NATIONAL NETWORK *of* DEPRESSION CENTERS

MOOD DISORDERS IN TRANSFORMATION:

NOVEL APPROACHES TO BIOLOGY, PSYCHOLOGY, AND ACCESS TO CARE

11th Annual NNDC Conference

September 24-25, 2019

Ann Arbor, MI

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For your convenience, we have included blank pages for notes at the back of this booklet.

Acknowledgments

We would like to thank all of our speakers and facilitators for their contributions both to this conference and their areas of study. We are proud to work with such highly respected and knowledgable clinicians, researchers, and advocates and hope to continue developing these adn other relationships with some of the world's brightest minds.

We would also like to thank the NNDC Conference Program and Planning Committees for putting together another engaging and innovative Annual Conference program.

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Meet the NNDC Team

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WELCOME TO THE 2019 NNDC ANNUAL CONFERENCE!

The theme of this year's conference – Mood Disorders in Transformation: Novel Approaches to Biology, Psychology, and Access to Care – was chosen to highlight the latest and greatest advances in mood disorders research and care delivery. By focusing on such cutting-edge research, we seek to accelerate the pace of treatment innovations in treating patients with depression and bipolar disorders. Special attention was given in this year's program to population-based approaches to understanding, diagnosing, and treating mood disorders – including those among children and adolescents – and beginning to address disparities in mental health care.

We are honored to welcome Dr. Myrna Weissman, the Diane Goldman Kemper Family Professor of Epidemiology and Psychiatry at Columbia University, as our keynote speaker this year. Dr. Weissman is a hero to clinicians who yearn for progress in translating research into real, meaningful treatments and care practices. In her keynote address, titled "30 Years of Studying Families at Risk for Depression: What's Been Learned Along the Way", Dr. Weissman will explore the unique insights that can be learned by studying the transmission of depression across generations.

We are also pleased to welcome Dr. Roy Perlis, Director of the Center for Quantitative Health at Massachusetts General Hospital, as our Seventh Annual David Mrazek Memorial Lecturer. His talk, titled "Beyond Artisanal Prescribing: Can Machine Learning Save Us from Ourselves?", details how machine learning can be used to process large collections of biomarker data to guide next-generation treatment selection for depression.

As it is every year, the 2019 NNDC Annual Conference is the perfect time to start thinking about how you can get more involved with the NNDC. We would love to discuss how your center's experts and areas of interest might fit into the work our Task Groups are doing

Thank you for joining us, as always.

Sagar Parikh, MD
Medical Director, NNDC

Ray DePaulo, MD
Chair of the Board, NNDC

FROM THE NNDC TEAM

On behalf of the whole NNDC Team, we are pleased to welcome you to Ann Arbor for our 11th Annual Conference! Each year we the conference program highlights the ways the NNDC is uniquely positioned to improve diagnosis and treatment of mood disorders by facilitating knowledge sharing across the nation and expediting large scale, multi-site research initiatives – and this year's program is no exception. Our members are engaging in some of the most innovative and exciting research in the field, and the Annual Conference is a great way to show off some of that work, whether through main stage presentations, poster session discussions, or even casual conversation with your fellow attendees over the duration of the program.

Thank you for joining us as we kick off the start of the NNDC's second decade! We hope to see you again next year – we will be taking the Annual Conference on the road to the Mayo Clinic in Rochester, Minnesota from September 30 to October 2, 2020.

Pat Rinvelt, MBA
Executive Director, NNDC

Dane Larsen
Director of Operations, NNDC

Featured Speakers

Keynote Lecturer

MYRNA WEISSMAN, PHD

Diane Goldman Kemper Family Professor of Epidemiology and Psychiatry
Columbia University Vagelos College of Physicians and Surgeons
Chief, Division of Translational Epidemiology
New York State Psychiatric Institute

Dr. Weissman is the Diane Goldman Kemper Family Professor of Epidemiology and Psychiatry, Vagelos College of Physicians and Surgeons and the Mailman School of Public health at Columbia University and Chief of the Division of Translational Epidemiology at New York State Psychiatric Institute. Until 1987, she was a Professor of Psychiatry and Epidemiology at Yale University School of Medicine and Director of the Depression Research Unit. She was a Visiting Senior Scholar at the Institute of Medicine, National Academy of Sciences, Washington, D.C. In 1974, she received a Ph.D. in chronic disease epidemiology from Yale University. Her current research includes the study of the transmission of depression across generations, the detection of biomarkers of transmission and treatment response, and the implementation of psychotherapy in low-income countries and populations.

