Abstracts for Poster Session 2 – Friday, October 2, 2020 at 2:00 pm ET

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2	Emily Belleau	McLean Hospital	Behavioral and Neural Indices of Reward Functioning in Adolescents at High Familial Risk for Major Depressive Disorder
3	Valeria Cuellar Leal	University of Texas Health Science Center at Houston	Deep brain stimulation in the medial forebrain bundle for treatment resistant depression: an open-label, long-term study
4	Daifeng Dong	McLean Hospital	Sex-specific Neural Responses to Acute Psychosocial Stress in Depression
5	Rif El-Mallakh	University of Louisville	NMDA Receptor Inhibition Prevents Intracellular Sodium Elevations Induced by the Sodium Ionophore Monensin in Human Olfactory Neuroepithelial Precursors Derived from Bipolar Patients
6	Brisa Fernandes	University of Texas Health Science Center at Houston	The kynurenine pathway in major depressive disorder, bipolar disorder, and schizophrenia: a meta-analysis of 101 studies
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8	Carolin Hoeflich	University of Florida	Comorbidity of moderate to severe depression and anxiety nearly triples over past decade among college students
9	Daniela Lopez	University of Michigan	Comparison of Side Effects Between "Remitters" and "Non-Remitters": A Bio-K Study Single Site Analysis
10	Sagar Parikh	University of Michigan	Safety of Using a Combinatorial Pharmacogenomic Test for Patients with Major Depressive Disorder in the GUIDED trial
11	Jane Persons	University of Iowa	Moderators of the association between depressive, manic, and mixed mood symptoms and suicidal ideation and behavior: An analysis of the National Network of Depression Centers Mood Outcomes Program
12	Jessica Poskus	Brigham & Women's Hospital	How Depression Symptoms Affect Quality of Life for Menopausal Women with Major Depressive Disorder
13	Katherine Reeves	University of California San Francisco	Characteristics and Temporal Patters of Suicidal Ideation - A Systematic Review
14	Giselli Scaini	University of Texas Health Science Center at Houston	Dysregulation of Mitochondrial Dynamics, Mitophagy and Apoptosis in Major Depressive Disorder: Does inflammation play a role?
15	Parker Schwab	Emory University	Efficacy of Treating Late-Life Bipolar Disorder with Right Unilateral Electroconvulsive Therapy
16	Cortney Sera	University of Michigan	Neurocognitive Effects of Intravenous Ketamine Treatment in Treatment Resistant Depression
17	Paul Thomas	University of Illinois at Chicago	Spectral embedding of the structural connectome reveals diffusion-based brain subnetwork correlates of clinical measures in a transdiagnostic psychiatric cohort.
18	Elizabeth Wenzel	University of Illinois at Chicago	The Natural History of Depression and Anxiety Symptoms Across Pregnancy and the Postpartum in Low-Income Black and Hispanic Women

Presenting Author	Nina Ahlers	University of California San Francisco

1. Exposure to Ambient Particulate Matter and Depressive Symptoms during Pregnancy

Nina Ahlers MPH[1]; Sandra J. Weiss PhD RN FAAN[1]

[1.] School of Nursing, University of California San Francisco, San Francisco, CA 94122

Background: An estimated 12% of women experience perinatal depression[1], affecting their own and their children's health outcomes[2,3]. Perinatal depression is defined as depression during pregnancy or within the first year post-partum[4]. A proposed mechanism of perinatal depression is the dysregulation of the maternal hypothalamic-pituitary-adrenal (HPA) axis[5]. Adult studies have also linked increased air pollution exposure to elevated serum levels of HPA axis hormones[6] and cortisol[7], implicating air pollutants as stressors on the stress response system by HPA activation. It is well documented that long-term activation of the stress system has lethal effects and increases the risk of depression[8]. Very recent studies have found an association between prenatal air pollution exposures to an increased risk of postpartum depression. While most studies have focused on the detection and treatment of postpartum mental health problems[4,9,], the majority of incident depressive symptoms occur during pregnancy rather than afterward[10]. As such, our aim is to gain a better understanding on how different types of stressors including air pollution exposure impact the maternal HPA axis linked to antenatal depression and how this relationship is mediated by cortisol biomarkers.

Methods: Women (n=50) were recruited in obstetric clinics during their third trimester. They completed the Patient Health Questionnaire-9 to assess depression and provided salivary samples at 4 times during the day for 2 days. Four measures of cortisol were calculated from salivary assays: average cortisol levels, cortisol awakening response (CAR), diurnal cortisol slope (DCS), and area under the curve (AUCG). We acquired data on particulate matter (PM2.5) within each woman's residential area from public records of the air quality control district. Structural equation modeling was used to analyze the aims.

Results: Increased PM2.5 exposure during the 1st trimester was associated with more severe depressive symptoms (0.05, p=0.047) and higher cortisol AUCG (6.74, p=0.01) and average levels (0.38, p=0.02) during the 3rd trimester. DCS is associated to increased 3rd trimester depressive symptoms in the 1st trimester and average PM2.5 exposure models (-.892, p=.046, -.949, p=.048, respectfully). The PM2.5 and DCS interaction term variable had a significant association to increased depressive symptoms (1T PM2.5: .195, p= .037, Avg. PM2.5: .460, p=.048) in regression adjusted models. Further, the risk of depressive symptoms decreases as the DCS steepness increases in the lowest exposure group (p=.002). Cortisol did not show a mediating relationship between PM2.5 exposure and depressive symptoms, but rather PM2.5 appeared to moderate the effect of cortisol on depression.

Conclusions: Exposure to pollution during the first trimester appears to have a significant impact on depression in the 3rd trimester, suggesting that effects of pollution on the brain take time to develop. Particulate matter may disrupt cortisol regulation during pregnancy. Mothers with lower prenatal exposure to air pollution are more likely to have stable cortisol diurnal slopes and a lower risk of developing depressive symptoms versus mothers with higher exposure to air pollution during the prenatal period. These findings suggest pregnancy is a critical window of PM2.5 exposure for perinatal depression risk, thus early depression assessment appears warranted for pregnant women in regions known for high pollution.

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Presenting Author	Emily Belleau	McLean Hospital

2. Behavioral and Neural Indices of Reward Functioning in Adolescents at High Familial Risk for Major Depressive Disorder

Emily L. Belleau, Ph.D., Rebecca Kremens, B.A., Yuen-Siang Ang, D.Phil., Angela Pisoni, M.A., Erin Bondy, M.A., Katherine Durham, Ph.D., Randy P. Auerbach, Ph.D., & Diego A. Pizzagalli, Ph.D.

