

Conclusions: We identified multimodal imaging predictors of response to SKI that generalized to predict ECT and TSD response.

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Keywords: Major Depressive Disorder (MDD), Treatment Response, Machine Learning, Multimodal Imaging, Ketamine

Direct Social Transmission of Chronic Stress

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Background: Stress-related disorders have complex biopsychosocial causes, yet also shape the social environment. Accordingly, there is an increased risk of mood and anxiety disorders among the peers of affected individuals. Yet, how stress in one individual seeds the behavior of another is poorly understood.

Methods: Eight twelve-week-old male and female C57BL/6J or transgenic Thy1-jRGECO1a (a genetically encoded calcium indicator) mice underwent the Chronic Variable Stress (CVS) model, where restraint, tail suspension, or foot shocks occur daily for 21 days. Animals were group housed, however only a subset within each cage underwent CVS. As a control, a subset of animals were placed in a novel environment (NE) daily, instead of CVS. Animals were tested in the open field, the elevated plus maze (EPM), the novelty suppressed feeding and the social interaction (SI) tests. Thy1-jRGECO1a animals received 9°9mm chronic cranial windows, and spontaneous cortical activity (30Hz, 18,000 frames) was sampled during head-fixation at baseline and at the conclusion of the protocol to characterize change in cortical functional connectivity.

Results: CVS and CVS-peer animals spent less time in the interaction zone, travelled a shorter total distance, spent less time in the arena centre, had longer latency to feed, but showed no EPM differences. We observed changes in large-scale cortical networks with increases functional connectivity in both CVS and CVS-peer animals.

Conclusions: We find evidence for the social transmission of stress-related pathological behavior and cortical functional connectivity in mouse. Exposure to a chronically stressed peer produces alterations mirroring that of their stressed counterparts.

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Keywords: Chronic Stress, Calcium Imaging, Animal Model of Depression

Disruptions in Attentional Control and Interoception in Dissociative Traumatized Individuals: Psychophysiological Correlates and Neural Network Profiles

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Background: Highly dissociative traumatized people experience disruptions in attention and interoception. These problems may be mechanisms through which dissociation affects functioning and interferes with treatment outcomes. We used

baseline multimodal data from our breath-focused (BF) meditation intervention to examine how dissociation is associated with disruptions in attentional control and interoception.

Methods: Sixty-one traumatized women were recruited from primary-care clinics of a publicly funded hospital and from community advertisements. Participants received clinical measures of dissociation, interoceptive awareness, and PTSD. Psychophysiological data, including electrocardiogram, galvanic skin response and respiration data were collected at rest and during BF (n= 45); a subset completed neuropsychological testing, including measures of sustained attention (continuous performance task, CPT; n=32) and 17 of these participants also performed an affective stroop attentional control task during fMRI; timeseries data were analyzed.

Results: Dissociation was inversely associated with interoceptive ability, particularly the ability to experience physical discomfort without emotional distress, even after accounting for PTSD symptoms ($r=-.37$, $p=.004$). High dissociation with associated with poorer CPT performance ($F_{1,32}=4$, $p=.05$), lower heart rate at rest ($F_{1,44}=5.4$, $p=.03$), and relatively unchanging, low BOLD response over time in both attentional control and interoceptive networks in response to distracting trauma-related stimuli. In comparison, low levels of dissociation were characterized by significant fluctuations in these networks over time.

Conclusions: Our findings indicate that dissociation is associated with disrupted attention and interoception, and these disruptions have distinct physiological and neural network signatures. We will discuss how these findings inform treatment indications for dissociative traumatized people and describe how our intervention targets these mechanisms.

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Keywords: Dissociation, PTSD - Posttraumatic Stress Disorder, Clinical Trials, Attentional Control, Interoception

Failure of Attentional Control is a Vulnerability Factor for PTSD: An Identical Twin Study

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Background: Posttraumatic stress disorder (PTSD) is an often-debilitating psychiatric disorder that emerges in some people after experiencing a traumatic event such as sexual assault, natural disaster, or combat. Attention-related symptoms such as "hypervigilance" and "problems with concentration" are considered in the DSM-5 to reflect symptoms that begin or worsen after the traumatic event. However, an important question is whether these disruptions are triggered by the experience of trauma or if they are actually a premorbid vulnerability factor.

Methods: We used a simple Posner cueing task with a unique cohort of Vietnam-era identical male twins, discordant for PTSD and combat exposure. Half of the combat-exposed individuals had PTSD (14) and half did not (17); each of these individuals had a combat-unexposed identical twin brother (14 and 17, respectively). All participants completed exogenous and endogenous cue version of a Posner cueing task.

