

Neural and Multimodal Signatures of Threat Learning, Generalization, and Return of Fear linked to Adverse Childhood Experiences

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**Neural and Multimodal Signatures of Threat Learning, Generalization, and Return of Fear
Linked to Adverse Childhood Experiences**

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Author note

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Abstract

Adverse childhood experiences (ACEs) are well established and strong risk factors for mental health challenges later in life, but the underlying mechanisms remain largely unclear. Associative learning, which shapes emotional and cognitive responses to environmental cues, may play a critical role in this relationship. However, the neural underpinnings linking ACEs and ACE load to alterations in associative threat and safety learning remain poorly understood. In this multimodal fMRI study, 171 participants (97 with ACEs, 74 without ACEs) underwent a fear conditioning paradigm, which included fear acquisition, generalization, extinction, and a return of fear test (ROF) after reinstatement. During fear acquisition, generalization and the ROF test, higher ACE load was associated with reduced discrimination between threat and safety cues, primarily driven by blunted responses to the threat cue across arousal ratings and central nodes of the fear network key brain regions (striatal regions and the vmPFC). During fear generalization, individuals with ACEs showed reduced activation in key brain regions to the CS+ (and GS+) but no differences in generalization gradients. In contrast, ACEs were neither related to expectancy ratings for nor aversiveness ratings for the unconditioned aversive event. These findings indicate a dissociation between cognitive and affective threat processing - putatively originating from a reduced transfer of US-related arousal to the CS+ as a hypothesized mechanistic pathway through which ACEs may become neurobiologically embedded, thereby potentially mediating the risk for mental health challenges.

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Introduction

Adverse childhood experiences (ACEs) can be defined as ‘experiences that are likely to require significant adaptation by an average child and that represent a deviation from the expectable environment’ (cf. 1). This umbrella definition covers a broad range of experiences, such as physical, sexual and emotional abuse, physical and emotional neglect, domestic violence, peer victimization and institutional rearing (e.g., 1, 2). Beyond their high prevalence - 43.7% of the general German population report having experienced at least one adverse event (3) - ACEs are linked to considerable individual suffering and have been estimated to account for 29.8% of all mental health disorders (2,4–9). This highlights the need to better understand the mechanisms linking ACEs to mental health in order to inform targeted prevention and intervention approaches (e.g., 10,11). One potential pathway underlying this association is a disruption of the neurobiological systems supporting associative learning (12,13). Through associative learning, environmental cues acquire predictive value for specific outcomes and thereby gain motivational significance, shaping emotional and cognitive processes and ultimately behavior. Threat learning mechanisms can be investigated under laboratory conditions using fear conditioning paradigms (14): In the fear acquisition phase, one inherently neutral cue (conditioned stimulus, CS+) is repeatedly paired with an aversive unconditioned stimulus (US, e.g., electro-tactile stimulation), which leads to the CS+ eliciting a conditioned response (CR), which closely resembles the unconditioned response to the US. A second neutral cue is presented but never paired with the US and serves as a control or safety cue (CS-). In a fear generalization phase, additional generalization stimuli (GS) resembling the CSs are included and (defensive) responses to the GS reflect

generalization of the CR. During the extinction phase, both the CS+ and CS- are presented but without the CS+ being paired with the US any longer, typically leading to a gradual reduction of the CR (15,16). In a return of fear (ROF) test phase, the recurrence of the CR can be investigated following unannounced re-exposure to the US (i.e., reinstatement). Fear acquisition and extinction serve as a model for the development and exposure-based treatment of anxiety- and stress-related disorders, while ROF test phases have been used to experimentally model relapse phenomena (16,17). Reinstatement-based mechanisms are considered to have transdiagnostic relevance beyond anxiety-related disorders, given that exposure to stressful or aversive life events is a well-established risk factor for the recurrence or worsening of symptoms across diverse psychopathological conditions.

The neural network implicated in threat learning, extinction and generalization is well established (18–20). More precisely, in humans, fear acquisition is typically linked to the dorsal anterior cingulate cortex (dACC), insula, striatal regions, and thalamus, whereas fear extinction is associated with activation in the dACC, medial prefrontal cortex (mPFC), insula, dorsolateral prefrontal cortex (dlPFC), putamen, caudate, pallidum, thalamus, motor cortical regions, and the pons. (19). Generalization gradients have been described as positive gradients (i.e., highest response to the CS+) in the anterior insula, dACC and thalamus and negative gradients (i.e., highest response to the CS-) in the hippocampus, ventromedial prefrontal cortex (vmPFC) and amygdala (20). While our recent review (21) provides first evidence for blunted responding towards threat signals in individuals with a history of ACEs, an integrative interpretation of the current evidence base is challenging as the existing studies have largely examined single experimental phases which correspond to different learning processes and outcome measures in isolation. This provides an incomplete picture as results for the extinction phase cannot be interpreted without knowledge of results from the preceding fear acquisition training phase - leaving critical mechanistic questions

(i.e., threat vs. safety learning) open. Likewise, different outcome measures tap into slightly different mechanisms and timing of stimulus processing. Fragmented evidence is hence difficult to integrate into a coherent picture. Crucially, studies focusing on the neural underpinnings of these associations are rare and results inconsistent (21) with only a single study investigating the link between ACEs and threat generalization at a neuro-functional level (22). Similarly, the operationalization of ACEs differed considerably across studies (e.g., dimensional vs. categorical approaches including median-split dichotomization, or focussing on specific adversity types only, (21)). Hence, for the present study we decided to include both, a categorical as well as a dimensional (cumulative risk approach) analysis approach to enhance comparability. The primary aim of this pre-registered study is to systematically integrate results from different outcome measures - including measures of neural activation (fMRI) - across all experimental phases in a single well-powered study. This design enables both the direct comparisons of different outcome measures within the same study and allows findings to be interpreted comprehensively in reference to preceding or subsequent experimental phases. In particular, we aim to elucidate mechanistic pathways through which ACEs may contribute to mental health symptoms by examining alterations in threat learning processes, focusing on neural activation patterns in key brain regions implicated in these mechanisms (18). Based on our prior work (21), we hypothesize an association between a history of ACEs and ACE load and reduced CS discrimination, driven by attenuated CS+ responding during fear acquisition and generalization across outcome measures. At the neural level, we expect corresponding differences in threat-related regions (18). During generalization, group differences in generalization gradients are explored in regions implicated in fear generalization (20), while analyses for the extinction phase and the ROF phase are exploratory due to limited evidence (21). A secondary aim is to explore potential interactions between ACE load, CS-discrimination and the general level of psychological, social and occupational functioning (i.e.,

GAF; Global Assessment of Functioning). We chose the GAF score as a continuous measure based on the individuals' clinical symptom load over categorical diagnostic grouping because the latter would not account for substantial within-diagnosis variance or comorbidities. Further, the resulting diagnostic subgroups would have been too small for adequately powered analyses. Hypotheses and analyses were pre-registered unless mentioned otherwise (OSF; <https://doi.org/10.17605/OSF.IO/W3ARJ>; January-12-2024; see **Table S4** for minor deviations).

Methods

Sample

We recruited 183 participants from a pre-screened sample and group assignment was based on the German version of the MACE questionnaire (Maltreatment and Abuse Chronology of Exposure; 23; i.e., KERF-I. Belastende Kindheitserfahrungen, 24). A full list of questionnaires as well as details on the sample are provided in chapter 1.1 the **supplementary material**. Participants recruited for the study additionally completed a telephone screening for current and lifetime psychiatric disorders using the Structured Clinical Interview for DSM-5 Disorders – Clinical Version (SCID-5-CV; 25) and were rated on their “general level of functioning” (Global Assessment of Functioning (GAF), American Psychiatric Association, 2000). Due to procedural and technical problems, the final sample consisted of 171 participants (for details see **Table 1** and chapter 2.1 in the **supplementary material**).

Paradigm

Participants underwent a fear conditioning task in an MR scanner with habituation, fear acquisition, fear generalization, fear extinction and a ROF test phase following a fear reinstatement manipulation, with all phases completed on the same day. Colored circles (presented using

Presentation Software (Neurobehavioral Systems, Inc., Albany, California) served as conditioning stimuli (CS). Prior to the experiment, the electrotactile stimulation (i.e., the unconditioned stimulus; US) was calibrated to the maximum tolerable intensity aiming for a 7-8 on a scale from 1 (not unpleasant at all) to 10 (extremely unpleasant; see **Figure 1** and chapter 1.2 in the **supplementary material** for details).

Data Acquisition and Preprocessing

Fear-potentiated startle response (FPS) and skin conductance responses (SCR) were acquired pre-processed following published guidelines (26–28) and previous work within the MRI (29). (f)MRI data were acquired on a 3-Tesla MR-scanner (MAGNETOM Prisma, Siemens) with a 64-channel head coil. Details on data acquisition and pre-processing are described in the **supplementary material**.

Statistical Analyses (physiological and rating data)

As pre-registered, to examine the differences between individuals with and without ACEs (i.e., categorical analyses) and differential conditioned responding, two-way mixed ANOVAs were conducted, including CS type (CS+ vs. CS-) and ACE group (ACE vs. noACE) as independent variables for all outcome measures (arousal, valence, fear and US-expectancy ratings as well as SCR and FPS) and experimental phases. Significant group interactions were always followed up by post hoc independent samples t-tests. For the generalization phase, the linear deviation score (LDS) was used as an index of the linearity of the generalization gradient (30,31). It was calculated by subtracting the mean responses to all GS from the mean responses to both CS and compared between ACE groups using t-tests. To examine the relationship between ACE load (i.e., cumulative risk approach) - operationalized as the KERF sumscore - and conditioned responding, we conducted linear regressions for subjective ratings and the LDS. An additional exploratory

regression analysis with ACE group and CS-discrimination as predictors and the GAF score as continuous measure of general level of functioning as a dependent variable was performed. Further, we conducted a formal mediation-analysis to explore if the association of ACE load and GAF is mediated by CS-discrimination. For SCR and startle data, we used linear mixed-effects models (LMMs), including the KERF sumscore, stimulus type and their interaction as fixed effects, with random intercept for subject and random slope for CS type. All statistical tests for physiological and behavioral outcome measures were performed using R (R Core Team, 2023) with the significance level set to $\alpha < .05$ (two-sided). Post-hoc t-tests were corrected for multiple comparisons by using Bonferroni-Holm correction. For data analyses and visualizations, as well as for the creation of the manuscript, we used the following R packages¹.