Background: Offspring of parents with major depressive disorder (MDD) have a two- to three-fold higher risk of developing MDD. Deficits in reward processing has emerged as a potential mechanism that may be mediating familial transmission of risk. Early adolescence, particularly the ages spanning 12-14, is marked by a heightened response to rewarding stimuli and increased rates of MDD, suggesting that this is an especially critical developmental period for studying reward functioning. The aim of the current study was to evaluate whether, relative to adolescents without a maternal MDD history (low-risk), adolescents at high-risk for MDD owing to a maternal history of MDD (high-risk) exhibit abnormalities in behavioral measures of reward processing and resting state function of core reward neural circuitry regions, including the ventral striatum (VS) and medial prefrontal (mPFC).

Methods: Low-risk and high-risk 12-14-year-old adolescents completed a probabilistic reward task (*n* = 74 low-risk, *n* = 27 high-risk) and a resting state MRI scan (*n* = 61 low-risk, *n* = 25 high-risk). Group differences in bias toward choosing the more frequently rewarded stimulus (i.e., response bias) as well as VS and mPFC resting activity were examined. Moreover, computational modeling analyses were conducted to test which reward process, specifically reward sensitivity (an index of consummatory pleasure) and learning rate (a measure of the ability to learn from rewarding stimuli), may be impacted by familial risk for MDD. Resting frontostriatal activity was examined by computing the fractional amplitude of low frequency fluctuation (fALFF), a measure of the strength of resting activity within a single brain region.

Results: High-risk adolescents were characterized by a blunted response bias (i.e., less propensity to choose the more frequently rewarded stimulus) compared to low-risk adolescents. Computational modeling analyses clarified that, relative to low-risk adolescents, high-risk adolescents exhibited less reward sensitivity, but an intact learning rate. Although there were no group differences in resting VS and mPFC fALFF, group differences emerged in how mPFC fALFF related to reward response bias. Namely, among high-risk adolescents, a lower reward response bias was associated with higher resting mPFC fALFF. However, there were no significant fALFF-response bias associations amongst low-risk adolescents.

Conclusions: High-risk adolescents exhibited reward responsiveness deficits, suggesting that reward alterations may be a promising premorbid vulnerability marker for MDD. Future studies should evaluate whether high-risk adolescents exhibiting both blunted reward responsiveness and hyperactive mPFC resting activity may be especially vulnerable to a future onset of a major depressive episode.

Presenting Author	Valeria Cuellar Leal	University of Texas Health Science Center at Houston

3. Deep brain stimulation in the medial forebrain bundle for treatment resistant depression: an open-label, long-term study

Valeria A. Cuellar Leal[1], Alexandre Paim Diaz[1], Flavio N. e Silva[1], Taya Bockmann[1], Elizabeth Vinson[1], Robert Suchting[1], Sudhakar Selvaraj[1], Joao De Quevedo[1], Marsal Sanches[1], Albert J. Fenoy[2], Jair C. Soares[1]

[1]The University of Texas Health Science Center at Houston, Louis A. Faillace, M.D, Department of Psychiatry and Behavioral Sciences, Houston, Texas, U.S.A.
[2]The University of Texas Health Science Center at Houston, Department of Neurosurgery, McGovern Medical School, Houston, TX, U.S.A

Background: Major Depressive Disorder (MDD) is one of the leading causes of disability in adults. It is estimated that at least 50% of patients with depression will not achieve and sustain remission following multiple antidepressant medications. (1) Deep brain stimulation (DBS) has emerged as a potential therapeutic intervention for treatment-resistant depression (TRD). (2) In this study, we investigated the rates of treatment response and remission, as well as the mean change in depressive symptoms, at one- and two-years follow-up of 11 (6 females, 5 males; 34-64 years old) patients with treatment resistant depression who underwent DBS in the medial forebrain bundle.

Methods: The diagnosis of MDD was determined using the Structured Clinical Interview for the DSM-IV Axis I Disorders (SCID-I). TRD was defined as no response to adequate trials of primary antidepressants from at least three different classes, using at least two different augmenting/combination agents, more than 6 bilateral treatments of electroconvulsive therapy (ECT) or inability to tolerate ECT, and 20 or more sessions of individual psychotherapy. Response was defined as a 50% or more decrease in the Montgomery-Asberg Depression Rating Scale (MADRS) compared to baseline. Remission was defined as a score of 7 or less on the MADRS. A paired-samples t-test was conducted to compare the MADRS scores from baseline to 1 year and from baseline to 2 years.

Results: Of the 11 participants that had the surgical intervention, 10 completed the evaluation at 1 year and 8 at 2 years. 60% achieved response and 50% achieved remission at 1-year follow-up. At the 2-year follow-up, 50% of the participants achieved response and 25% achieved remission. There was a significant decrease in the mean MADRS scores at 1 year (-20.50, standard deviation (SD)= 12.51, 95% confidence interval (CI) -29.45 – -11.55, p=0.001) and at 2 years (-19.75, SD 15.54, 95% CI= -32.74 – -6.76, p= 0.009).

Conclusion: Medial forebrain bundle DBS showed early promising results regarding treatment response and remission.

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Presenting Author	Daifeng Dong	McLean Hospital

4. Sex-specific Neural Responses to Acute Psychosocial Stress in Depression

Daifeng Dong[1,2], Maria A. Ironside[2,3], Emily L. Belleau[2,3], Shuqiao Yao[1], Diego A. Pizzagalli[2,3,4]

[1]Medical Psychological Center, The Second Xiangya Hospital of Central South University, Changsha, Hunan, P.R. China
[2]Center for Depression, Anxiety, and Stress Research, McLean Hospital, Belmont, MA, USA
[3]Harvard Medical School, Boston, MA, USA
[4]McLean Imaging Center, McLean Hospital, Belmont, MA, USA

Background: Increased stress sensitivity has been implicated in major depressive disorder (MDD) but preclinical studies highlight possible sex-specific effects in neural stress responses in limbic regions. In light of this evidence, we speculated that stress response abnormalities in MDD might be further modulated by sex. In the present study, our goal was to investigate the potential interaction effect between sex and diagnosis in limbic regions during stress processing.

Methods: The Montreal Imaging Stress Task (MIST; three runs, each run lasting 7min) was administered to 124 patients with first-episode MDD (48 males/76 females, mean age ± SD = 25.32 ± 6.96) and 243 heathy controls (HC;106 males/137 females, mean age ± SD = 20.98 ± 3.52) in conjunction with fMRI scanning. Subjective stress and cortisol levels were collected throughout the task. Amygdala, hippocampus and medial orbitofrontal cortex were selected as a priori regions of interest. A repeated measures ANCOVA with *Hemisphere* and *Time* (three runs) as within-subject factors, *Sex* and *Diagnosis* as between-subject factors, and age as covariate was run on contrast values (stress vs. control) extracted from three regions of interest.

