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

Daniel Grupe, Joseph Wielgosz, Jack Nitschke, and Richard Davidson

University of Wisconsin-Madison

**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.

**Supported By:** NSF Graduate Research Fellowship Program; UW-Madison Institute for Clinical & Translational Research; Dana Foundation; NICHD (P30-HD003352)

**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

Janna Marie Bas-Hoogendam, Henk van Steenbergen, J. Nienke Pannekoek, Jean-Paul Fouche

University of Amsterdam

**Supported By:** Leiden University Research Profile ‘Health, Prevention and the Human Life Cycle’; Netherlands Organization for Scientific Research (NWO); EU 7th Framework Marie Curie Actions International Staff Exchange Scheme grant ‘European and South African Research Network in Anxiety Disorders’ (EUSARNAD); South African Medical Research Council National Health Scholarship; German Research Society (SFB/TRR-58, project C07 and STR 987/6-1); ZonMw, grant number 10-000-1002; Swedish Research Council and the Swedish Research Council for Health, Working Life and Welfare.

**Keywords:** Social Anxiety Disorder, Voxel Based Morphometry
17. Emotional Processing in OCD - A Meta-Analysis of 23 Functional Neuroimaging Studies

Anders Thorsen1, Pernille Hagland1, Joaquim Radua2, David Mataix-Cols3, Gerd Kvale1, Bjarne Hansen1, and Odile A. van den Heuvel4

1OCD-team, Haukeland University Hospital; University of Bergen, Norway, 2FIDMAG Germanes Hospitalàries, CIBERSAM, Barcelona, Spain; Department of Clinical Neuroscience, Centre for Psychiatry Research, Karolinska Institutet, Stockholm, Sweden; Department of Psychiatry Studies, Institute of Psychology, Psychiatry, and Neuroscience, King’s College London, 3Karolinska Institute, 4VU University Medical Center

Background: Dysfunctional emotional processing of intrusive thoughts, images and impulses is an important aspect of obsessive-compulsive disorder (OCD). Different designs have been used to study emotional processing in OCD, including symptom provocation and cognitive paradigms using emotional stimuli. However, studies show considerable variability in findings, methodology, and patient characteristics.

Methods: 23 functional neuroimaging studies comparing OCD patients and healthy controls using fMRI or PET were analyzed using seed-based d mapping. We performed a main meta-analysis comparing patients and healthy controls, and meta-regressions of medication usage, stimulus duration, symptom severity using Y-BOCS, and comorbidity. Jackknife and publication bias analyses were also performed.

Results: OCD patients, compared with healthy controls, show increased activity in the bilateral amygdala, right putamen, orbitofrontal, middle temporal, and left inferior occipital cortex during emotional processing. Right amygdala hyperactivity was most pronounced in unmedicated patients and in studies with short stimulus durations. Symptom severity was related to increased activity in the orbitofrontal, anterior cingulate cortex and precuneus. Comorbid anxiety disorders were associated with more right amygdala and putamen activity, while comorbid mood disorders were associated with more activity in the right insula and cerebellum. Comorbidity in general predicted decreased activity in the left amygdala. Jackknife analysis showed that activity in the inferior prefrontal cortex in patients and dorsomedial prefrontal cortex in controls were possibly underestimated. There was no evidence of publication bias.

Conclusions: OCD patients show increased emotional processing related activity in limbic, frontal and temporal regions. Both methodology and patient characteristics likely influence neuroimaging findings, especially regarding the amygdala activity.

Supported By: Helse Vest Health Authority (No. 911754 and 911880)

Keywords: Obsessive Compulsive Disorder (OCD), Neuroimaging, Meta-analysis, Amygdala, Anxiety

18. In Vivo Quantification of mGluR5 Availability in Posttraumatic Stress Disorder

Margaret Davis1, Sophie Holmes1, Robert Pietrzak2, Nicole DellaGioia1, Nabeel Nabuisi1, David Matuskey1, Steven Southwick2, Richard Carson1, John Krystal1, and Irina Esterlis3

1Yale University School of Medicine, 2VA National Center for PTSD

Background: Posttraumatic stress disorder (PTSD) is associated with considerable emotional, financial, and social burden (McCrone et al., 2003) and heightened risk for suicide (Ramsawh et al., 2014). Yet, relatively little is known about the pathophysiology of PTSD on a molecular level. The metabotropic glutamatergic receptor (mGluR5) is implicated in animal models of fear extinction (Fontanez-Nuix, et al., 2011) and may contribute to the pathophysiology of PTSD. This study examined the relationship between mGluR5 availability and suicidality in vivo in PTSD.

Methods: Sixteen individuals with PTSD and 16 age-, sex-, and smoking-matched healthy controls participated in an [18F]FPEB PET scan and comprehensive clinical assessment. Volume of distribution (VT: ratio of activity in tissue relative to that in blood) in grey matter regions was computed.

Results: We observed significantly greater mGluR5 availability in individuals with PTSD compared to controls in brain regions implicated in the neurobiology of PTSD [dorsolateral PFC (dPFC); 19% higher; Cohen’s d = 0.88), ventromedial PFC (vmPFC; 18% higher; Cohen’s d = 0.88), and orbitofrontal cortex (OFC; 18% higher; Cohen’s d = 0.88). Higher mGluR5 availability was associated with greater PTSD symptom severity (p < .04) and presence of suicidal ideation on scan day (p < .05).

Conclusions: This is the first in vivo investigation implicating mGluR5 dysregulation in PTSD, which may be indicative of lower glutamate levels or dysregulation in the glucocorticoid system. Importantly, higher mGluR5 availability was associated with increased PTSD symptom severity and presence of suicidal ideation. Our findings suggest a potentially crucial role for mGluR5 in the pathophysiology and suicide risk in PTSD.

Supported By: NIH T32 (Davis); NIH K01 (Esterlis); NIH R01 (Esterlis); VA National Center for PTSD

Keywords: PTSD, glutamate, PET, suicide, imaging

19. Amygdala Subnuclei Volumes Differ among PTSD, Asymptomatic Trauma-Exposed and Healthy Individuals

Nicolina Bruno1, Marie-France Marin2,3, Mohammed Milad1, and Joan Camprodon2

1Massachusetts General Hospital, 2MGH/Harvard Medical School, 3University of Montreal

Background: The clinical consequences of trauma differ across individuals: while some develop post-traumatic stress disorder (PTSD), others may not present with significant psychopathology. A growing body of evidence is pointing to the anatomical and physiological properties of the fear conditioning circuitry, and the amygdala in particular, as the substrate that explains different trauma-related clinical