Statistical models (fMRI):

For all phases, for the first level general linear model (GLM), separate regressors for the stimuli (CS+, CS-, three GS for generalization) were included. US presentations, startle probes and ratings were included as additional regressors. For fear acquisition and extinction, the first CS+

¹ R (Version 4.2.3; 32) and the R-packages *afex* (Version 1.4.1; 33), *apa* (Version 0.3.4; 34,35), *car* (Version 3.1.3; 36,37), *carData* (Version 3.0.5; 37), *dplyr* (Version 1.1.1; 38), *effectsize* (Version 1.0.1; 39), *emmeans* (Version 1.10.5; 40), *ez* (Version 4.4.0; 41), *ggplot2* (Version 4.0.1; 42), *ggpubr* (Version 0.6.0; 43), *here* (Version 1.0.1; 44), *knitr* (Version 1.42; 45), *lme4* (Version 1.1.35.5; 46), *lmerTest* (Version 3.1.3; 47), *MASS* (Version 7.3.58.2; 48), *Matrix* (Version 1.5.3; 49), *mediation* (Version 4.5.1; 50,51–54), *mvtnorm* (Version 1.3.2; 55), *papaja* (Version 0.1.4; 35), *psych* (Version 2.5.6; 56), *readxl* (Version 1.4.3; 57), *reshape2* (Version 1.4.4; 58), *rstatix* (Version 0.7.2; 59), *sandwich* (Version 3.1.1; 60,61,62), *sjPlot* (Version 2.9.0; 63), *tidyr* (Version 1.3.1; 64), *tinylabels* (Version 0.2.4; 65), and *xlsx* (Version 0.6.5; 66)

and CS- were included as separate regressors and for the extinction phase, contrasts for early and late extinction were estimated separately. For the ROF test phase only the first two trials after reinstatement were included as regressor of interest, the remaining trials were modeled as separate regressors. Further, movement parameters were included as nuisance regressors in all analyses. The contrast estimates “CS+ > CS-” and “CS- > CS+” were taken to the second-level analyses. To test for differences in CS-discrimination between individuals with and without ACEs, two-sample t-tests for the CS+ > CS- contrast were calculated, for each phase separately. Additionally, linear regressions were conducted to investigate if ACE load predicted a reduction in the CS+ > CS- contrast during fear acquisition. Correction for multiple comparisons was done on the whole-brain level and within predefined anatomical regions of interest (ROI): bilateral amygdala, hippocampus, caudate nucleus, putamen, pallidum, nucleus accumbens and thalamus as well as dlPFC, dACC and vmPFC. To investigate potential differences in neural generalization gradients (30) between groups, we extracted ROI-level beta estimates from regions identified in fear generalization in a meta-analysis (i.e., anterior insula, caudate, thalamus, dlPFC, dACC, hippocampus, amygdala and vmPFC; 20). For bilateral ROIs, values were averaged across hemispheres. This approach was chosen because corresponding statistical analyses to calculate the linear deviation scores (LDS) cannot readily be implemented in SPM. Instead, these analyses were conducted in R using the extracted ROI-based parameter estimates.

Results

Sample characteristics

The full sample consisted of 171 participants (see **Table 1**; 124 women, 47 men, age range: 18 - 53 years, mean age = 25.64, *SD* = 4.78).

Threat-Safety Discrimination:

In the full sample, the expected pattern of stronger responses to the CS+ (and GS) compared to the CS- across all behavioral and physiological outcome measures was observed for fear acquisition and generalization, while results for the fear extinction phase indicated successful fear extinction. During the ROF test phase, a re-occurrence of the conditioned response was observed (i.e., differential reinstatement with CS+ > CS- across all ratings, generalized reinstatement to both CSs in SCRs. See **supplementary material** and **Table S1** for details. At a neural level, whole brain analyses for the CS+ > CS- contrast during the fear acquisition and generalization phase showed widely distributed activation patterns typically observed for differential fear conditioning. For extinction (whole phase as well as early versus late extinction), no significant effects for the CS+ > CS- contrast were observed.

Associations between CS-discrimination and ACEs

During the fear acquisition phase, CS discrimination in arousal ratings was reduced in individuals with ACEs as compared to those without ($p = .011$, see **Table 2** and **Figure 2B**) driven by trend-wise but non-significantly blunted CS+ responding ($M_{ACE} = 70.08$) in individuals with a history of ACEs ($M_{noACE} = 77.40$, $t(167) = 1.92$, $p = .057$) while no significant differences were observed for the CS- ($M_{ACE} = 16.9$; $M_{noACE} = 13.4$, $t(167) = -1.17$, $p = .243$). No significant group differences were observed for other outcome measures, even though at a descriptive level (see **Figure 2E**) individuals with a history of ACEs showed generally - although statistically not significant - reduced SCRs to the CS+ and a trend-wise reduction in CS discrimination at the neural level in the left anterior insula as well as striatal ROIs (caudate, pallidum, putamen, see **Table S5** and **Figure S2**). During the generalization phase, individuals with ACEs showed reduced CS-discrimination in the left caudate ($p_{FWE} = .022$), dlPFC ($p_{FWE} = .049$) as well as the left nucleus

accumbens ($p_{\text{FWE}} = .012$; see **Table S2**). Extracted parameter estimates from ROIs show blunted CS+ (dACC: $t(159) = 2.04, p = .04$, vmPFC: $t(159) = 2.05, p = .04$) and GS+ (amygdala: $t(159) = 2.96, p = .004$) responses while generalization gradients are comparable (see **Figure 3**). No significant differences in CS discrimination were observed between both groups in any other outcome measure (all $p > .05$, **Table 2**), nor for Linear Deviation Scores (LDS; all $p > .05$, see **Table S2**). During the extinction phase, no significant group differences in CS discrimination were observed (all $p > .05$, **Table 2**). At the ROF-test, group differences as observed during acquisition re-emerged (i.e., reduced CS-discrimination in individuals with ACEs) for arousal ratings but now also for expectancy and fear ratings. As during acquisition, this was driven by significantly lower CS+ ratings in individuals with ACEs (expectancy: $t = 2.89, df = 153, p = .004, d = 0.47$; arousal: $t = 3.03, df = 153, p = .003, d = 0.49$; fear: $t = 2.12, df = 153, p = .036, d = 0.345$) in absence of differences for the CS- (all $p > .05$; see **Table 2**). For valence ratings, a similar pattern, yet only at a non-significant descriptive level ($p = .062$) was observed. No group differences emerged for SCRs and BOLD fMRI.

Associations between CS-discrimination and ACE Load

As in the categorical analyses, higher ACE load was associated with significantly reduced CS discrimination in arousal ratings during acquisition ($p = .019$, see **Table 2**) resulting from non-significantly reduced CS+ responding ($b = -0.218, t(334) = -1.85, p = .065$) as well as nonsignificantly increased CS- responding ($b = 0.203, t(5678) = 1.72, p = .086$, see **Figure 4A**). At a descriptive but statistically not significant level (see **Figure 2E**) individuals with higher ACE load showed reduced CS discrimination in fear and valence ratings as well as SCRs. This pattern was mirrored at the neural level with ACE load being significantly associated with a reduction in CS-discrimination in the right caudate ($p_{\text{FWE}} = .016$), bilateral nucleus accumbens ($p_{\text{FWE}} = .027$ and

$p_{FWE} = 0.046$), left putamen ($p_{FWE} = .024$), bilateral pallidum ($p_{FWE} = .046$ and $p_{FWE} = .035$) and the vmPFC ($p_{FWE} = .017$; see **Figure 5** and **Table S5**). No significant association between ACE load and CS discrimination was observed in any other outcome measure during acquisition or during generalization and extinction - also matching categorical analyses. One exception to this is the neural level during generalization: Higher ACE load was significantly associated with a reduction in CS-discrimination in left lateralized striatal areas (i.e., caudate, $p_{FWE} = .01$; putamen, $p_{FWE} = .01$; pallidum, $p_{FWE} = .003$). Again matching categorical analyses, for the ROF test phase, higher ACE load was significantly associated with reduced CS discrimination in arousal ($p = .048$) and expectancy ratings ($p = .036$) and at the neural level with reduced CS discrimination in the dACC ($p_{FWE} = .01$) but increased CS discrimination in the left caudate ($p_{FWE} = .039$; see **Figure 5**). No such effects were observed in any outcome measure (all $p > .05$).

ACEs and Psychological Functioning

Exploratory analyses focused on arousal ratings, as these showed the most consistent effects across phases. Reduced CS-discrimination in post-acquisition arousal ratings was associated with lower global level of functioning (GAF; ($b = .49$, $t(144) = 3.19$, $p = .002$, **Figure 6A**). Importantly, this effect was only significant in exposed individuals ($b = .14$, $t(85) = 2.74$, $p = .007$) but not unexposed ($b = .02$, $t(57) = 0.31$, $p = .756$, see **Figure 6B**). A formal - albeit cross-sectional - mediation-analysis revealed that the association of ACE load and GAF is, in fact, (statistically) partially mediated (9%, $p = .044$) by reduced CS-discrimination in post-acquisition arousal ratings. This is consistent with a mediating role in the association between ACE load and GAF, as the indirect effect of ACE load on GAF reached significance (ACME = -0.036 , 95 % CI [-0.1061 , -0.0006], $p = .044$). When controlling for CS discrimination in post-acquisition arousal ratings, this effect remained statistically significant (ADE = -0.36 , $p < .001$).