Results: When considering subjective and cortisol stress levels, there was a significant main effect of *Time* (cortisol, $F(7,357) = 10.53$, $p < 0.001$; subjective stress, $F(1,363) = 156.67$, $p < 0.001$), indicating the stress was successfully elicited by the MIST task. Main effects of *Diagnosis* and *Sex* were not found in amygdala, hippocampus and medial orbitofrontal cortex. However, a significant *Diagnosis* × *Sex* interaction emerged for the amygdala and hippocampus (amygdala, $F(1,362) = 5.76$, $p = 0.017$; hippocampus, $F(1,362) = 4.73$, $p = 0.030$). Bonferroni-corrected simple effects analyses showed that the female MDD had significantly higher activation in comparison to female HC in the amygdala and hippocampus (amygdala, $p_{Bonferroni} = 0.011$; hippocampus, $p_{Bonferroni} = 0.032$); the male HC showed significant higher activation in comparison to female HC in the amygdala and hippocampus (amygdala, $p_{Bonferroni} = 0.003$; hippocampus, $p_{Bonferroni} = 0.007$).

Conclusions: Our results highlight the importance of considering sex differences when investigating neural stress responses. Case-control differences in neural stress responses observed in females may provide evidence for sex differences in the etiology and pathophysiology of depression.

Presenting Author	Rif El-Mallakh	University of Louisville

5. NMDA Receptor Inhibition Prevents Intracellular Sodium Elevations Induced by the Sodium Ionophore Monensin in Human Olfactory Neuroepithelial Precursors Derived from Bipolar Patients

Yonglin Gao, MD[1]; Aaron Mack, MD[1]; Nick Delamere, PhD[2]; Rif S. El-Mallakh, MD[1]

[1]Mood Disorders Research Program, Depression Center, Department of Psychiatry and Behavioral Sciences, University of Louisville School of Medicine, Louisville, Kentucky
[2]Head, Department of Physiology, University of Arizona, PO Box 245051, Tucson, AZ 85724-5051

Background: Dysregulation of ion flux across membranes and glutamate-induced excitotoxicity appear to be important pathophysiologic abnormalities in bipolar illness. Understanding ion control and responses to ionic stress is important to decipher the pathogenesis of this disorder.

Methods: Olfactory neuroepithelial precursors (ONPs) were obtained by biopsy from type I bipolar patients and non-bipolar controls matched for age, gender, and passage number (n=3 and n=6, respectively). ONPs were cultured in MEM, gentamycin 0.1mg/mL, and FBS 10%, in 5% CO2. ONPs in culture produce neurons, glia, and undifferentiated neural precursors cells. ONPs were treated with, 1 µM monensin (sodium ionophore) for 6 hours, 0.1mM AP_5 (NMDA receptor antagonist) for 6 hours, Or pretreated AP5 30 minutes followed by monensin for 6 hours. Intracellular sodium ($[Na]_i$) was measured with flame spectroscopy and expressed as concentration per protein as measured by Lowery.

Results: Monensin alone significantly increased $[Na]_i$ in ONPs from bipolar individuals (5.08 ± 0.71 vs baseline 3.13 ± 0.93, P =0.03) and AP_5 had no effect (2.0 ± 1.2 vs baseline 3.13 ± 0.93, P =0.27). However, the combination of AP_5 and monensin resulted in normalization of $[Na]_i$ (3.25 ± 1.28 vs baseline 3.13 ± 0.93, P =0.89). This effect was not observed in cells from non-bipolar individuals (monensin alone, 1.72 ± 1.10 vs baseline 2.42 ± 1.80, P =0.25; AP_5 alone, 1.37±0.74 vs baseline 2.42±1.80; AP_5 combined with monensin, 1.53 ± 0.98 vs baseline 2.42 ± 1.80, P =0.31).

Discussion: Sodium regulation is central to neuronal function and may be disturbed in patients with bipolar disorder. Monensin is an ionophore, meaning that it incorporates itself into the membrane and allows sodium to enter independent of cellular membrane proteins. While the mechanism remains obscure, the observation that the NMDA receptor antagonist, AP_5, normalizes $[Na]_i$ only in olfactory neuroepithelial precursors obtained from bipolar illness may provide novel insights into ion regulation in tissues from subjects with bipolar illness.

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Presenting Author	Brisa Fernandes	University of Texas Health Science Center at Houston

6. The kynurenine pathway in major depressive disorder, bipolar disorder, and schizophrenia: a meta-analysis of 101 studies

Brisa S. Fernandes, MD, PhD [1,] Wolfgang Marx, PhD [2], Amelia J McGuinness, MSc [2], Alexandre P. Diaz, MD, PhD [1], João Quevedo, MD, PhD [1], Jair C. Soares, MD, PhD [1]

[1]Center of Excellence on Mood Disorders, Faillace Department of Psychiatry and Behavioral Sciences, McGovern Medical School, The University of Texas Health Science Center at Houston (UTHealth), Houston, TX, USA.
[2]Deakin University, IMPACT – the Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Barwon Health, Geelong, Australia.

Background: The importance of tryptophan as a precursor for neuroactive compounds has long been acknowledged. The metabolism of tryptophan along the kynurenine pathway and its involvement in mental disorders is an emerging area in psychiatry. We performed a meta-analysis to examine the differences in kynurenine metabolites in major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SZ).

Methods: Electronic databases were searched for studies that assessed metabolites involved in the kynurenine pathway (tryptophan, kynurenine, kynurenic acid, quinolinic acid, 3-hydroxykynurenine, and their associate ratios) in people with MDD, SZ, or BD, compared to controls. We computed the difference in metabolite concentrations between people with MDD, BD or SZ, and controls, presented as Hedges' g with 95% confidence intervals.

Results: A total of 101 studies with 10,912 participants were included. Tryptophan and kynurenine are decreased across MDD, BD, and SZ; kynurenic acid and the kynurenic acid to quinolinic acid ratio are decreased in mood disorders (i.e., MDD and BD), whereas kynurenic acid is not altered in SZ; kynurenic acid to 3-hydroxykynurenine ratio is decreased in MDD but not SZ. Kynurenic acid to kynurenine ratio is decreased in MDD and SZ, and the kynurenine to tryptophan ratio is increased in MDD and SZ.

Conclusions: Our results suggest that there is a shift in the tryptophan metabolism from serotonin to the kynurenine pathway, across these psychiatric disorders. In addition, a differential pattern exists between mood disorders and SZ, with a preferential metabolism of kynurenine to the potentially neurotoxic quinolinic acid instead of the neuroprotective kynurenic acid in mood disorders but not in SZ.

