

processes in both healthy and clinical populations, including the study of anxiety disorders and their treatment.

**Keywords:** Fear Extinction, fMRI, Anxiety Disorders, ventromedial prefrontal cortex, Anterior Cingulate Cortex

### 15. Respiratory Sinus Arrhythmia and Ventromedial Prefrontal Function in Veterans with Posttraumatic Stress Symptoms

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**Background:** Adaptive emotional responding requires flexible regulatory control of autonomic response systems, thought to involve the ventromedial prefrontal cortex (vmPFC). Individuals with posttraumatic stress disorder (PTSD) show compromised vmPFC function and parasympathetic tone—as reflected by reduced respiratory sinus arrhythmia (RSA)—yet previous studies have not drawn a direct link between these deficits.

**Methods:** We conducted fMRI scanning during an unpredictable threat anticipation task in 51 male veterans with a broad range of PTSD symptoms. We calculated RSA during a separate resting scan, and conducted voxelwise regression analysis across the medial prefrontal cortex to identify associations between resting RSA and task-related anticipatory threat activation.

**Results:** Replicating and extending previous findings, re-experiencing symptoms of PTSD were inversely correlated with resting RSA ( $r = -0.37$ ,  $p < 0.05$ ). Re-experiencing symptoms were also associated with relatively undifferentiated vmPFC activation across conditions of safety and threat ( $p < 0.05$ , small-volume corrected). Directly linking these two findings, we identified a novel relationship between resting RSA and vmPFC activation: veterans with reduced RSA showed less differentiated responses across conditions of safety and threat in an anatomically overlapping aspect of the vmPFC ( $p < 0.05$ , small-volume corrected).

**Conclusions:** The present data tie together reduced resting RSA, undifferentiated vmPFC activation, and elevated re-experiencing symptoms in combat veterans. These findings provide a theoretically parsimonious account in which intrusive trauma symptoms are associated with reduced neural control over flexible autonomic responding. More broadly, these data underscore the importance of considering individual differences in discrete symptom clusters when investigating neurobiological mechanisms of PTSD.

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**Keywords:** PTSD - Posttraumatic Stress Disorder, ventromedial prefrontal cortex, Respiratory Sinus Arrhythmia, Veterans, Parasympathetic Arousal

### 16. Sample Size Matters: A Voxel-Based Morphometry Multi-Center Mega-Analysis of Gray Matter Volume in Social Anxiety Disorder

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**Background:** Social Anxiety Disorder (SAD) is a disabling psychiatric disorder, associated with high co-morbidity. Previous research on structural brain alterations associated with SAD has yielded inconsistent results concerning changes in gray matter (GM) in various brain regions, as well as on the relationship between GM and SAD-symptomatology. These heterogeneous findings are possibly due to limited sample sizes. Multi-site imaging offers new possibilities to investigate SAD-related GM changes in larger samples.

**Methods:** An international multi-center mega-analysis on the largest database of SAD brain scans to date was performed to compare GM volumes of SAD-patients ( $n=174$ ) and healthy participants ( $n=213$ ) using voxel-based morphometry. A hypothesis-driven region of interest (ROI) approach was used, focusing on the basal ganglia, amygdala-hippocampal complex, prefrontal cortex and parietal cortex.

**Results:** SAD-patients had larger GM volume in the dorsal striatum when compared to healthy participants. This increase correlated positively with the level of social anxiety symptoms. No SAD-related differences in GM volume were present in the other ROIs.

**Conclusions:** The results suggest a role for the dorsal striatum in SAD, but previously reported SAD-related changes in GM in the amygdala, hippocampus, precuneus, prefrontal cortex and parietal regions were not replicated. Thereby, our findings indicate that sample size matters and stress the need for meta-analyses like those performed by the Enhancing Neuroimaging Genetics through Meta-Analysis (ENIGMA) Consortium and its working groups. Actually, the collaborative effort for this work has resulted in the start of the ENIGMA-Anxiety workgroup.

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