Discussion

We investigated how a history of ACEs and cumulative ACE load relate to key threat learning processes (acquisition, generalization, extinction, and ROF) across outcome measures, including neurofunctional measures. Using a pre-registered, multimodal experimental design in a large pre-screened sample ($N = 171$), this study aimed to provide the most comprehensive and mechanistic account of experience-dependent alterations in threat and safety processing as well as threat generalization to date. In sum, ACEs - particularly cumulative ACE load - was associated with reduced CS discrimination during fear acquisition and ROF, driven primarily by blunted CS+ responding while US expectancy ratings, US intensity and perceived US aversiveness were comparable between groups. This pattern emerged in arousal ratings and most prominently within the striatal salience circuitry (i.e., incl. accumbens, caudate, putamen, pallidum) as well as the vmPFC and was less consistent in “classical” threat-related areas (e.g., insula, amygdala, hippocampus, dACC, see 18) and fear ratings. Notably, these associations were restricted to experimental phases characterized by imminent threat (fear acquisition and generalization). Importantly, neither ACE exposure nor ACE load were related to the shape of generalization gradients (i.e., LDS) highlighting that effects are restricted to the CS+ (and partly the GS+, see **Figure 3**) - thereby replicating previous work (22,32,33). The prominence of striatal and arousal-based effects in absence of group differences in threat responding may reflect altered salience or value assignment to the threat cue (CS+), such that their affective impact is diminished despite preserved explicit knowledge about CS–US contingencies. Importantly however, the literature on associative threat learning in individuals with a history of ACEs is overall heterogeneous (for a review, see 21), with many studies reporting null findings but also studies that report enhanced responding to threat cues in individuals with a history of ACEs (e.g., 34). Recent work suggests, that this variability might reflect the influence of factors such as the developmental timing (35, 36)

and severity (35) of adverse experiences, which may differentially affect learning-related processes and subsequent symptom development (36). Notably, Sisk and colleagues identified distinct neural response profiles using a latent profile approach integrating both adversity characteristics and neural activation patterns, whereas cumulative ACE load alone did not account for the observed patterns. This highlights that sample characteristics as well as characteristics of adversity beyond cumulative exposure - such as developmental timing and severity - should be taken into account in future work to advance our understanding of how different aspects of adverse experiences shape developmental trajectories and may, in turn, help explain the heterogeneous findings in the existing literature.

Our results highlight the value of multimodal experimental approaches in providing mechanistic insights. Specifically, we demonstrate a dissociation between arousal and expectancy ratings in individuals with a history of ACEs, suggesting that ACEs are primarily associated with blunted flexible affective threat responses - potentially reflecting a reduced transfer of US-related arousal to the CS+ (37) - while leaving cognitive contingency learning intact. Typically, this transfer occurs as the CS+ becomes a reliable predictor of the (imminent) US thereby acquiring the ability to activate neural pathways and behavioral responses similar to those involved in processing the US itself (18,37). We speculate that this reduced transfer, seemingly specific to the arousal component, may have developed as an adaptive mechanism in environments characterized by high levels of unpredictability and uncontrollability - common features of ACEs (10,38). In such environments, attenuated arousal responding in the face of an uncontrollable predictor of threat - as the US in a fear conditioning experiment - may constitute an experience-dependent adaptive and energy efficient strategy (12,39). However, in more stable environments later in life, this response pattern may become maladaptive. A potentially reduced motivation to escape aversive states may interfere with the pursuit of goals (e.g., rewards) and manifest as anhedonia-like behavior - a core

symptom of mood disorders (40). Because the present paradigm offers little opportunity for control through action, future studies should explore in more detail whether alterations in the affective anticipatory threat response also affect subsequent decision-making processes and approach-avoidance behavior (41,42).

A notable exception to this dissociation emerged in the ROF test phase - an experimental model of relapse (17) - where ACE history and load were associated with reduced US-expectancy to the CS+ - accompanied by similarly blunted CS+ responses in arousal and fear ratings. Unlike the acquisition and generalization phase which involve strong and predictable CS+–US contingencies (i.e., 80% reinforcement rate, strong situation; 43), the ROF test phase is characterized by ambiguity following unsignalled US re-exposure (17). Individuals with a history of ACEs may therefore be less likely to trust that prior threat contingencies remain valid in ambiguous contexts, potentially reflecting heightened exposure to environmental unpredictability during development (10,38). At the neural level, individuals with higher ACE load were characterized by reduced discrimination in the dACC during the ROF test - a region known to be implicated in the threat learning and particularly tagging emotional events as action-relevant (44,45). In contrast, we observed enhanced discrimination-related activity in the (left) caudate, a region implicated in prediction error signalling in ambiguous contexts. .

Thus, under conditions of uncertainty, individuals with higher ACE load showed reduced discrimination between threat and safety at the level of explicit US-expectancy in contrast to phases with more certainty (acquisition, generalization), in which this effect was only present in arousal-based measures. In addition, discrimination-related activity in the striatum was enhanced in individuals with higher ACE load under uncertain conditions but reduced when contingencies were more certain. This dissociation between reduced explicit discrimination (i.e., expectancy ratings)

and increased striatal engagement under uncertainty may suggest a link between a history of ACEs and biases in threat learning toward more implicit, striatum-based representations that are engaged when environmental conditions are ambiguous but are less accessible to conscious expectancy evaluations. In addition to these main findings, in a secondary, exploratory set of analyses, we examined how ACEs, threat responding and global psychological functioning are interrelated to indirectly tackle an apparent paradox in the literature. Stress- and anxiety-related disorders are consistently and primarily linked to deficits in safety learning (i.e., enhanced responding to the CS-; 46, 47, 48) while a history of ACE, as a well established risk factor (5,8,9), has been linked to blunted threat responding (i.e., CS+; 21). Strikingly, both lines of research show effects particularly pronounced in affective ratings but not in physiological measures. These exploratory analyses revealed an association of lower CS discrimination in arousal ratings and lower general functioning (i.e., lower GAF scores), yet, this was only true for individuals with a history of ACEs. Even though our study was not explicitly designed to solve the paradox outlined above, our exploratory analysis suggests that aberrant CS-discrimination might partially mediate the association of ACEs and the subsequent development of mental health symptoms.

Limitations and Outlook

While a large sample and the inclusion of multiple outcome measures provides possibilities that were not given in previous studies, they also come with challenges including higher data loss for physiological measures inside the MR and potential selection biases as compared to behavioral-lab settings. In addition, despite the broad range of outcome measures included, reliance on post-phase ratings limits temporal precision and future studies should focus on trial-by-trial ratings to capture learning dynamics and individual trajectories. Moreover, the cross-sectional design precludes causal or mechanistic conclusions and limits the interpretation of the mediation analysis,

hence longitudinal studies are needed to clarify the causal relationships. Finally, we relied on a traditional binary categorization of ACEs as well as on a cumulative load score relying on implicit assumptions of simple additive effects of adversity types (49). Both approaches represent a simplification of the heterogeneity inherent in ACEs (e.g., 50) and do not capture dimensions such as chronicity, severity, timing, or type of ACE (49).

Conclusion

In conclusion, the results of the current study suggest that reduced CS-discrimination in arousal-based measures linked to ACEs does not appear to reflect alterations in declarative threat learning (i.e., associative learning of the cue-outcome contingencies) or threat reactivity per se. Rather, ACEs seem to be linked to a reduced transfer of US-related arousal to the CS+, a core mechanism of aversive learning in which the CS comes to predict the imminent US and thereby gains the ability to engage neural pathways involved in US processing. Similarly, reduced US-expectancy during the ROF test indicated that individuals with ACEs are less likely to rely on learned contingencies in a new, ambiguous situation. Investigating how these alterations shape real-world anticipatory behavior and their long-term consequences represents a promising direction for future research. These processes, particularly the hypothesized reduced transfer of US-related arousal, should be examined in more detail using experimental paradigms specifically designed to probe these mechanisms and their translation into behavioral response patterns (42).

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Data availability Statement

This article has been posted on a preprint server: https://osf.io/preprints/psyarxiv/8u5wx_v1

AI Technologies

AI tools (i.e., ChatGPT 5.3) were used to debug code and for stylistic editing.

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Conflict of Interest

The authors declare no competing financial interests.

References

1. McLaughlin KA, Sheridan MA, Gold AL, Duys A, Lambert HK, Peverill M, *et al.* (2016): Maltreatment Exposure, Brain Structure, and Fear Conditioning in Children and Adolescents. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 41: 1956–1964.
2. Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, *et al.* (2006): The enduring effects of abuse and related adverse experiences in childhood. *European archives of psychiatry and clinical neuroscience* 256: 174–186.
3. Witt* A, Sachser* C, L. Plener P, Brähler E, M. Fegert J (2019): The Prevalence and Consequences of Adverse Childhood Experiences in the German Population. *Deutsches Ärzteblatt International* 116: 635–642.
4. Kessler RC, McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, *et al.* (2010): Childhood adversities and adult psychopathology in the WHO World Mental Health Surveys. *The British Journal of Psychiatry: The Journal of Mental Science* 197: 378–385.
5. Kirkbride JB, Anglin DM, Colman I, Dykxhoorn J, Jones PB, Patalay P, *et al.* (2024): The social determinants of mental health and disorder: Evidence, prevention and recommendations. *World Psychiatry* 23: 58–90.
6. McLaughlin KA, Greif Green J, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC (2012): Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents. *Archives of General Psychiatry* 69: 1151–1160.
7. Green JG, McLaughlin KA, Berglund PA, Gruber MJ, Sampson NA, Zaslavsky AM, Kessler RC (2010): Childhood Adversities and Adult Psychiatric Disorders in the National Comorbidity Survey Replication I: Associations With First Onset of DSM-IV Disorders. *Archives of General Psychiatry* 67: 113–123.
8. Teicher MH, Gordon JB, Nemeroff CB (2022): Recognizing the importance of childhood maltreatment as a critical factor in psychiatric diagnoses, treatment, research, prevention, and education. *Molecular Psychiatry* 27: 1331–1338.
9. Struck N, Krug A, Yuksel D, Stein F, Schmitt S, Meller T, *et al.* (2020): Childhood maltreatment and adult mental disorders – the prevalence of different types of maltreatment and associations with age of onset and severity of symptoms. *Psychiatry Research* 293: 113398.
10. McLaughlin KA, DeCross SN, Jovanovic T, Tottenham N (2019): Mechanisms linking childhood adversity with psychopathology: Learning as an intervention target. *Behaviour Research and Therapy* 118: 101–109.