Presenting Author	Gabriel Fries	University of Texas Health Science Center at Houston

7. Lack of association between epigenetic aging acceleration and oxidative stress in bipolar disorder

Camila N. C. Lima[1], Jair C. Soares[2], Joao Quevedo[1,2], Gabriel R. Fries[1]*

[1]Translational Psychiatry Program, Department of Psychiatry and Behavioral Sciences, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, Texas;
[2]UT Center of Excellence on Mood Disorders, Department of Psychiatry and Behavioral Sciences, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, Texas
*presenting author

Background: Bipolar disorder (BD) has been associated with many signs of accelerated aging, early-onset dementia, and a higher incidence of age-related conditions. As a marker of biological aging predicted based on genome-wide DNA methylation levels, we have recently reported on alterations in epigenetic aging in BD patients compared to controls, although the mechanisms underlying this acceleration are unknown. Of note, aging has been repeatedly linked to an accumulation of molecular oxidative damage (free radical theory of aging), and the methylation of numerous blood CpGs sites has been correlated with markers of oxidative stress. We aimed to investigate the cross-talk between oxidative stress markers and epigenetic aging in a sample of patients with BD and controls.

Methods: Euthymic BD patients (n = 93) and healthy controls (n = 40) matched for chronological age, sex, ethnicity, and body mass index were enrolled for this analysis. Peripheral blood samples were analyzed for genome-wide DNA methylation levels using the EPIC BeadChip (Illumina) and assessed for epigenetic age and intrinsic epigenetic age acceleration (IEAA) using the Horvath calculator. Oxidative stress was measured with commercial kits and included the following markers: 8-oxo-2'-deoxyguanosine (8-oxo-dG), thiobarbituric acid reactive substances, protein carbonyl content, and total antioxidant capacity. We compared groups showing slower (IEAA < 0) or accelerated aging (IEAA > 0) using univariate analyses. Binary logistic regressions were also performed to check for the combined effects of the markers and covariates on the likelihood that participants would show a slower or accelerated epigenetic aging.

Results: Oxidative stress markers were not significantly different between aging acceleration groups within patients or controls ($p>0.05$ for all comparisons). In a multiple regression, TBARS, PCC, antioxidant capacity, and 8-oxo-dG significantly predicted epigenetic aging acceleration in the whole sample ($F(4,89) = 3.227$, $p = 0.016$, $R2 = 0.127$), but not when the analysis was performed within each group (controls – $F(4,26) = 1.766$, $p = 0.166$, $R2 = 0.214$; patients – $F(4,58) = 1.344$, $p = 0.265$, $R2 = 0.085$). Similarly, binary logistic regression models were not statistically significant in controls ($X2(6)=8.956$, $p=0.176$) or in patients ($X2(7)=3.502$, $p=0.835$).

Conclusion: We did not find major influences of oxidative stress on epigenetic aging acceleration in patients or controls. Epigenetic aging is thought to result from a chronic exposure to stress, inflammation, and many other aging-inducing stimuli, which may not be captured by an acute assessment of oxidative stress.

Presenting Author	Carolin Hoeflich	University of Florida

8. Comorbidity of moderate to severe depression and anxiety nearly triples over past decade among college students

Carolin Hoeflich, MS[1]; Sara Nutley, MS[1]; Marcia R. Morris, MD[2]; & Catherine W. Striley, PhD, MSW, ACSW, MPE[1]

[1]Department of Epidemiology, College of Public Health & Health Professions and College of Medicine, University of Florida, Gainesville, Florida
[2]Department of Psychiatry, College of Medicine, University of Florida, Gainesville, Florida

Background: A fourth of college students reported twelve-month prevalence of a mental disorder diagnosis or treatment in 2015[1], and prior research indicates that the frequency of depression[2, 3] and anxiety[3] are rising. However, few research studies have assessed recent trends in the prevalence and pharmacological treatment of mood disorders among college populations. Thus, the present study examined the temporal prevalence of depressive- and anxiety-based disorders, as well as psychiatric medication treatment, among undergraduate and graduate students over the past decade.

Methods: Responses from 261,483 college students in the United States and Canada who consented and completed the annual Healthy Minds Study (HMS) questionnaire between 2007 through 2018-2019 were analyzed. Prevalence of moderate to severe depression in the sample was determined through a positive screening on the Patient Health Questionnaire-9 (PHQ-9), and rates of moderate to severe anxiety were assessed using the anxiety items of the Patient Health Questionnaire (PHQ) for the 2007 – 2012 HMS surveys and the Generalized Anxiety Disorder 7-item (GAD-7) for the 2013 through 2018-2019 HMS questionnaires. The proportion of students who reported depression only, anxiety only, or both conditions were calculated across each wave of the survey.

Results: Prevalence of comorbid depression and anxiety among the college population was relatively stable from 8.2% in 2007 to 7.3% in 2012, but subsequently increased to 22.2% in 2018-2019. Among students with either depression or anxiety, a 17% increase in the proportion of co-morbid depression and anxiety was observed since 2007. Though the proportion of students with moderate to severe anxiety (i.e. no depression) quadrupled from 1.8% in 2007 to 7.6% in 2018-2019, the prevalence of moderate to severe depression only (i.e. no anxiety) was relatively stable over the past decade, ranging from 10.2% to 14.2%. College students also reported increased use of prescription psychiatric medications; in particular, past-year use of anti-depressants, anti-anxiety medications, psychostimulants, mood stabilizer, and anti-psychotics each doubled from 2007 to 2018-2019. Upward trends were also observed in the current use of anti-depressants and anti-anxiety medications among those with depression or anxiety.

Conclusions: Among North American college students, the prevalence of anxiety, as well as co-morbid depression and anxiety is rapidly increasing. Increased past-year and current use of psychiatric pharmacological treatment - specifically anti-depressants and anti-anxiety medications - among this population may suggest increasing acceptability of psychiatric medication use or increasing disorder severity. These findings may inform psychiatric practice by alerting clinicians to rising trends in psychiatric symptomatology among college students.

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Presenting Author	Daniela Lopez	University of Michigan

9. Comparison of Side Effects Between "Remitters" and "Non-Remitters": A Bio-K Study Single Site Analysis

Sagar V. Parikh[1], Dan Maixner[1], Karina Drake[1], Brendan Watson[1], Daniela Lopez[1], Cortney Sera[1], Erica Vest-Wilcox[1], Ivana Senic[1], Liz Jewell[1], Ashley Bade[1], Geoff Collins[1], Jessica Singley[1], Abby Machoka[1], the Bio-K Study Team[1] and John Greden[1]

[1]University of Michigan Department of Psychiatry and Depression Center

Introduction: The Bio-K Study is a biomarker development study analyzing response of intravenous racemic ketamine delivered at 100- or 40-minute durations at .5mg/kg for treatment refractory depression across four national sites. Currently, biomarkers are being analyzed to determine why certain participants (n=75) responded to IV-ketamine versus those that did not. Furthermore, while information on ketamine side effects are well-documented there is still little information as to who experiences what type and frequency of side effects (Short et al, 2018). As part of a sub-analysis, we wanted to compare whether participants who met study-defined remission status experienced different side effects than those who did not remit as a potential additional signifier of remission status.

