but fewer studies have measured parasympathetic function using high frequency Heart Rate Variability (HF-HRV). While previous research suggests that individuals with lower resting HF-HRV may exhibit more exaggerated responses to threat, task-related HF-HRV may be more closely associated with behavior (Whitney et al., under review). However, few studies have examined individual differences in HF-HRV during threat learning or investigated the impacts of task-related HF-HRV on subsequent appraisals and approach-avoidance behavior to threats.

Methods: In an MRI session, thirty-one adults (17 females), ages 18-30 ($M = 20.32$, $SD = 2.55$) underwent a threat conditioning task. Two women with neutral facial expression served as the conditioned stimuli, CS+ and CS-. A fearful facial expression of the CS+ co-terminating with a loud, aversive scream served as the unconditioned stimulus (US). The CS+ was paired with the US using a 50% reinforcement rate, whereas the CS- was never paired with the US. Subjective ratings of the CS+ and CS- were obtained to assess threat conditioning. Following threat conditioning, individuals viewed morphed images of the CS+ and CS- in the context of two tasks. In response to each morphed image during a threat appraisal task, individuals rated the explicit probability of the US, current fear of the CS, and likelihood of avoiding the CS in the future. All morphed images were assessed in each appraisal block. In an implicit approach-avoidance task (AAT), individuals viewed morphed images on a colored background (e.g., blue or green). Participants identified the background color via button press until the image disappeared. With each button press, the image either increased or decreased size, mimicking approach and avoidance of the image, respectively. Heart rate, skin conductance (SCR), and respiration were collected continuously during each task: rest, threat conditioning, threat appraisal, and implicit AAT. For each task, HF-HRV was extracted using the spectral power within the 0.15-0.40 Hz frequency band and log transformed. In SPSS, statistical significance of main effects and group differences were determined using alpha = 0.05.

Results: In the whole group, evidence of threat conditioning was detected in subjective report of US awareness (CS + >CS-, $t(28) = 6.69$, $p < .001$) and skin conductance differences (US>CS + >CS-, $F(1, 29) = 14.38$, $p < 0.001$). Analysis of self-reported anxiety ratings revealed two patterns: a group that failed to exhibit threat conditioning ($n = 11$; CS+Anx = CS-Anx) and a group that exhibited successful threat conditioning ($n = 18$; CS+Anx > CS-Anx). Although group differences in HF-HRV were only at trend-level significance ($p < 0.09$), we investigated group differences in HF-HRV during each task, controlling for resting state HF-HRV. In the group that failed to exhibit threat conditioning, HF-HRV reactivity increased throughout the threat conditioning task, such that HF-HRV was significantly greater in the late acquisition phase ($M = 2.76$, $SD = 0.45$) compared to pre-acquisition ($M = 2.52$, $SD = 0.59$), $t(10) = -1.93$, $p = 0.04$. Within this group, HF-HRV was significantly lower in the threat appraisal condition ($M = 3.19$, $SD = 0.28$) compared to the explicit memory condition ($M = 3.27$, $SD = 0.29$, $t(12) = 2.620$, $p < 0.02$). In the group that demonstrated successful threat conditioning, no changes in HF-HRV reactivity were observed in conditioning ($p = 0.16$) and no differences in HF-HRV across appraisal types were observed ($p < 0.73$). Group differences in HF-HRV were not observed in the AAT task between the non-conditioning and threat conditioning groups ($p = 0.66$).

Conclusions: Individuals that self-reported unsuccessful or successful threat conditioning exhibited divergent patterns of HF-HRV during threat conditioning and threat appraisal. Lower HF-HRV during pre-conditioning compared to later acquisition of conditioning among individuals that failed to demonstrate successful threat conditioning may indicate greater demands on emotion regulation during early threat conditioning. Therefore, lower HF-HRV when individuals are learning and appraising threat may have clinical implications. In addition, these data highlight differences in HF-HRV between explicit and implicit threat processing, which may suggest that explicit and implicit threat processing differentially captures active demands on emotion regulation. Regardless, future threat processing studies should expand the investigation of autonomic function to include HRV as a measure to understanding parasympathetic mechanisms underlying anxiety disorders.

Keywords: Threat Conditioning, Heart Rate Variability, Approach/Avoidance

Disclosure: Nothing to disclose.