11. Romeo RR, Segaran J, Leonard JA, Robinson ST, West MR, Mackey AP, *et al.* (2018): Language Exposure Relates to Structural Neural Connectivity in Childhood. *The Journal of Neuroscience* 38: 7870–7877.
12. Gerin MI, Puetz VB, Blair RJR, White S, Sethi A, Hoffmann F, *et al.* (2017): A neurocomputational investigation of reinforcement-based decision making as a candidate latent vulnerability mechanism in maltreated children. *Development and Psychopathology* 29: 1689–1705.
13. Morelli NM, Liuzzi MT, Duong JB, Kryza-Lacombe M, Chad-Friedman E, Villodas MT, *et al.* (2021): Reward-related neural correlates of early life stress in school-aged children. *Developmental Cognitive Neuroscience* 49: 100963.
14. Lonsdorf TB, Menz MM, Andreatta M, Fullana MA, Golkar A, Haaker J, *et al.* (2017): Don't fear "fear conditioning": Methodological considerations for the design and analysis of studies on human fear acquisition, extinction, and return of fear. *Neuroscience & Biobehavioral Reviews* 77: 247–285.
15. Milad MR, Quirk GJ (2012): Fear Extinction as a Model for Translational Neuroscience: Ten Years of Progress. *Annual Review of Psychology* 63: 129–151.
16. Vervliet B, Craske MG, Hermans D (2013): Fear Extinction and Relapse: State of the Art. *Annual Review of Clinical Psychology* 9: 215–248.
17. Haaker J, Golkar A, Hermans D, Lonsdorf TB (2014): A review on human reinstatement studies: An overview and methodological challenges. *Learning & Memory (Cold Spring Harbor, NY)* 21: 424–440.
18. Fullana MA, Harrison BJ, Soriano-Mas C, Vervliet B, Cardoner N, Àvila-Parcet A, Radua J (2016): Neural signatures of human fear conditioning: An updated and extended meta-analysis of fMRI studies. *Molecular Psychiatry* 21: 500–508.
19. Fullana MA, Albajes-Eizagirre A, Soriano-Mas C, Vervliet B, Cardoner N, Benet O, *et al.* (2018): Fear extinction in the human brain: A meta-analysis of fMRI studies in healthy participants. *Neuroscience & Biobehavioral Reviews* 88: 16–25.
20. Webler RD, Berg H, Fhong K, Tuominen L, Holt DJ, Morey RA, *et al.* (2021): The neurobiology of human fear generalization: Meta-analysis and working neural model. *Neuroscience & Biobehavioral Reviews* 128: 421–436.
21. Ruge J, Ehlers MR, Kastrinogiannis A, Klingelhöfer-Jens M, Koppold A, Abend R, Lonsdorf TB (2024): How adverse childhood experiences get under the skin: A systematic review, integration and methodological discussion on threat and reward learning mechanisms ((C. M. Gillan & K. M. Wassum, editors)). *eLife* 13: e92700.

22. Lange I, Goossens L, Bakker J, Michielse S, van Winkel R, Lissek S, *et al.* (2019): Neurobehavioural mechanisms of threat generalization moderate the link between childhood maltreatment and psychopathology in emerging adulthood. *Journal of Psychiatry and Neuroscience* 44: 185–194.
23. Teicher MH, Parigger A (2015): The “Maltreatment and Abuse Chronology of Exposure” (MACE) Scale for the Retrospective Assessment of Abuse and Neglect During Development. *PLOS ONE* 10: e0117423.
24. Isele D, Teicher MH, Ruf-Leuschner M, Elbert T, Kolassa I-T, Schury K, Schauer M (2014): KERF–Ein Instrument zur umfassenden Ermittlung belastender Kindheitserfahrungen: Erstellung und psychometrische Beurteilung der deutschsprachigen MACE (Maltreatment and Abuse Chronology of Exposure) Scale. *Zeitschrift für Klinische Psychologie und Psychotherapie* 43: 121–130.
25. First MB, Williams JBW, Karg RS, Spitzer RL (2016): *User’s Guide for the SCID-5-CV Structured Clinical Interview for DSM-5 Disorders: Clinical Version*. Arlington, VA, US: American Psychiatric Publishing, Inc., pp xii, 158.
26. Measures S for PRAHC on E (2012): Publication recommendations for electrodermal measurements. *Psychophysiology* 49: 1017–1034.
27. Kuhn M, Gerlicher AMV, Lonsdorf TB (2022): Navigating the manyverse of skin conductance response quantification approaches – A direct comparison of TROUGH-TO-PEAK , baseline correction, and model-based approaches in Ledalab and PSPM. *Psychophysiology* 59. <https://doi.org/10.1111/psyp.14058>
28. Blumenthal TD, Cuthbert BN, Filion DL, Hackley S, Lipp OV, van Boxtel A (2005): Committee report: Guidelines for human startle eyeblink electromyographic studies. *Psychophysiology* 42: 1–15.
29. Kuhn M, Wendt J, Sjouwerman R, Büchel C, Hamm A, Lonsdorf TB (2020): The Neurofunctional Basis of Affective Startle Modulation in Humans: Evidence From Combined Facial Electromyography and Functional Magnetic Resonance Imaging. *Biological Psychiatry* 87: 548–558.
30. Stegmann Y, Reutter M, Hutterer K, Hildebrandt L, Deckert J, Deserno L, *et al.* (2025): Psychometric Considerations in Assessing Fear Generalization as a Predictor of Anxiety. *Biological Psychiatry Global Open Science* 100570.
31. Kaczurkin AN, Burton PC, Chazin SM, Manbeck AB, Espensen-Sturges T, Cooper SE, *et al.* (2017): Neural Substrates of Overgeneralized Conditioned Fear in PTSD. *American Journal of Psychiatry*. <https://doi.org/10.1176/appi.ajp.2016.15121549>

32. Klingelhöfer-Jens M, Hutterer K, Schiele MA, Leehr EJ, Schümann D, Rosenkranz K, *et al.* (2025): Reduced discrimination between signals of danger and safety but not overgeneralization is linked to exposure to childhood adversity in healthy adults ((M. J. Frank, editor)). *eLife* 12: RP91425.
33. Qiu Y, Dou H, Dai Y, Li H, Lei Y (2022): The influence of being left behind on fear acquisition and academic performance—a study of left-behind children. *Current Psychology*. <https://doi.org/10.1007/s12144-022-03914-1>
34. Machlin L, Sheridan MA, Lurie LA, Kasparek SW, Kim SG, Peverill M, *et al.* (2024): Alterations in fear learning as a mechanism linking childhood exposure to violence with PTSD symptoms: A longitudinal study. *Psychological Medicine* 54: 3389–3397.
35. Sisk LM, Keding TJ, Ruiz S, Odriozola P, Kribakaran S, Cohodes EM, *et al.* (2025): Person-centered analyses reveal that developmental adversity at moderate levels and neural threat/safety discrimination are associated with lower anxiety in early adulthood. *Communications Psychology* 3: 31.
36. Zhu J, Zhou L, Zou Y, Zhang Y, Liu Y, Teicher MH (2026): Opposing sensitive period effects of early and late childhood maltreatment on corticolimbic responses in fear conditioning. *Molecular Psychiatry* 1–12.
37. Onat S, Büchel C (2015): The neuronal basis of fear generalization in humans. *Nature Neuroscience* 18: 1811–1818.
38. Frankenhuys WE, Panchanathan K, Nettle D (2016): Cognition in harsh and unpredictable environments. *Current Opinion in Psychology* 7: 76–80.
39. Murphy RJ (2023): Depersonalization/Derealization Disorder and Neural Correlates of Trauma-related Pathology: A Critical Review. *Innovations in Clinical Neuroscience* 20: 53–59.
40. Oltean L-E, Soflău R, Miu AC, Szentágotai-Tătar A (2022): Childhood adversity and impaired reward processing: A meta-analysis. *Child Abuse & Neglect* 105596.
41. Taylor JJ, Neitzke DJ, Khouri G, Borckardt JJ, Acierno R, Tuerk PW, *et al.* (2014): A pilot study to investigate the induction and manipulation of learned helplessness in healthy adults. *Psychiatry Research* 219: 631–637.
42. Smith KE, Xu Y (Lillian), Pollak SD (2025): How childhood adversity affects components of decision making. *Neuroscience & Biobehavioral Reviews* 169: 106027.

43. Lissek S, Pine DS, Grillon C (2006): The strong situation: A potential impediment to studying the psychobiology and pharmacology of anxiety disorders. *Biological Psychology* 72: 265–270.
44. Shackman AJ, Salomons TV, Slagter HA, Fox AS, Winter JJ, Davidson RJ (2011): The integration of negative affect, pain and cognitive control in the cingulate cortex. *Nature Reviews Neuroscience* 12: 154–167.
45. Etkin A, Egner T, Kalisch R (2011): Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences* 15: 85–93.
46. Kausche FM, Carsten HP, Sobania KM, Riesel A (2025): Fear and safety learning in anxiety- and stress-related disorders: An updated meta-analysis. *Neuroscience & Biobehavioral Reviews* 169: 105983.
47. Duits P, Cath DC, Lissek S, Hox JJ, Hamm AO, Engelhard IM, *et al.* (2015): Updated meta-analysis of classical fear conditioning in the anxiety disorders. *Depression and Anxiety* 32: 239–253.
48. Lissek S, Powers AS, McClure EB, Phelps EA, Woldehawariat G, Grillon C, Pine DS (2005): Classical fear conditioning in the anxiety disorders: A meta-analysis. *Behaviour Research and Therapy* 43: 1391–1424.
49. Smith KE, Pollak SD (2021): Rethinking Concepts and Categories for Understanding the Neurodevelopmental Effects of Childhood Adversity. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science* 16: 67–93.
50. Breslin FJ, Ratliff EL, Cohen ZP, Croff JM, Kerr KL (2025): Measuring adversity in the ABCD Study: Systematic review and recommendations for best practices. *BMC Medical Research Methodology* 25: 77.