Methods: We looked at the University of Michigan site's participants (n=24) side effects and MADRS data and completed a chi-square analysis to analyze the association of side effects in each participant type. The participants at this site completed three-IV ketamine infusions at both 100min (infusion#1) and 40min (infusions 2 and 3) duration, and MADRS scores were collected across all three infusions prior to beginning the infusion, immediately following the infusion, and 24-hours after the infusion. Participants were considered to be "remitters" if their MADRS scores was ≤9 at post 24-hours infusion#3. Side effect data was collected using three different scales, included the Ketamine Side Effects Scale, Young Mania Rating Scale, and an Open-Ended Treatment Emergent Side Effects questionnaire during several timepoints across infusions.

Results: Of the 24 participants, 42% met study-defined remission status at the end of 24-hours post infusion#3. Mean MADRS score for remitters was 4.7 ± 2.62; while non-remitters had a mean score of 20.14± 5.62. All participants experienced some side effect that ranged from very mild to severe during the infusion; however, none required medical intervention or discontinuation of the infusion and all symptoms dissipated 60 min post infusion. The proportion of participants who had study-induced hypertension did not differ between those who met study-defined remission status than those who did not, X^2 (1, N = 24) = 3.4, p > .05. This was similar for other side effects as well.

Conclusion: Participants who achieved remission status did not differ from those who did not meet remission status in their experience of side effects at the University of Michigan site. However, there may be an association at other sites and further analysis may be warranted with other participants.

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Presenting Author	Sagar Parikh	University of Michigan

10. Safety of Using a Combinatorial Pharmacogenomic Test for Patients with Major Depressive Disorder in the GUIDED trial

Sagar V. Parikh, MD[1]; Gabriela K. Khazanov, PhD[2]; Michael E. Thase, MD[2]; Anthony J. Rothschild, MD[3]; Boadie W. Dunlop, MD[4]; Charles DeBattista, DMH, MD[5]; Charles R. Conway, MD[6]; Brent P. Forester, MD, MSc[7]; Richard C. Shelton, MD[8]; Matthew Macaluso, DO[9]; James Li, PhD[10]; Kunbo Yu, MS[10]; Stephanie Meek, PhD[11]; Michael R. Jablonski, PhD[10]; John F. Greden, MD[1]

[1]University of Michigan Comprehensive Depression Center and Department of Psychiatry and NNDC, Ann Arbor, MI
[2]Perelman School of Medicine of the University of Pennsylvania & the Corporal Michael Crescenz VAMC, Philadelphia, PA
[3]University of Massachusetts Medical School and UMass Memorial Healthcare, Worcester, MA
[4]Emory University School of Medicine, Atlanta, GA
[5]Stanford University School of Medicine, Stanford, CA
[6]Washington University School of Medicine, St. Louis, MO
[7]McLean Hospital, Belmont, MA
[8]The University of Alabama at Birmingham, Birmingham, AL
[9]University of Kansas School of Medicine-Wichita, Wichita, KS
[10]Myriad Neuroscience, Mason, OH
[11]Myriad Genetics, Inc., Salt Lake City, UT

Background: Pharmacogenomic testing has emerged to aid medication selection for patients with major depressive disorder (MDD) by identifying potential gene-drug interactions (GDI). Many pharmacogenomic tests are available with varying levels of supporting evidence, including direct-to-consumer and physician-ordered tests. We retrospectively evaluated the safety of using a physician-ordered combinatorial pharmacogenomic test (GeneSight) to guide medication selection for patients with MDD in a large, randomized, controlled trial (GUIDED).

Methods: Patients diagnosed with MDD who had an inadequate response to ≥1 psychotropic medication were randomized to treatment as usual (TAU) or combinatorial pharmacogenomic test-guided care (guided-care). All received combinatorial pharmacogenomic testing and medications were categorized by predicted GDI (no, moderate, or significant GDI). Patients and raters were blinded to study arm, and physicians were blinded to tests results for patients in TAU, through week 8. Measures included adverse events (AEs, present/absent), worsening suicidal ideation (increase of ≥1 on the corresponding HAM-D17 question), or symptom worsening (HAM-D17 increase of ≥1). These measures were evaluated based on medication changes [add only, drop only, switch (add and drop), any, and none] and study arm, as well as baseline medication GDI.

Results: Most patients had a medication change between baseline and week 8 (938/1,166; 80.5%), including 269 (23.1%) who added only, 80 (6.9%) who dropped only, and 589 (50.5%) who switched medications. In the full cohort, changing medications resulted in an increased relative risk (RR) of experiencing AEs at both week 4 and 8 [RR 2.00 (95% CI 1.41-2.83) and RR 2.25 (95% CI 1.39-3.65), respectively]. This was true regardless of arm, with no significant difference observed between guided-care and TAU, though the RRs for guided-care were lower than for TAU. Medication change was not associated with increased suicidal ideation or symptom worsening, regardless of study arm or type of medication change. Special attention was focused on patients who entered the study taking medications identified by pharmacogenomic testing as likely having significant GDI; those who were only taking medications subject to no or moderate GDI at week 8 were significantly less likely to experience AEs than those who were still taking at least one medication subject to significant GDI (RR 0.39, 95% CI 0.15-0.99, p=0.048). No other significant differences in risk were observed at week 8.

Conclusion: These data indicate that patient safety in the combinatorial pharmacogenomic test-guided care arm was no worse than TAU in the GUIDED trial. Moreover, combinatorial pharmacogenomic-guided medication selection may reduce some safety concerns. Collectively, these data demonstrate that combinatorial pharmacogenomic testing can be adopted safely into clinical practice without risking symptom degradation among patients.

Presenting Author	Jane E. Persons	University of Iowa

11. Moderators of the association between depressive, manic, and mixed mood symptoms and suicidal ideation and behavior: An analysis of the National Network of Depression Centers Mood Outcomes Program

Jane E. Persons, PhD[1], Jess G. Fiedorowicz, MD, PhD[2], Michael J. Ostacher, MD, MPH[3], William H. Coryell, MD[4]

[1]Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, Iowa, United States
[2]Department of Psychiatry, The Ottawa Hospital, Ottawa, Ontario, Canada
[3]Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Palo Alto, California, United States
[4]Department of Psychiatry, University of Iowa, Iowa City, Iowa, United States

BACKGROUND: Mixed depressive and manic symptoms are a high-risk state for suicide, although it is not established that this risk is any greater than that of the component symptoms.

METHODS: The National Network of Depression Centers Mood Outcomes Program collected data from measurement-based care for 17,179 visits from 6,105 individuals with clinic diagnoses of mood disorders (998 bipolar disorder, 5,117 major depression). The Patient Health Questionaire-8 (PHQ-8) captured depressive symptoms and the Altman Self-Rating Mania scale (ASRM) measured hypomanic/manic symptoms. Generalized linear mixed models assessed associations between depressive symptoms, manic symptoms, and their interaction (to test for synergy with mixed symptoms) on the primary outcome of suicidal ideation or behavior from the Columbia-Suicide Severity Rating Scale (C-SSRS).