Results: Combat-exposed veterans with PTSD and their combat-unexposed identical twin brothers demonstrated attention capture by exogenous, but not endogenous cues, while combat exposed veterans without PTSD and their combat-unexposed identical twin brothers did not demonstrate attention capture by either task version.

Conclusions: These results demonstrate for the first time that propensity for exogenous attentional capture, even by neutral cues, is a familial vulnerability factor for PTSD. These results are consistent with attentional control deficits as a fundamental and pre-trauma deficit. As attention is a fundamental cognitive process, potential relationships to specific symptoms including hypervigilance and reexperiencing are discussed.

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Keywords: PTSD, Attention, Cognitive Control, Anterior Cingulate Cortex, Twins

Modelling Dynamic Changes in Thalamo-Cortical and Thalamo-Cerebellar Functional Connectivity in the Early Stage of Psychosis

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Background: Thalamo-cortical and thalamo-cerebellar connectivity has been shown to be abnormal in psychosis and associated with cognition and conversion risk. Few studies have explored dynamic functional connectivity (FC) changes within the crucial early stage of psychosis (ESP).

In this study, we explored thalamo-cortical and thalamo-cerebellar FC between ESP patients and controls, and within patients throughout the first five years of psychosis illness.

Methods: Resting state-fMRI data were collected from 230 participants (154 ESP patients, 76 controls), and processed in the CONN toolbox. A ROI-to-ROI analysis was conducted between the thalamus and 14 ROIs (7 cortical networks and 7 cerebellar networks), with group (patient or control) as the between-subjects contrast. The shape of the thalamus-ROI trajectory in patients over time was then explored with generalized additive models (GAM) using the mgcv package in R.

Results: ESP patients had significantly higher thalamo-cortical connectivity than controls in the visual, somatomotor, dorsal attention and limbic cortical networks (all p -FDR < 0.05), and between the thalamus and cerebellar regions associated with the visual network (p -FDR = 0.003745). Trending hypoconnectivity was observed between the thalamus and cerebellar regions associated with the default mode (DMN; p -FDR = 0.05495) and frontoparietal (FPN; p -FDR = 0.0614) networks. GAM analysis

revealed decreasing curvilinear thalamo-cerebellar connectivity in patients over time in the DMN- and FPN-associated regions (p < 0.01) and an increasing linear pattern of hyper-connectivity for the limbic and motor cortical networks.

Conclusions: A greater understanding of the trajectories of thalamo-cortical and thalamo-cerebellar FC during ESP could potentially reveal greater insights into behavioral outcomes.

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Keywords: Early Stage Psychosis, Thalamocortical Connectivity, Thalamo-Cerebellar Connectivity

Targeting Emotion Regulation Circuitry With a Psychobehavioral Intervention to Reduce Hopelessness in Bipolar Disorder

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Background: Hopelessness is an important behavioral construct that is a robust predictor of suicide. The identification and targeting of brain circuitry underlying hopelessness may therefore help in preventing suicide, yet, such study is rare. This study examined hopelessness in bipolar disorder (BD), which carries one of the highest risks for suicide. Using magnetic resonance imaging (MRI) data, we investigated (a) regional and connectome-based patterns of brain circuitry dysfunction that underlie hopelessness, and (b) aspects of the circuitry that change in association with reductions in hopelessness following a 12-week psychobehavioral intervention, Brain Emotion Circuitry Targeted Self-Monitoring and Regulation Therapy for Emotion Regulation (BE-SMART-ER).

Methods: MRI data were acquired in subjects with BD and healthy controls (N=100; ages 16-79 years). Functional activation and intrinsic connectivity were assessed, while subjects performed an explicit emotion regulation (ER) task, to identify brain circuitry patterns associated with hopelessness and its subconstructs: loss of motivation, feelings about the future, and future expectations. Analyses were also performed, in a subset of sample (16-24 years) who were administered the BE-SMART-ER intervention, to examine brain circuitry changes associated with reductions in hopelessness.

Results: Dysfunction in brain circuitry that subserves ER, including in medial orbitofrontal cortex (mOFC), was associated with hopelessness in BD, particularly due to loss of motivation (p <0.001). From pre-to-post BE-SMART, reductions in hopelessness were associated with increased mOFC and decreased amygdala (p <0.05).

Conclusions: This work provides new insights into the brain circuitry underlying hopelessness and a non-pharmacological intervention that may improve functioning in that circuitry and thereby reduce hopelessness.

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Keywords: Bipolar Disorder, Hopelessness, Emotion Regulation, Therapy, BOLD Functional MRI