P45. Rostral Anterior Cingulate Response to Emotional Conflict is Modulated by Trauma Exposure Burden in Resilient World Trade Center Responders

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Background: People vary widely in ability to successfully adapt after potentially-traumatic events. For example, a subset of 9/11 World Trade Center (WTC) responders have remained consistently psychologically well despite having endured considerable WTC-related exposures. Emotion regulation is one psychological factor that may support resilience: top-down cortical regulation of subcortical fear processing structures supports adaptive responding to environmental demands. Most neuroimaging studies have focused on effortful (explicit) emotion regulation. However, recent studies suggest that automatic (implicit) emotion regulation abnormalities constitute a core dysfunction in PTSD and could be key to resilience as well: Offringa and colleagues (2013) found greater rostral anterior cingulate (rACC) activation during implicit emotion regulation in trauma-exposed controls vs. symptomatic individuals. However, few neuroimaging studies investigated implicit emotion regulation in trauma-exposed adults across both dimensions of exposure severity and presence or absence of psychopathology.

In the present study, we sought to examine rACC functioning (as a region subserving automatic emotion regulation) using an established picture-word emotional Stroop task. We hypothesized that (1) highly resilient WTC responders with high WTC-trauma exposure burden [Resilient-High group] would demonstrate the greatest degree of rACC BOLD activation in response to emotional conflict, while the lower-WTC-exposed responders [Resilient-Low group] would show lesser but still positive rACC activation, and (3) responders with PTSD would not exhibit significantly different rACC activation on incongruent (vs. congruent) trials.

Methods: Rescue and recovery workers ($N = 97$) involved in WTC recovery efforts following the 9/11/01 attacks in New York City were enrolled in a neuroimaging study. All participants were administered the Structured Clinical Interview for DSM-5 and the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5). We categorized WTC trauma-exposed responders with no current or lifetime psychopathology (i.e., resilient) into two groups (Resilient-High and Resilient-Low) based on number of specific 9/11-related exposures (e.g., participated in search and rescue, exposed to human remains, experienced death of a colleague or loved one). The PTSD group met DSM-5 criteria for WTC-related PTSD, based on the CAPS-5. Groups were matched on age and sex, with approximately 82% males in each group.

Participants attended a fMRI session during which they completed a task involving photos of fearful or happy faces, overlaid with a word ("AFRAID" or "HAPPY") that was either

congruent or incongruent with the face. They were instructed to indicate the emotion in the photo by pressing a button as quickly as possible, while ignoring the overlaid word.

fMRI data preprocessing used fMRIPrep 21.0.2 to generate individual motion-, susceptibility distortion-, and slice timing-corrected echoes, which were subsequently denoised using TE-dependent independent components analysis (TEDANA 0.0.12) and smoothed with a 6-mm FWHM Gaussian kernel before single-subject and group-level analysis via SPM12.

Ninety-six participants completed the FaceStroop task, of which 85 were included in the final FaceStroop task analyses (Resilient-High n = 31, Resilient-Low n = 26, PTSD n = 28) after excluding data from 7 participants for excessive motion in the scanner and from 4 participants for task performance below conventional thresholds for this task (>25% missed trials and/or <75% accuracy).

Results: There were no significant group differences in FaceStroop task performance (mean reaction time and accuracy), matching results from Offringa et. al (2013).

Incongruent > Congruent fMRI single-subject contrast images were aggregated across the sample to assess for whole-brain effects of task and group. We found typical task-related activation in regions reflecting conflict processing (e.g., dorsal ACC, bilateral anterior insula) and cognitive control (inferior frontal gyrus, dorsolateral prefrontal and parietal cortices), among others (FWE-corrected $p = .05$, $k = 10$).

To test our a priori region of interest hypotheses, we created an 8-mm sphere around the rACC peak MNI coordinates reported by Offringa et al. (2013) [x = 16, y = 36, z = 34] and extracted participants' Incongruent > Congruent BOLD activation estimates within the mask. As predicted, there was an omnibus effect of group, $F(2,82) = 3.20$, $p = .046$, such that the Resilient-High group showed the greatest rACC response to emotional conflict, followed by the Resilient-Low group, with minimal to no rACC activation in the PTSD group. Linear contrast results supported our specific directional hypotheses: rACC in Resilient-High > PTSD ($t(82) = 2.48$, $p = .015$), Resilient-High > Resilient-Low ($t(82) = 0.72$, $p = .48$), and Resilient-Low > PTSD ($t(82) = 1.67$, $p = .098$). We obtained similar results using an anatomically-defined rACC mask.