RESULTS: PHQ-8 scores were strongly associated with suicide-related outcomes across diagnoses. ASRM scores showed no association in bipolar disorder and an inverse association in major depression. The PHQ-8*ASRM interaction was not significant, showing no evidence of synergy between depressive and manic symptoms.

CONCLUSION: There does not appear to be any additional risk of mixed depressive and manic symptoms beyond that explainable by the depressive symptoms alone. Depressive symptoms are strongly linked to suicidal ideation and suicidal behavior and represent an important and potentially modifiable risk factor for suicide.

Presenting Author	Jessica Poskus	Brigham and Women's Hospital

12. How Depression Symptoms Affect Quality of Life for Menopausal Women with Major Depressive Disorder

J. Poskus, M. Shanahan, M. Shanahan, KE. Burdick

Mood and Psychosis Research Program, Dept. of Psychiatry, Brigham and Women's Hospital, Harvard Medical School

Background: Women with Major Depressive Disorder tend to exhibit more maladaptive coping mechanisms, which can be defined as cognitive and behavioral efforts to manage stressful demands. This can contribute to a more severe course of illness, as it increases risk for recurrence and reduces quality of life.

Methods: 51 postmenopausal adult women with MDD and an average baseline Premorbid IQ of 104 were administered the Menopause-Specific Quality of Life (MENQOL) Questionnaire, which is used to measure severity of past menopausal symptoms (vasomotor, psychosocial, physical, and sexual). The MATRICS Consensus Cognitive Battery (MCCB) was used as well to assay cognitive functioning. All participants completed the Brief-COPE scale (BCOPE) to measure the patients' self-described habitual use of a variety of coping mechanisms, which are determined to be either adaptive (e.g. humor) or maladaptive (e.g. self-blame). A multiple regression analysis was used to determine how number of depressive episodes, age of onset of menopause, cognitive functioning, and coping styles influence quality of life.

Results: Significant differences were found in patients with more depressive symptomology tended to exhibit more maladaptive coping mechanisms ($p<0.05$). Individuals with more maladaptive coping mechanisms tended to perform worse on the MCCB ($p<0.05$).

Conclusions: As the menopausal transition places women at risk for depression and cognitive decline, this is a critical window to study, particularly in those with a recurrent mood disorder. Our results support the hypothesis that both depression and cognitive impairment contribute to lower quality of life. Aspects that are related to reproductive status will be further analyzed, as will hormonal levels and inflammation-based biomarkers to better understand the biological risk factors for poor outcome.

Presenting Author	Katherine Reeves	University of California San Francisco

13. Characteristics and Temporal Patters of Suicidal Ideation – A Systematic Review

Katherine W Reeves, MS PMHNP-BC[1,2]; Genesis Vascones, MS PMHNP-BC[1]; Sandra Weiss, PhD DNSc RN[1,2]

[1]Department of Community Health Systems, University of Californian San Francisco
[2]UCSF Depression Center

Background: Suicide is a growing public health concern across demographics in the United States. Despite significant efforts, there has been no substantial progress in our ability to predict suicide risk over the last 50 years, contributing to a dearth of effective suicide prevention interventions. Recent evidence suggests that this stall may be due to a lack of information about the experience of Suicidal Ideation (SI). This systematic review aimed to identify, synthesize and critique literature assessing descriptive characteristics of SI (e.g. temporality, severity, duration, etc.) in order to decipher what is known about how one experiences thoughts of suicide.

Methods: Four databases were searched (Pubmed, Embase, Web of Science, and PsychInfo). Studies were included that measured characteristics of SI in any population and were excluded if they analyzed a dichotomous (yes/no) SI variable or if the dependent variable included characteristics of the individual (e.g. personality traits, one's environment, etc).

Results: Of 1,478 articles generated in the initial search, 10 peer-reviewed publications were included in the review. Findings suggested four takeaways: 1) There is little information identifying typical patterns of how SI fluctuates over short periods of time; 2) There is significant evidence to show that SI varies significantly over short periods of time (e.g. day to day); 3) There is preliminary evidence for the presence of SI subtypes based on phenotypic distinctions of one's experience with SI; and 4) There are conceptual discrepancies in this literature around the operationalization of SI and its associated characteristics as a concepts and how they should be applied to suicide research.

Conclusions: The emerging body of literature about suicidal thoughts shows promising progress in suicide prevention research. However, this body of literature is small and there are conceptual discrepancies among studies that threaten its progress. Future research should focus on identifying a set of universally agreed on characteristics of SI that can be used across studies to better understand patterns of SI as well as subtypes of SI that may lead to more effective, targeted suicide prevention strategies.

Presenting Author	Giselli Scaini	University of Texas Health Science Center at Houston

14. Dysregulation of Mitochondrial Dynamics, Mitophagy and Apoptosis in Major Depressive Disorder: Does inflammation play a role?

Giselli Scaini[1]*, Alexandre P. Diaz[1], Brittany Mason[2], Manish Jha[2], Jair C. Soares[1], Madhukar H. Trivedi[2], and João Quevedo[1]

[1] Louis A. Faillace, MD, Department of Psychiatry and Behavioral Sciences, McGovern Medical School, The University of Texas Health Science Center at Houston (UTHealth), Houston, TX, USA; [2]Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, TX, USA

Background: Recent studies have suggested that mitochondrial dysfunction and dysregulated neuroinflammatory pathways are involved in the pathophysiology of major depressive disorder (MDD). Thus, in this study, we tested the hypotheses that the changes in mitochondrial morphology and number are associated with an imbalance in the mitochondrial dynamics and mitophagy in MDD patients. We assessed differences in molecular markers of mitochondrial dynamics, mitophagy, general autophagy, and apoptosis in peripheral blood mononuclear cells (PBMCs) of MDD patients and healthy controls (HCs). Moreover, we studied inflammation engagement as a moderator of mitochondria dysfunctions on the severity of depressive symptoms.

Methods: Our sample included 24 healthy controls (HC; 39.45 ± 2.60 years; 16 females), and 84 MDD (44.91 ± 1.48 years; 59 females). PBMCs were separated using LeucoPREP brand cell separation tubes, and Immunoblotting and Multi-Plex interrogated the MQC, autophagy, and intrinsic apoptotic-related proteins.