Figure Legends

Figure 1

Figure 1. **A.** Schematic overview of the fear conditioning paradigm. Participants completed five consecutive experimental phases: habituation, acquisition, generalization, extinction, and return of fear following a reinstatement manipulation, which consisted of two unsignalled presentations of the unconditioned stimulus (US, electro-tactile stimulation). The CS-US reinforcement rate during acquisition and generalization was 80%. The generalization phase included four additional generalization stimuli (GS) varying in perceptual similarity between the CS+ and CS-. Subjective ratings of US-expectancy, arousal, valence and fear) were obtained at the end of each phase. **B.** Schematic illustration of exemplary trials from the acquisition phase. CSs were presented for 6 - 8 seconds. On reinforced CS+ trials, the US was delivered 200 ms before CS offset. Inter-trial intervals (ITI) varied between 10 and 16 seconds. During the ITI, a fixation cross was displayed. Acoustic startle probes were presented in 30% of all trials and ITIs, occurring 3 - 5.5 seconds after CS or ITI onset, respectively.

Figure 2

Figure 2. Differences in mean **(A)** arousal, **(B)** expectancy, **(C)** fear, and **(D)** valence ratings, as well as **(E)** SCR and **(F)** FPS between individuals with and without a history of ACEs across all experimental phases for the CS+ (blue) and CS- (green). Solid lines and circles represent data from individuals without a history of ACEs compared to dotted lines and triangles for individuals with a history of ACEs. Error bars represent the standard error of the mean. Asterisks indicate significant group differences ($p < .05$, see **Table 2** for details).

Figure 3

Figure 3. Positive **(A)** and **(B)** negative generalization gradients based on ROI-level parameter estimates extracted from regions of interest derived from a meta-analysis of the neural correlates of fear generalization. The gradients illustrate group differences between individuals with and without ACEs in responses to the CS-, CS+, and the three generalization stimuli (GS-, GSA, GS+). Error ribbons represent the standard error of the mean. dACC = dorsal anterior cingulate cortex; dlPFC = dorsolateral prefrontal cortex; vmPFC = ventromedial prefrontal cortex. Red and blue colors indicate the ROIs included in the fMRI analyses.

Figure 4

Figure 4. Association between ACE load, operationalized as KERF sumscore, and mean **(A)** arousal, **(B)** expectancy, **(C)** fear and **(D)** valence ratings after fear acquisition phase, **(E)** mean SCR amplitude (log-transformed and range corrected) during fear acquisition phase, **(F)** and mean FPS amplitude (t-transformed) during fear acquisition phase for the CS+ (blue) and CS- (green). Dots represent the participant's mean value. Ribbons represent the standard error of the mean.

Figure 5

Figure 5. Negative association between ACE load, operationalized as the KERF sum score, and the CS+ > CS- contrast during **(A)** fear acquisition and **(B)** return of fear (ROF). First-level parameter estimates for the CS+ and CS- were extracted from the peak voxel that was identified in the regression analysis showing a negative association between ACE load and the CS+>CS- contrast. These extracted peak-voxel parameter estimates were not used for statistical inference, but for visualization purposes only. Points represent the beta estimates for individual subjects. Ribbons indicate the standard error of the mean. The visualization threshold was set to $p = .01$

Figure 6

Figure 6. (A) Association between clinical symptom load, operationalized as GAF and post-acquisition arousal ratings for the conditioned stimuli. Dots represent individual participants' values. Ribbons represent the standard error of the mean. **(B)** Association between CS discrimination for post-acquisition arousal ratings and clinical symptom load, operationalized as GAF for individuals with and without history of ACEs. Dots represent individual participant's values. Ribbons represent the standard error of the mean. **(C)** Cross-sectional mediation analysis indicates that higher ACE load predicts lower GAF scores both directly and indirectly via reduced post-acquisition CS discrimination in arousal ratings. Both the indirect effect and the direct effect were significant. The association of ACE load and GAF is (statistically) partially mediated (9%) by CS discrimination

Table 1

N = 171	no ACE (n = 74)	ACEs (n = 97)	group comparison
Age	25.5 (5.38)	25.8 (4.3)	$p = .616$
Sex ¹	46w / 28m	78w / 19m	$p = .013$
KERF sumscore	6.68 (5.4)	26.14 (13.4)	$p < .001$
CTQ sumscore	32.1 (5.9)	47.2 (14.4)	$p < .001$
Education			
<i>lower</i>	5	4	$p = .120$
<i>high school diploma</i>	40	40	
<i>bachelor degree</i>	21	45	
<i>master degree or higher</i>	7	8	
GAF	86.7(11.1)	75.7 (13.7)	$p < .001$
SKID - acute vs. lifetime diagnosis (N = 151²)			
<i>no diagnosis</i>	39	30	$p < .001$
<i>lifetime</i>	18	36	
<i>acute</i>	4	24	
STAI	35.6 (9.4)	44.4 (10.1)	$p < .001$
Subjective socio- economic status - childhood	6.2 (1.5)	5.3 (1.7)	$p < .001$
Subjective socio- economic status - current	5.9 (1.5)	5.3 (1.1)	$p = .010$
Saliva cortisol baseline (nmol/l)³	3.92 (2.43)	3.35 (2.95)	$p = .100$
US intensity	2.60 (2.3)	2.43 (1.5)	$p = .581$
US aversiveness ratings	69.6 (17.7)	69.7 (19.8)	$p = .959$
startle aversiveness ratings	34.17 (20.93)	38.37 (25.78)	$p = .331$
SCR to US [rc, log]	0.51 (0.26)	0.53 (0.26)	$p = .388$

Table 1. Demographical data for individuals with and without ACEs. ¹see **supplementary material** for sensitivity analyses; ²the sample size for the clinical interview data is smaller, as we decided to conduct the interviews as exploratory measure when the first 22 participants had already completed the study; ³see **supplementary material** for details

Table 2

Phase	Measure	b	SEb	df ¹	F/t1	p	f ² / η^2	95% CI
Acquisition								
categorical	Expectancy			1, 167	1.62	.205		
dimensional	Expectancy	0.167	0.118	334	1.410	.16		[-0.066, 0.398]
categorical	Arousal			1, 167	6.68	.011	0.015	
dimensional	Arousal	0.42	0.17	334	2.52	.012	0.019	[0.093, 0.748]
categorical	Valence			1, 167	2.78	.097		
dimensional	Valence	0.163	0.16	334	1.021	.31		[-0.151, 0.478]
categorical	Fear			1, 167	3.05	.083		
dimensional	Fear	0.24	0.185	334	1.290	.198		[-0.125, 0.602]
categorical	SCR			1, 125	2.24	.137		
dimensional	SCR	0.001	0.001	125.3	1.66	.099		[-0.0002, 0.0022]
categorical	FPS			1, 116	0.13	.716		
dimensional	FPS	0.038	0.048	278	0.81	.422		[-0.055, 0.132]
Generalization								
categorical	Expectancy			1, 161	0.34	.599		
dimensional	Expectancy	-0.03	0.11	322	0	.82		[-0.25, 0.199]
categorical	Arousal			1, 161	1.07	.301		
dimensional	Arousal	0.16	0.16	322	1.01	.314		[-0.15, 0.48]
categorical	Valence			1, 161	0.16	.69		
dimensional	Valence	0.04	0.16	322	0	.8		[-0.27, 0.35]
categorical	Fear			1, 161	0.51	.478		
dimensional	Fear	0.08	0.17	322	0	.65		[-0.26, 0.42]
categorical	SCR			1,119	0.86	.355		
dimensional	SCR	0.001	0.001	118.7	1.6	.113		[-0.0002, 0.0023]
categorical	FPS			1, 108	1.17	.281		
dimensional	FPS	0.005	0.051	129	0.104	.917		[-0.095, 0.105]

Extinction								
categorical	Expectancy			1, 157	2.02	.157		
dimensional	Expectancy	-0.29	0.17	314	-2	.09		[-0.63, 0.047]
categorical	Arousal			1, 157	1.06	.305		
dimensional	Arousal	-0.19	0.17	314	-1.1	.29		[-0.53, 0.157]
categorical	Valence			1, 157	2.61	.108		
dimensional	Valence	-0.25	0.16	314	-2	.13		[-0.56, 0.07]
categorical	Fear			1, 157	0.76	.384		
dimensional	Fear	-0.18	0.15	314	-1	.243		[-0.48, 0.122]
categorical	SCR			1,114	1.45	.231		
dimensional	SCR	0.0003	0.0003	108.1	0.93	.356		[-0.00028, 0.0008]
categorical	FPS			1, 107	0.24	.627		
dimensional	FPS	0.007	0.037	105	0.178	.859		[-0.066, 0.079]
Return of Fear								
categorical	Expectancy			1, 153	6.42	.012	0.014	
dimensional	Expectancy	0.451	0.21	314	2	.032	0.015	[0.039, 0.86]
categorical	Arousal			1, 153	5.67	.018	0.01	
dimensional	Arousal	0.415	0.211	314	1.97	.0498	0.012	[0.0004, 0.83]
categorical	Valence			1, 153	3.53	.062		
dimensional	Valence	0.349	0.21	314	2	.094		[-0.06, 0.757]
categorical	Fear			1, 153	9.23	.003	0.012	
dimensional	Fear	0.334	0.21	314	2	.12.		[-0.087, 0.755]
categorical	SCR			1, 113	6.8	.01		
dimensional	SCR	0.001	0.001	96.6	1.54	.128		[-0.0002, 0.002]
Extinction to Return of Fear								
categorical	Expectancy			1,153	9.41	0.993	0.009	
categorical	Arousal			1,153	7.93	0.006	0.005	
categorical	Valence			1,153	9.43	0.003	0.006	
categorical	Fear			1,153	11.19	0.001	0.006	