Conclusions: We replicated prior findings that rACC engagement during automatic regulation of emotional conflict is modulated by presence/absence of psychopathology, and further expanded these results by identifying differences in trauma exposure severity as another modulator in resilient individuals. These findings contribute to understanding the neural instantiation of psychological factors that enable some individuals to be highly resilient despite high trauma exposure burden.

Keywords: Stress Resilience, World Trade Center Rescue and Recovery Work, PTSD, fMRI, Trauma Exposure

Disclosure: Nothing to disclose.

P46. Fear Generalization and Extinction are Related to Peripheral 2-AG Levels and Distinct Neural Connectivity Patterns in Humans

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Background: The endocannabinoid system is believed to play a critical role in fear learning. In particular, the ability to distinguish between fear-related and safe stimuli is a process critical to well-being but believed to be impaired in some individuals following trauma exposure. As several cannabinoid-targeted compounds are moving forward in clinical trials related to trauma exposure (i.e., PTSD), we aimed to explore the relationship between fear learning, neural connectivity, and eCB function in a clinically heterogenous sample of adults with or without prospectively assessed histories of childhood trauma exposure or substance use disorders.

Methods: In this study, adult male and female humans (N = 102 total) with or without histories of prospectively assessed childhood trauma exposure and/or substance use disorders (N = 24-26/group) completed a single-day laboratory model of fear conditioning and extinction and provided blood samples for analysis of peripheral endocannabinoid levels (AEA, 2-AG) using mass spectrometry. A resting state functional neuroimaging scan was collected on a separate occasion. Given the role of the amygdala as a mediator of fear behavior, the left/right amygdala were used as seeds in a seed-based connectivity analysis with target regions of the dorsolateral prefrontal cortex (dlPFC) and anterior cingulate cortex (ACC) and were assessed for covariance with peripheral measures of endocannabinoids and behavioral measures of fear conditioning. Results were further validated by extracting beta coefficients from the significant clusters for each participant to use in a regression analysis.

Results: Overall, those with trauma exposure histories had lower 2-AG levels ($F(3, 60) = 2.81$, $P = 0.047$). When the sample was assessed as a whole, lower levels of 2-AG were associated with generalization of fear ($p = 0.025$, 95% CI 0.007, 0.132), i.e., an impaired ability to distinguish between a fear-associated cue and a cue not associated with a fear stimulus. Higher levels of 2-AG were also associated with facilitated within-session fear extinction ($p = 0.005$, 95% CI 0.020, 0.130). Fear generalization was associated with reduced amygdala-dorsolateral prefrontal cortex activity ($p < 0.001$, 95% CI 0.022, 0.051), while fear extinction was associated with greater connectivity between the amygdala and anterior cingulate cortex ($p < 0.001$, 95% CI 0.037, 0.085).

Conclusions: Together, this data highlights potential novel therapeutic targets for individuals with histories of trauma exposure. New therapeutic interventions could include pharmacological interventions, such as increasing 2-AG via inhibition of the degradative enzyme monoacylglycerol lipase, or non-pharmacological interventions, such as neurostimulation of the dlPFC, which would constitute innovative treatment opportunities for individuals histories of trauma exposure

Keywords: Endocannabinoids, Childhood Trauma, Fear Conditioning

Disclosure: Nothing to disclose.

P47. Posttraumatic Stress Disorder (PTSD) is Associated With Abnormal Amygdala and Striatal Signaling of Temporal Prediction Errors During a Passive Reward Learning Task

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Background: Posttraumatic stress disorder (PTSD) is characterized by prominent symptoms of diminished positive affect (DPA), e.g., inability to experience pleasure, diminished interest in valued activities, and difficulty experiencing interpersonal closeness. In PTSD, these symptoms are subsumed by the symptom domain of "emotional numbing", where they are associated with greater distress and chronicity, greater functional impairment, poorer treatment outcomes, and increased suicidality. Despite these relationships to important clinical outcomes, the biological bases of PTSD DPA symptoms are not well characterized.