Results: One-Way ANCOVA after controlling for age, gender, ethnicity, BMI, smoking status, and antidepressant treatment showed that the protein levels of the mitochondrial fusion-related protein Mfn-2 and fission-related protein Fis-1 were increased in MDD patients when compared to HCs. Moreover, we observed a lower ratio of long to a short isoform of Opa-1 in PBMCs from patients with MDD, suggesting that mitochondrial morphology was shifted toward a fragmented network. We also found that MDD patients had higher levels of Pink-1, p62/SQSTM1, LC3B, and caspase-3 active compared to HCs. On the other hand, our study demonstrated lower levels of Parkin in MDD patients. Another notable finding was that CRP levels were a significant predictor of higher levels of Mfn-2, Pink-1, and LC3B levels, and this relationship persisted when depressive symptoms were controlled for. Moreover, MDD patients with low CRP levels, Opa-1 levels contribute to the depression severity. However, in MDD patients with higher CRP levels, Mfn-2 levels were a significant predictor of depression severity.

Conclusion: Overall, our study demonstrated that mitochondrial fragmentation caused by a disruption in mitochondrial fusion could initiate a cascade of abnormal changes relevant to the critical pathological changes during the course of MDD and lead to progression of the disease, and poor outcomes. Moreover, the subtle regulation of mitochondrial quality control network during disease progression may be a possible therapeutic strategy to improve treatment response and disease progression.

Presenting Author	Parker Schwab	Emory University

15. Efficacy of Treating Late-Life Bipolar Disorder with Right Unilateral Electroconvulsive Therapy

P. Parker Schwab, BBA[1]; Amitha Dhingra, MD[1]; Hannah Chapman, MA[1]; Autumn Lunceford[1]; A. Umair Janjua, MD[1]; Gregory Job, MD[2]; William McDonald, MD[2]; Patricio Riva-Posse, MD[1]; Amanda Tan, B.S.[2]; Rachel Hershenberg, Ph.D.[1],Adriana P. Hermida, MD[2]

[1]Department of Psychiatry and Behavioral Sciences, Emory University, 101 Woodruff Cir NE, Suite 4000, Atlanta, GA, 30322, USA
[2]Department of Psychiatry and Behavioral Sciences, Fuqua Center for Late-Life Depression, Emory University, 101 Woodruff Cir NE, Suite 4000, Atlanta, GA 30322, USA

Background: Bipolar Disorder (BPAD) accounts for 10-25% of all mood disorders in the geriatric population and 5% of all inpatient admissions to geropsychiatric units. It is a disabling illness in the elderly and is often treatment-resistant. Electroconvulsive therapy (ECT) is an effective treatment for all phases of BPAD, though only a few studies have focused on bipolar disorder in the geriatric population. There is insufficient evidence to determine which electrode placement is most efficacious in treating bipolar disorder. This study examines the safety and efficacy of right unilateral (RUL), namely ultra-brief right unilateral (UBRUL), ECT for patients with late-life BPAD.

Methods: A retrospective chart review was conducted of BPAD patients who received brief RUL and UBRUL ECT treatments. Symptomatic response was measured using pre- and post-ECT Quick Inventory of Depressive Symptomatology (QIDS) and Beck Depression Inventory (BDI) scores. Clinical improvement and cognitive change were measured using Clinical Global Impression improvement (CGI-I) and Electroconvulsive Cognitive Assessment (EcCA) scores.

Results: Forty elderly patients (28 women and 12 men, mean age 68.9 ± 7.1 years) were included in the analysis. 60.6% of patients showed ≥ 50% improvement and 51.5% achieved remission of ≤5 in QIDS scores (n = 33). 66.7% demonstrated ≥ 50% improvement and 50% achieved remission of ≤12 in BDI scores (n = 6). Average QIDS score was reduced by a statistically significant 46.2% (two-tailed, paired p-value <0.01) after ECT. 67.6% of patients attained a score of “much improved” or better in CGI-I (n = 37) and 35.1% achieved remission. 50% of patients saw ≥ 50% improvement in EcCA scores (n = 6).

Conclusions: RUL ECT is a safe and effective treatment for patients presenting with late-life BPAD. Additional studies are warranted to establish further treatment guidelines in this area.

Presenting Author	Cortney Sera	University of Michigan

16. Neurocognitive Effects of Intravenous Ketamine Treatment in Treatment Resistant Depression

Cortney E. Sera[1], Daniela Lopez[1], Dan Maixner[1], Karina Drake[1], Brendan Watson[1], Kelly Ryan[1], Eric Achtyes[2], Erica Vest-Wilcox[1], Ivana Senic[1], LeAnn Smart[2], John Greden[1], Sagar V. Parikh[1]

[1]Michigan Medicine, University of Michigan Department of Psychiatry and Depression Center, Ann Arbor, USA
[2]Pine Rest Christian Mental Health Services, Grand Rapids, USA

Background: Ketamine is an NMDA receptor antagonist associated with learning and memory. In pre-clinical research, limited evidence suggests neurotoxicity, but there is disagreement over how ketamine treatment for treatment resistant depression (TRD) impacts cognitive function[1,2,3,4,]. We investigated the possible effects of intra-venous ketamine on cognition using the Repeatable Battery for the Assessment of Neuropsychological Status Update®, (RBANS-Update) a brief, individually administered battery[5].

Methods: We conducted a clinical trial to examine biomarkers of remission to ketamine for resistant unipolar or bipolar depression, involving administering 3 IV ketamine infusions over an 11-day period. At baseline and 24 hours after the last infusion, the RBANS-Update was administered. RBANS-Update is a validated and reliable cognitive battery of 12 subtests focused on 5 indexes of cognition: immediate memory, visuospatial/constructional, language, attention, and delayed memory. Subtest raw scores are converted to standardized index scores by same-age peer groups.

Results: Twenty-nine subjects completed the acute phase of infusions at the University of Michigan and satellite Michigan State University – Pine Rest site. Preliminary analysis of 24 participants show, regardless of clinical outcome, there was a significant improvement in all five cognitive indexes and by percentile rank. Overall, there was significant improvement from percentile rank by age group at baseline (M=48.42, SD=25.95) to 24 hours post infusion 3 (M=70.45, SD=31.46) conditions; t(23)=-11.84, p = .000. A one-way between subjects ANOVA was conducted to compare the effect of remission on percentile rank. Remission was defined as a score of ≤ 9 on the Montgomery–Åsberg Depression Rating Scale MADRS. There was no significant difference in remitter group at baseline testing on percentile rank (F(1, 25) = .667, p = .422). Because there was no difference between participants that experienced remission and did not experience remission at baseline, baseline differences between groups cannot account for the overall improvement.

Conclusion: These preliminary data provide evidence of cognitive improvement, not decline, following administration of 3 IV ketamine infusions for depression. While cognitive improvement may be mediated by improvement in depression, even individuals not achieving remission demonstrated cognitive improvement. These data are clinically reassuring that low doses of ketamine do not cause neuro-cognitive deficits. Further analysis will be done to explore how depression improvement mediates improved cognition as well as how cognitive performance may be linked to suicidal ideation[1].

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Presenting Author	Paul Thomas	University of Illinois at Chicago

17. Spectral embedding of the structural connectome reveals diffusion-based brain subnetwork correlates of clinical measures in a transdiagnostic psychiatric cohort.