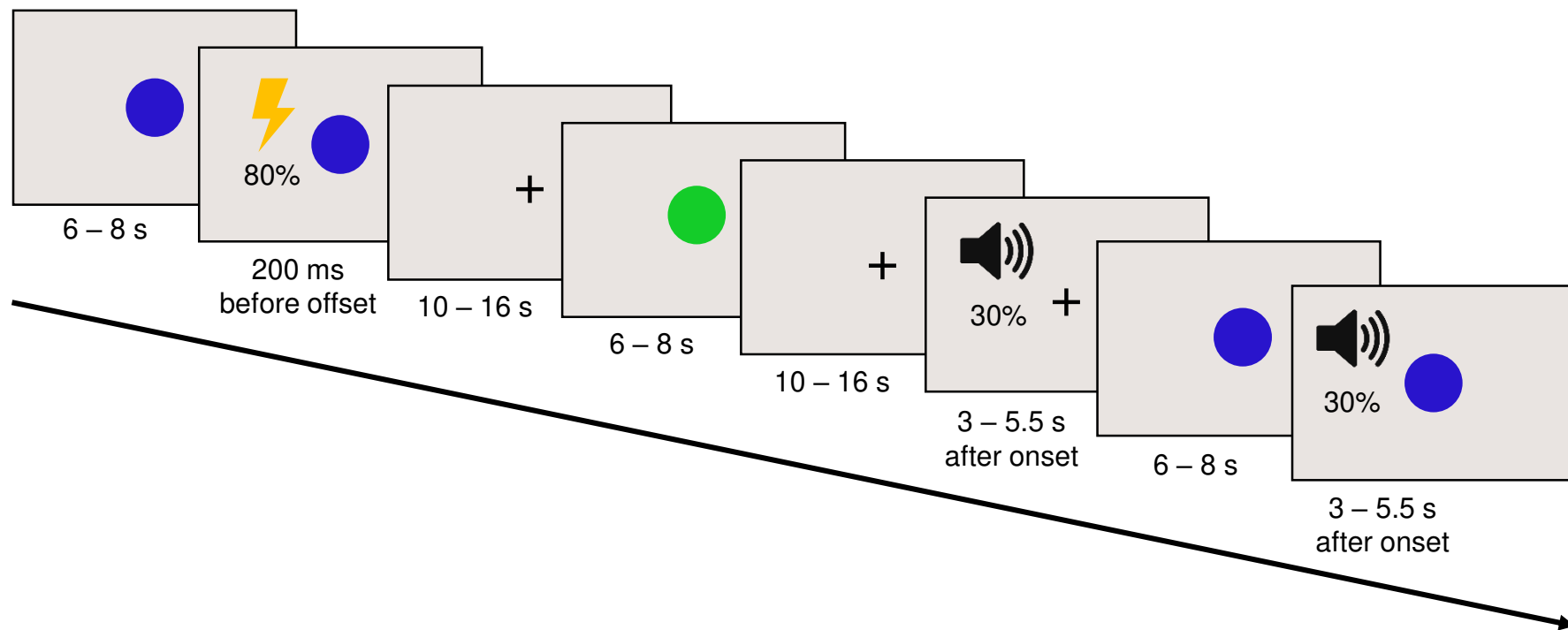
categorical	SCR			1,104	1,13	0.291		
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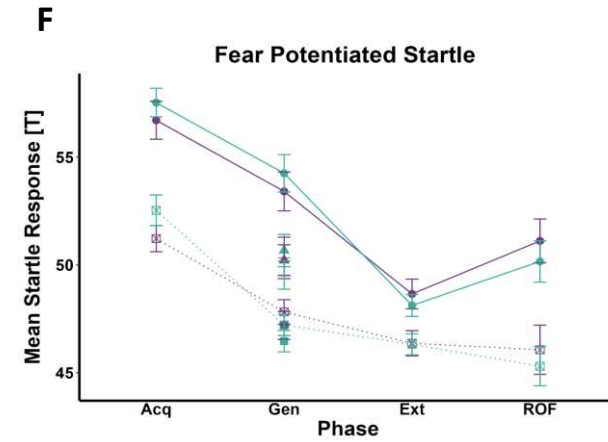
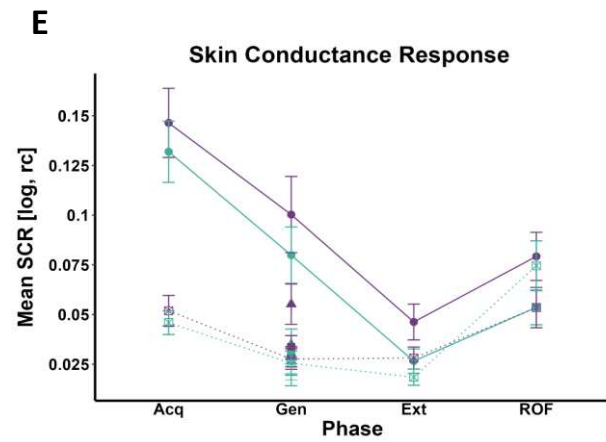
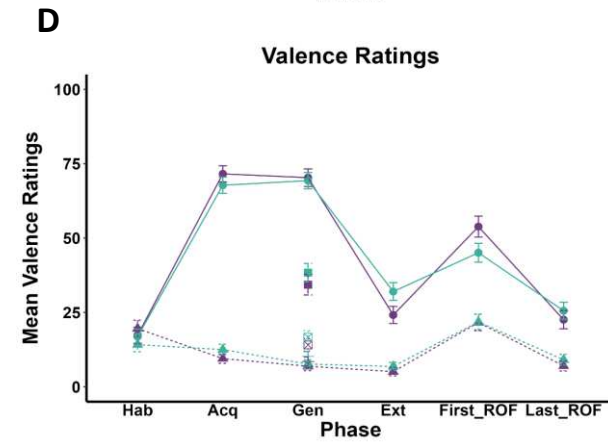
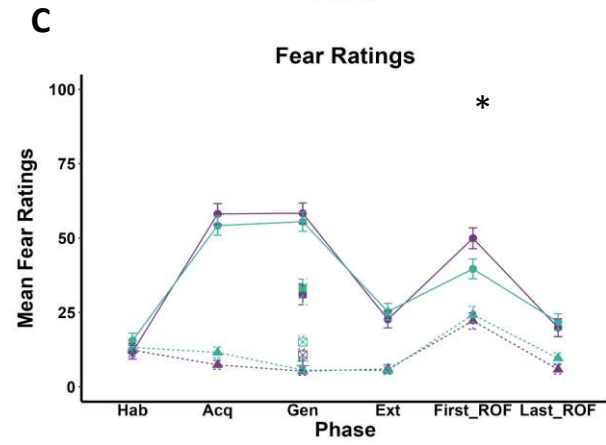
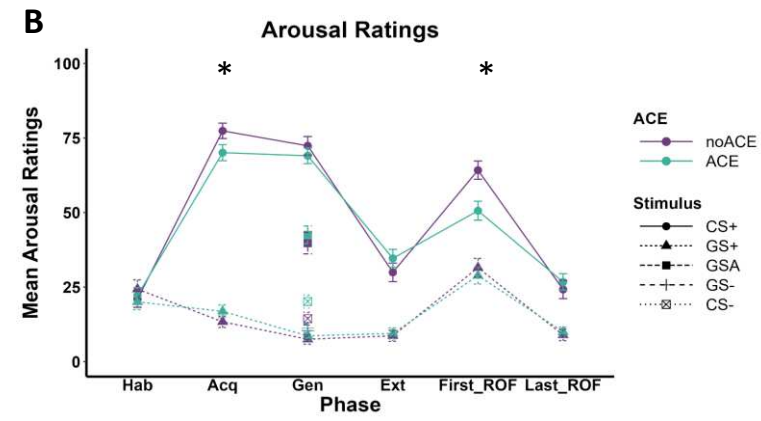
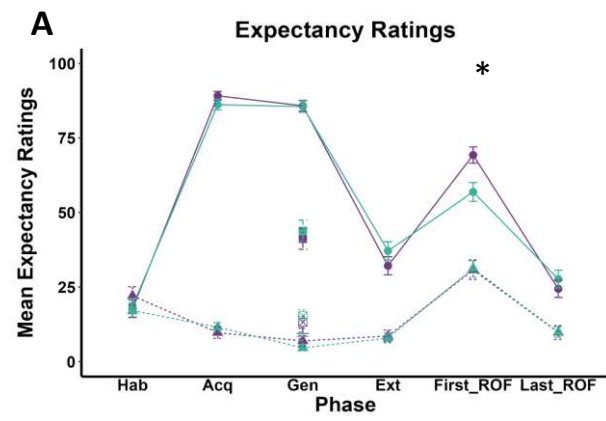
Table 2. Associations between CS-discrimination and a history of ACEs (categorical approach) as well as ACE load (cumulative risk approach). ¹Due to missing data for individual outcome measures and experimental phases, sample sizes vary. In brief, for **ratings**, the maximum number of valid data sets was 169, for **SCRs** 127, for **FPS** 118 and for **imaging** 166. For details see **supplementary material**.

