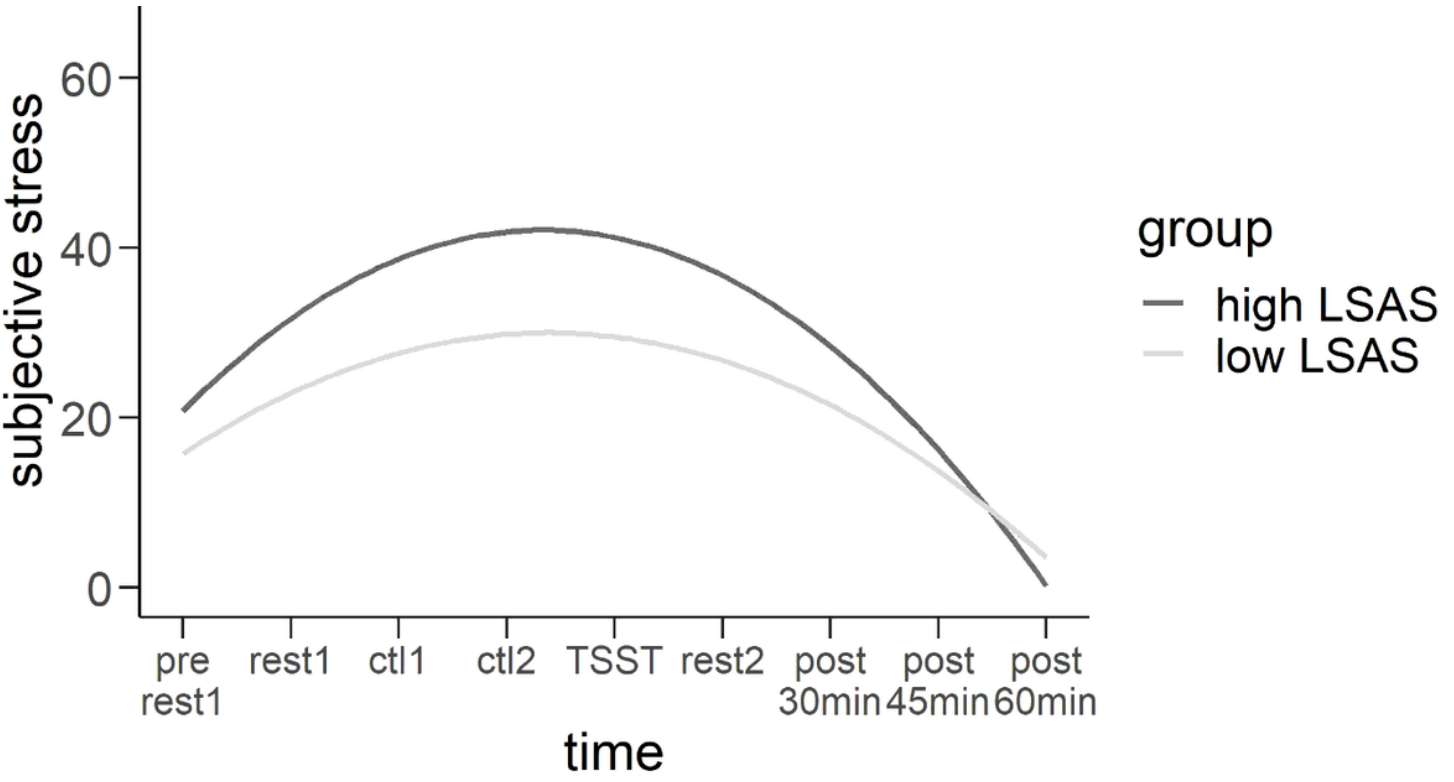

Figure 2

Predicted subjective stress ratings (VAS) in percent dependent on time according to the estimated parameters of the regression model including LSAS (rest1 = resting-state measurement 1, ctl1 = control task 1, ctl2 = control task 2, TSST = stress induction, rest2 = resting-state measurement 2). The significant interaction effect of LSAS and time has been categorized into low and high total scores (+/- 1 SD) for reasons of clearer visualization.

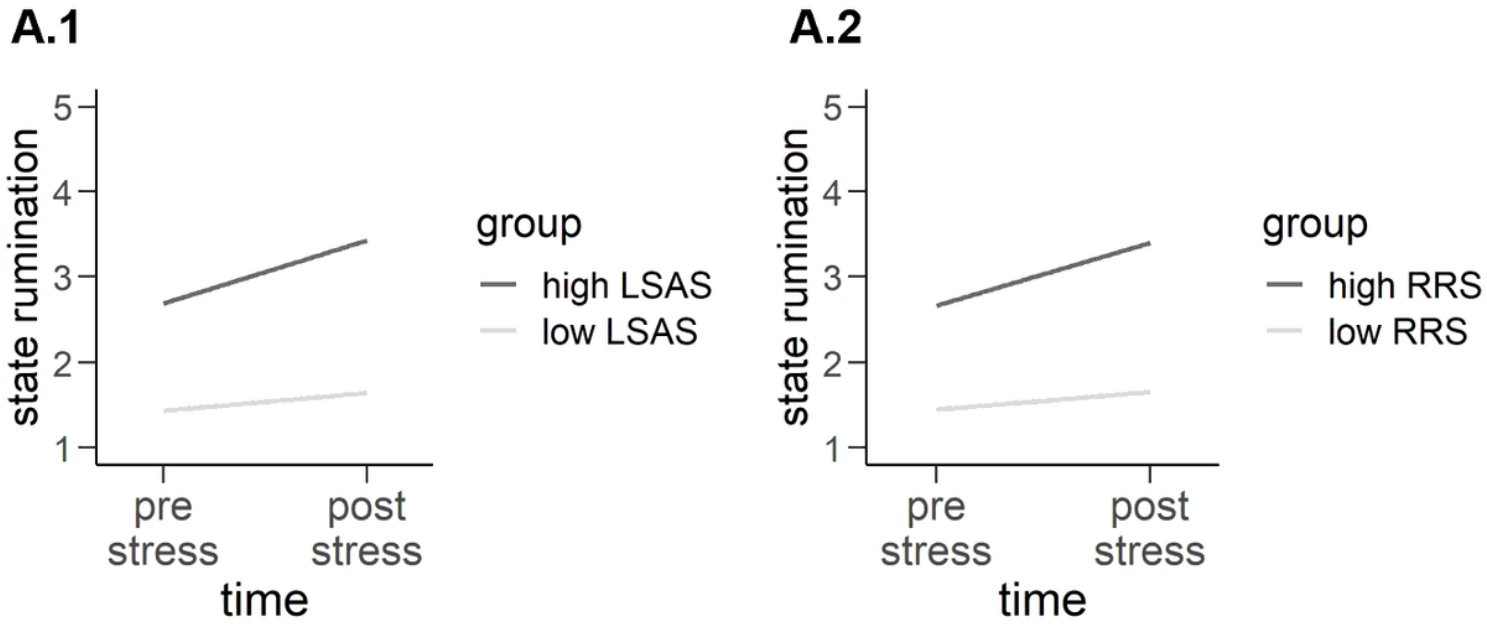

Figure 3

Predicted state rumination dependent on time (pre-stress vs. post-stress) according to the regression model including LSAS (A.1) and RRS (A.2), respectively. The significant interaction effects of LSAS and time (A.1) and RRS and time (A.2) have been categorized into low and high total scores (+/- 1 SD) for reasons of clearer visualization.

Supplementary Files

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