Paul J Thomas[1,2]; Alex Leow MD PhD[1,2]; Olusola Ajilore MD PhD[2]

[1]Department of Bioengineering, University of Illinois at Chicago, Chicago, IL 60612
[2]Department of Psychiatry, University of Illinois at Chicago, Chicago, IL 60612

Background: Graph theoretical models of brain networks are extensively studied in the field of psychiatry. Such networks are represented as a set of vertices (brain regions) and edges (connections between brain regions), which are defined based on imaging modality. Commonly, white matter tractography based structural connectomes are used directly for either edge-based or graph theoretical analysis. However, edge-centric studies are limited to pairwise comparison, and predefined graph features limit access to potentially informative latent network structure. Alternatively, the mathematical properties of connectome graph laplacian can be utilized to model the "heat" or "information" diffusion characteristics, which take into account the entire network topology, of brain networks. In this study, we propose a novel method for representing the structural connectome by defining edge weights between nodes as a similarity metric based on the spectral embedding of each subject's brain graph. We then apply the network-based statistic (NBS) framework to identify subnetworks that correlate with clinical traits of interest.

Methods: Data used are diffusion tensor imaging based structural connectomes from an Research Domain Criteria (RDoC) study, with N=66 patients (PT, mean age=27.5, male/female=20/46) with any form of internalizing psychopathology (e.g., major depressive disorder, generalized anxiety disorder, social anxiety disorder, post-traumatic stress disorder) and N=23 age and sex matched healthy controls (HC, mean age=24.7, male/female=8/15). The Depression Anxiety and Stress (DASS) questionnaire was administered to each subject. The symmetric normalized laplacian is computed and eigen-decomposed to obtain the eigenmodes (eigenvectors of the laplacian matrix) for each subject's structural adjacency matrix. Each element of an eigenmode corresponds to the spectral embedding of a node such that diffusion occurs more quickly between nodes with similar eigenmode values. Brain network eigenmodes are then used to determine the similarity (via Euclidean distance) of all nodes to one another in the embedding space. Next, an NBS-based framework is applied to the newly defined structural connectomes to identify subnetworks that either positively or negatively correlate with clinical traits of interest. As the connectomes used are similarity matrices based on the spectral embedding of nodes, a significant subnetwork using only positive correlations, for example, would indicate that faster diffusion in the subnetwork is positively correlated with the trait of interest.

Results: In a preliminary analysis, one subnetwork was found to correlate positively with the DASS depression subscale, indicating that faster diffusion within the subnetwork is positively associated with this scale. This subnetwork is composed of the bilateral precuneus, posterior cingulate cortices, amygdalae and left frontal cortical regions (*rho threshold* =-0.35, p=0.004). Edges in the subnetwork were predominantly adjacent to the bilateral precuneus, which are hubs of the default mode network, a major functionally defined subnetwork that has previously been implicated in depression and anxiety.

Conclusions: This preliminary study both proposes a novel method for the identification of brain subnetwork-based correlates of psychiatric disease and employs this method to successfully identify a subnetwork that includes brain regions that have been previously implicated in depression and anxiety. These results provide evidence that structural network features of the brain regions in a canonically functionally defined subnetwork may be transdiagnostic markers of disease across the swath of internalizing psychopathologies.

Presenting Author	Elizabeth Wenzel	University of Illinois at Chicago

18. The Natural History of Depression and Anxiety Symptoms Across Pregnancy and the Postpartum in Low-Income Black and Hispanic Women

Wenzel ES[1,2], Gibbons RD[3], Maki PM[1,2,4]

[1]Department of Psychology, University of Illinois at Chicago, Chicago, IL
[2]Women's Mental Health Research Program, Department of Psychiatry, University of Illinois at Chicago, Chicago, IL
[3]Center for Health Statistics and Departments of Medicine and Public Health Sciences, University of Chicago, Chicago, IL
[4]Department of Obstetrics & Gynecology, University of Illinois at Chicago, Chicago, IL

Background: The perinatal period is a time of increased vulnerability to affective disorders, with rates of perinatal depression (PND) between 6.5%-12.9% and comorbid perinatal anxiety (PNA) in as many as 50% of PND cases. While most research to date on the natural history of perinatal affective disorders (PNAD) has been conducted in White women, it is important to extend this work to women of color as Black and Hispanic women have shown higher rates of PNAD. Improved screening itself can lower rates of PNAD, and it is therefore important to allocate limited resources to periods of increased risk. To further our understanding of the natural history of PNAD in Black and Hispanic women, we investigated changes in PND and PNA symptoms at up to five timepoints in the perinatal period from the first trimester to 4-6 weeks postpartum using a computerized adaptive test for mental health (CAT-MH™), which includes a diagnostic screen for MDD (CAD-MDD), and a measures of the severity of depressive (CAT-DI) and anxiety (CAT-ANX) symptoms tailored for PND.

Methods: A total of 178 pregnant Black and Hispanic women (115 Black, 63 Latina) from an urban university obstetrics outpatient clinic were evaluated at 523 visits using CAT-MH™ as part of a longitudinal study on perinatal mental health. Linear mixed-effects models were used to evaluate time-dependent changes in PND and PNA symptoms, and logistic mixed-effects models were used to evaluate time-dependent changes in positive PND (a positive result on the CAD-MDD) and PNA (a moderate or severe result on the CAT-ANX) screenings, including covariates of race/ethnicity, income, age, and history of depression.

Results: There was a significant main effect of trimester on CAT-DI severity scores (b=-.15, p=.008), with scores declining overall across trimesters/postpartum. Among women who had at least one positive CAD-MDD screening across the perinatal period, the likelihood of a positive screening was highest in the first trimester (OR .63; 95% CI .33-.86), with a trend towards declining likelihood across subsequent trimesters/postpartum (b=-.31, p=.06). There was a significant main effect of trimester on CAT-ANX severity score (b=-.16, p=.02), with scores declining across trimesters/postpartum. Among women who had at least one positive CAT-ANX screening, the likelihood of a positive screening was highest in the first trimester (OR .34; 95% CI .13-.63) with rates declining across trimesters/postpartum (b=-.34, p=.03). However, there was a significant interaction between race/ethnicity and trimester on positive CAT-ANX screenings (p=.01). While Hispanic women showed the highest likelihood of a CAT-ANX positive screening in the first trimester (OR .34; 95% CI .13-.63), Black women showed the least likelihood of a positive screening in the first trimester (OR .07; 95% CI .02-.22), and the highest likelihood postpartum (OR.23; 95% CI .09-.46).

Conclusions: The present study suggests that screening for PND is especially important in the first trimester for low-income Black and Hispanic women, while screening for PNA may be most useful in the first trimester for Hispanic women and in later pregnancy and the postpartum for Black women.