glycerophospolipids, 1 sphingomyelin, 1 biogenic amine, and 1 acylcarnitine. GWAS for these metabolites yielded 8 SNPs ($p<1e-05$) that met our GTEx/dbSNP annotation criteria. These SNPs yielded 11 candidate genes expressed in brain tissue. Notably, one SNP ($p= 3.28E-06$) was a sex-biased-eQTL for hypothalamus URB2.

Conclusions: Using a multi-omic approach with independent cohort validation, we have identified for further functional validation 11 novel genes that might contribute to MDD pathophysiology and SSRI response in women.

Supported By: NSF Award Number 2041339, R01 GM28157, U19 GM61388, R01 MH108348

Keywords: Depression, Escitalopram-SSRI, Pharmacometabolomics, Pharmacogenomics

The Roles of Endogenous Opioid System in the Antidepressant Actions of Ketamine

Cheng Jiang[1], Ralph DiLeone[1], Christopher Pittenger[1], and Ronald Duman[1]

[1]Yale University School of Medicine

Background: Synaptic signaling in the medial prefrontal cortex (mPFC) plays an important role in the pathophysiology and treatment of depression. Recent clinical and preclinical studies demonstrate that naltrexone, which primarily blocks μ-opioid receptors, attenuates the antidepressant efficacy of ketamine. Here, we investigate whether the endogenous opioid system within mPFC is necessary for the antidepressant actions of ketamine.

Methods: Male Sprague Dawley rats were administered ketamine (10 mg/kg, i.p.) following intraperitoneal naltrexone (20 mg/kg), intra-mPFC naltrexone (20 μg/side) or intra-mPFC β-endorphin neutralizing antibody (0.5 μg/side) injections. Behavioral tests were carried out starting 24h after ketamine administration. Levels of phosphorylated components of mTOR signaling pathways and total amounts of synaptic proteins were determined by western blot at 1h and 24h after ketamine treatment, respectively. β-endorphin amount was measured in mPFC homogenate 1h after ketamine treatment using ELISA.

Results: Pretreatments with naltrexone (i.p. and intra-mPFC) and β-endorphin neutralizing antibody (intra-mPFC) block the antidepressant effects of ketamine in forced swimming test and female urine sniffing test without altering locomotor activity ($n = 8$ - 14; two-way ANOVA). Systemic pretreatment with naltrexone abolishes ketamine-induced elevations in phosphorylation of mTOR and p70S6K at 1h and in GluR1 and PSD-95 levels at 24h in mPFC synaptosome preparation ($n = 5$ - 6; two-way ANOVA). Ketamine treatment increases β-endorphin levels in mPFC at 1h time point ($n = 5$; t-test/$p<0.05$).

Conclusions: Our results suggest that the antidepressant actions of ketamine are mediated by μ-opioid receptor activation in mPFC, which is induced by increased β-endorphin levels in the region.

Supported By: R01MH093897, R01MH105910, R01NS101104, State of Connecticut

Keywords: Ketamine, Depression, Medial Prefrontal Cortex, Opioid System, β-Endorphin

Research Method: Physiology

Central Autonomic Network Association With Cardiac Autonomic Sleep-Wake Rhythm in Major Depression and Borderline Personality Disorder

Agustina Wainsztein[1], Camacho Vicente[2], Carolina Abulafia[2], Mirta F. Villarreal[2], Carles Soriano-Mas[3], Charles Nemeroff[4], Salvador M. Guinjoan[2], and Mariana N. Castro[2]

[1]Fleni, [2]FLENI Foundation, [3]Bellvitge Biomedical Research Institute-IDIBELL, [4]Dell Medical School at The University of Texas at Austin

Background: Resting heart rate variability (HRV), a measure of ANS activity, adaptability and health, has been shown to be altered in patients with Major Depressive Disorder (MDD) and Borderline Personality disorder (BPD). The Central Autonomic Network (CAN) comprises brain regions involved in both physiological and behavioral regulation. Evidence linking cortical thickness of CAN components and HRV circadian patterns is scarce. We explored this relationship in patients with BPD, MDD and healthy controls (CS).

Methods: Forty-two participants (15 BPD, 14 MDD, 13HC) underwent 24hr-HRV recordings following structural MRI. Cortical thickness analysis was performed (FreeSurfer). Sleep-wake HRV measures (i.e, HF and RMSSD) were calculated. Cortical thickness of CAN regions were tested as HRV predictors.

Results: Cortical thickness of right anterior cingulate and lateral orbitofrontal cortex predicted 50% of RMSSD ($p=.023$) and 58% of HF ($p=.008$) nocturnal variation respectively in BPD patients where greater cortical thickness was associated with increased HRV. HC exhibited this association between left inferior frontal gyrus (IFG) and middle frontal gyrus areas and sleep-HRV($p<.05$). Left triangular segment of IFG explained 86% variability of nocturnal RMSSD in this group ($p=.001$). MDD group did not show significant correlations.

Conclusions: Greater cortical thickness of CAN regions may be associated with increased sleep-HRV in BPD patients and HC. Nocturnal HRV patterns could serve as a biomarker of preserved neural architecture and functioning. Neural correlates of HRV may provide important insights into mechanisms involved in self-regulation that might be related to emotional well-being or psychopathology.

Supported By: CIBERSAM — Ministerio de Economía y Competitividad de España and Agencia Nacional de Promoción Científica y Tecnológica Argentina [PICT 2014: 20140633]

Keywords: Structural MRI, Central Autonomic Network, Heart Rate Variability, Borderline Personality Disorder, Major Depressive Disorder

Feeling Lonely and Heart Rate Variability in Autism and Schizophrenia

Sarah Haigh[1] and Tabatha Walford[1]

[1]University of Nevada Reno

Background: Lower heart rate variability (HRV) reflects chronic stress and is a potential biomarker of psychiatric