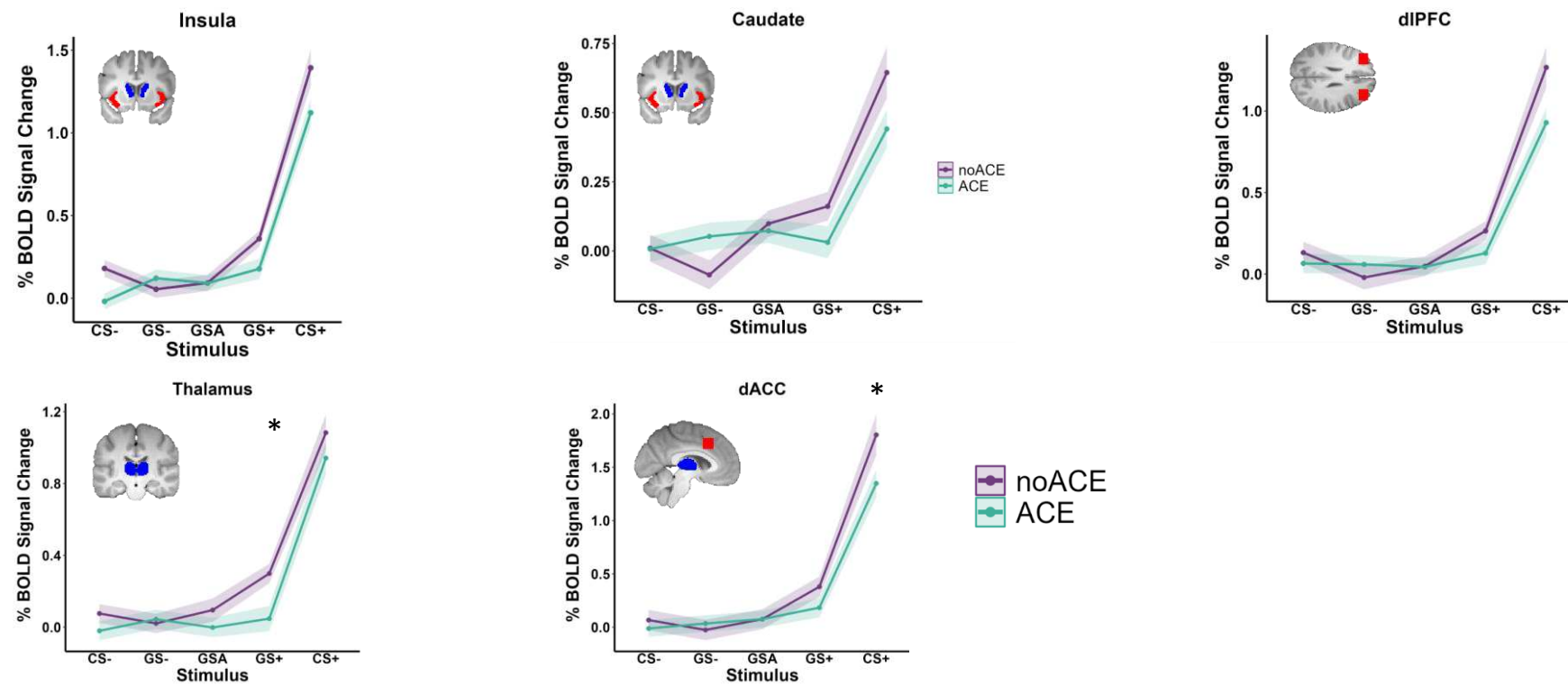
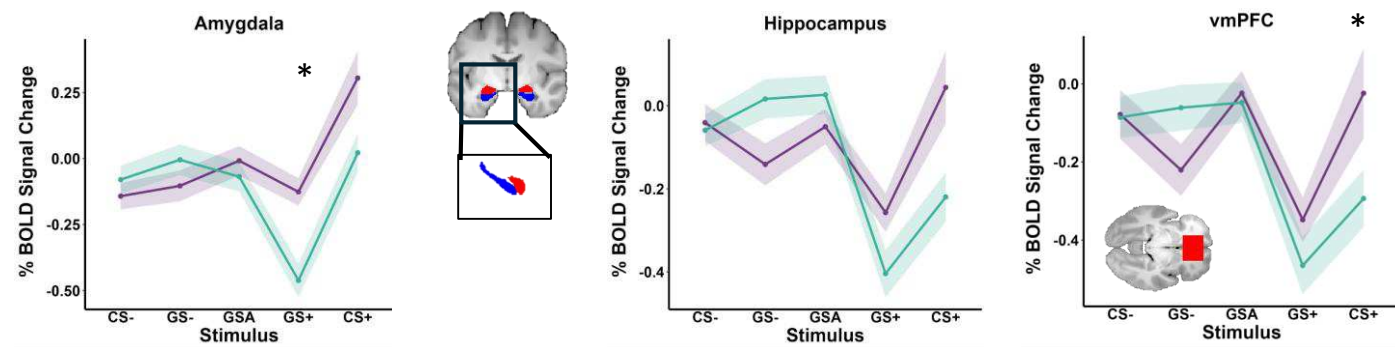
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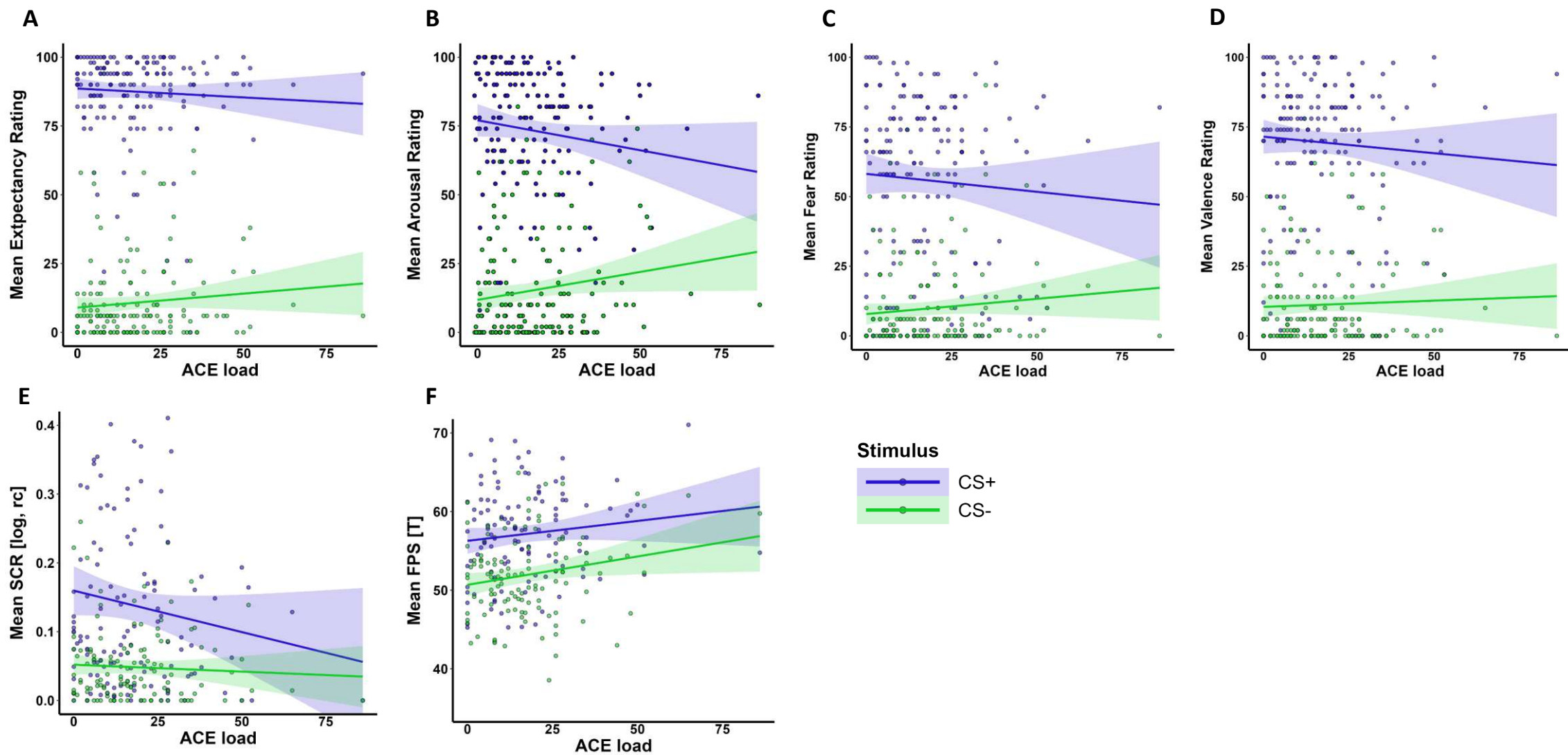
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B

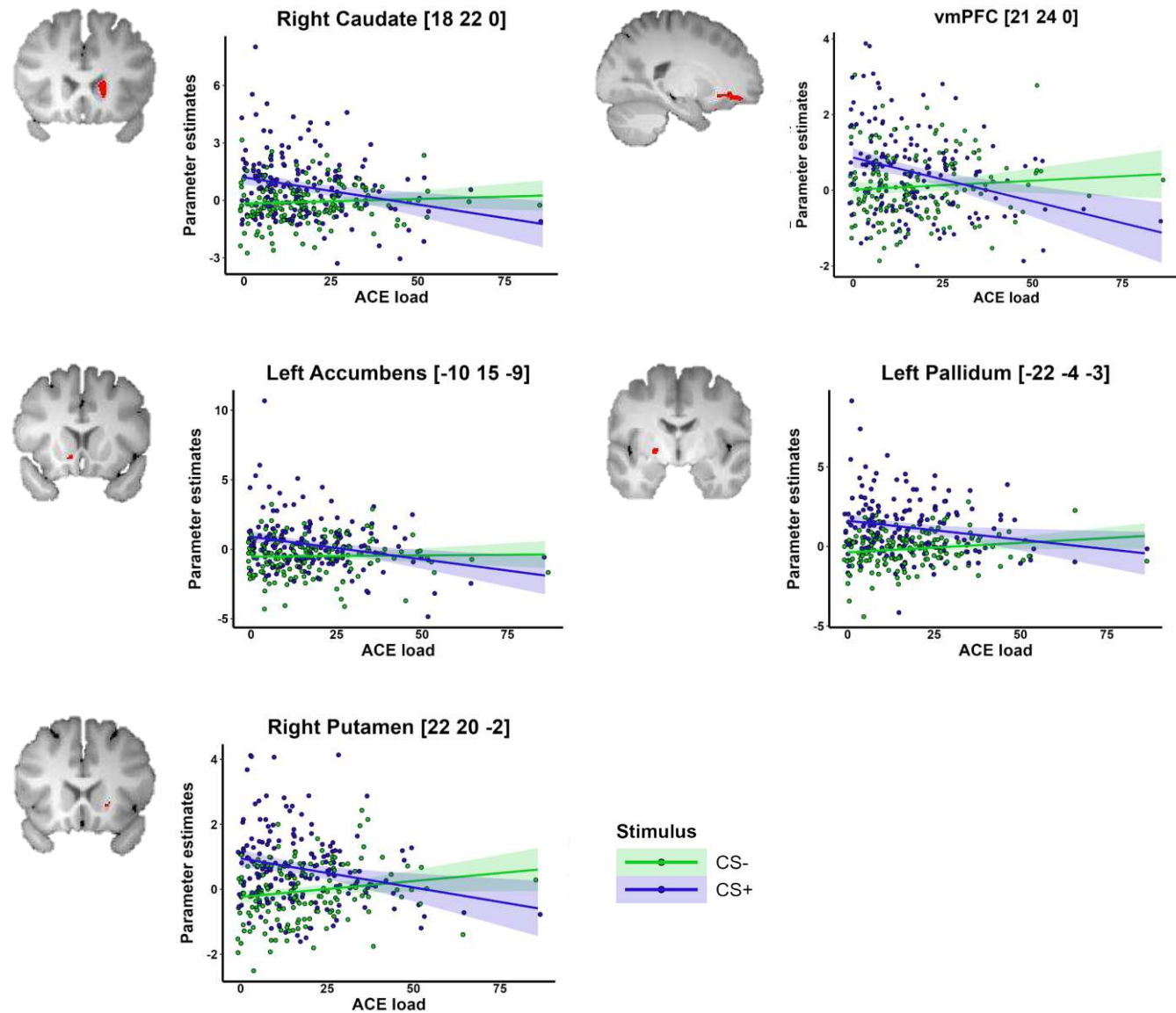




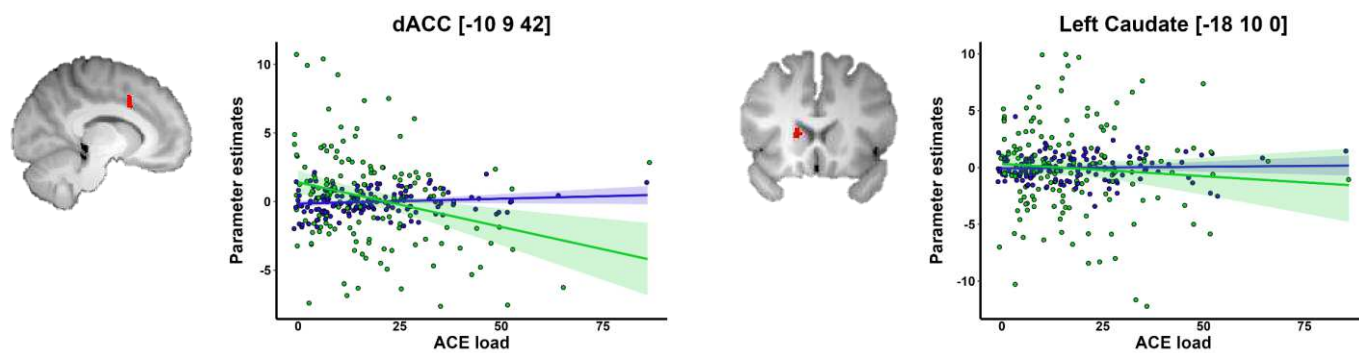
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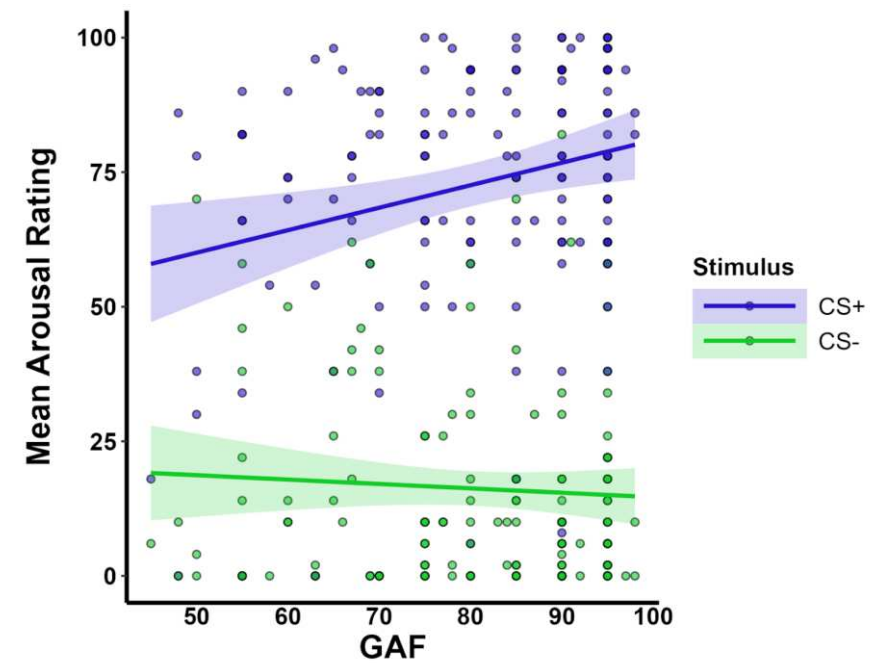
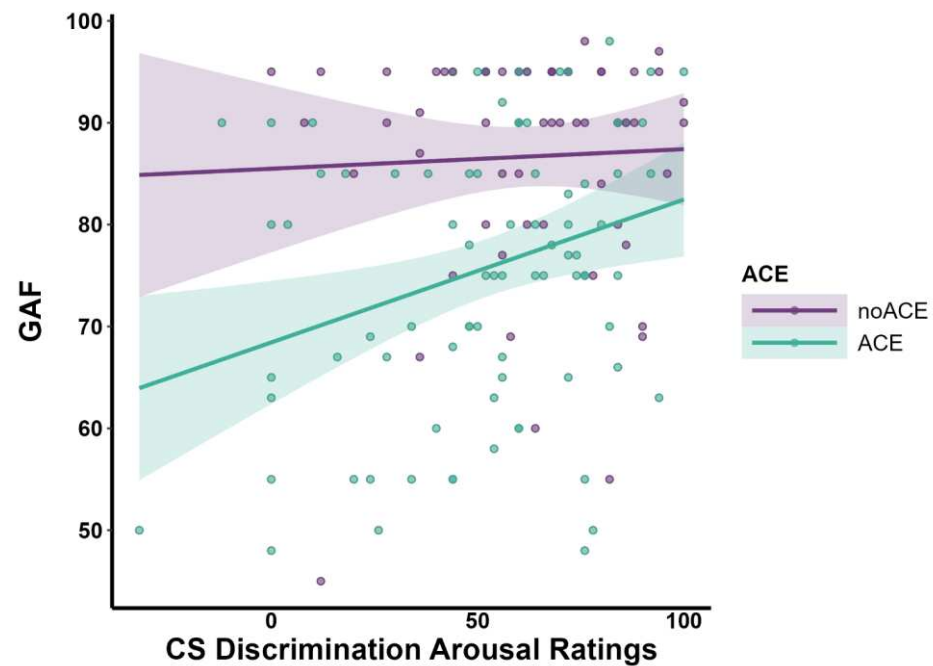
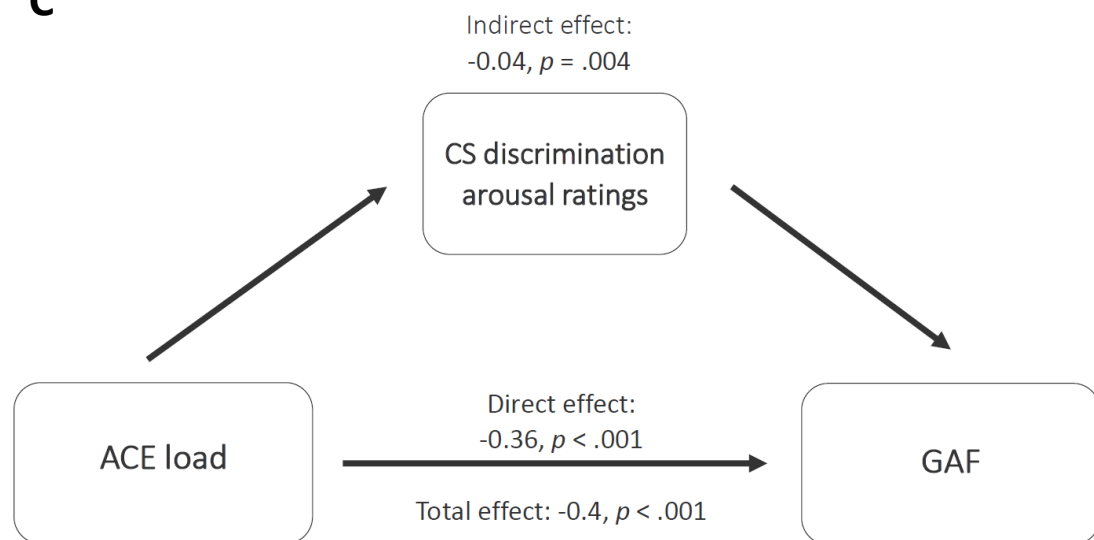


A



B



A**B****C**

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