Dr. Weissman has been a consultant to many private and public agencies, including the World Health Organization, Brain and Behavior, the American Foundation for Suicide Prevention, and more. She is also a member of the National Academy of Medicine. She has been the author or a co-author of over 600 scientific articles and chapters, and 12 books, the most recent being T*he Guide to Interpersonal Psychotherapy*, Oxford University Press, New York, NY, 2018. Along with her late husband Gerald Klerman, she developed Interpersonal Psychotherapy, an evidence-based treatment for depression and related disorders with over 100 clinical trials carried out worldwide.

In April 2009, she was selected by the American College of Epidemiology as 1 of 10 epidemiologists in the United States who has had a major impact on public policy and public health. The summary of her work on depression appears in a special issue of the *Annals of Epidemiology*, *Triumphs in Epidemiology*. In January 2016, she was listed as one of the 100 highly cited authors in all fields by Google Scholars Citation.

David Mrazek Memorial Lecturer

ROY PERLIS, MD, MSC

Professor of Psychiatry
Director, Pharmacogenomics Research
Department of Psychiatry and Center for Human Genetic Research
Medical Director, Bipolar Clinic and Research Program
Massachusetts General Hospital

Roy Perlis, MD, MSc is the Director of the Center for Quantitative Health at Massachusetts General Hospital. He is Professor of Psychiatry at Harvard Medical School, and Associate Editor for Neuroscience at *JAMA*'s new open-access journal, *JAMA Network - Open*. He graduated from Brown University, Harvard Medical School and Harvard School of Public Health, and completed his residency, chief residency, and clinical/research fellowship at MGH before joining the faculty.

Dr. Perlis's research is focused on identifying predictors of treatment response in brain diseases, and using these biomarkers to develop novel treatments. He directs two complementary laboratory efforts, one focused on patient-derived cellular models and one applying machine learning to large clinical databases. These two programs converge in the MGH NeuroBank, one of the largest cellular biobanks in the world for the study of neurodevelopmental and neurodegenerative disorders. The NeuroBank spans more than 400 cell lines associated with detailed clinical phenotypic assessment and links to electronic health records.

Dr. Perlis's laboratory has made a number of key contributions to understanding the biological basis of psychiatric disease. In work published in *Nature Neuroscience*, his team described abnormalities in synaptic pruning using neurons and microglia from individuals with schizophrenia, laying the groundwork for high-throughput screens to identify interventions with the potential to treat and potentially prevent schizophrenia and related disorders. In 2016 he co-led the team that identified the first genetic variation associated with major depressive disorder, published in *Nature Genetics*. His team was also the first to apply machine learning to predict antidepressant response and the first to complete genome-wide association studies of suicide and lithium response. They have also made major contributions to the application of electronic health records to study brain diseases in terms of longitudinal outcomes.

In total, Dr. Perlis has authored more than 250 articles reporting original research, in journals including *Nature Genetics*, *Nature Neuroscience*, *JAMA*, *NEJM*, the *British Medical Journal*, and the *American Journal of Psychiatry*. His research has been supported by awards from NIMH, NHGRI, NHLBI, NCCIH, and NSF, among others. In 2010 Dr. Perlis was awarded the Depression and Bipolar Support Alliance's Klerman Award; he now serves as a scientific advisor to the DBSA.

Schedule-at-a-Glance

MONDAY, SEPTEMBER 23, 2019

Start	End	Session
3:30 pm	4:30 pm	**NNDC Executive Committee Meeting** *Executive Committee and NNDC Staff only*
5:30 pm	8:00 pm	**NNDC Board Meeting** *Board of Directors and NNDC Staff only* *Working dinner planned for 7:00 pm*

TUESDAY, SEPTEMBER 24, 2019

Start	End	Session
7:30 am	8:30 am	**Breakfast and Registration**
8:30 am	8:45 am	**Opening Remarks**
8:45 am	10:45 am	**Symposium: Advances in Neuromodulation** Conor Liston, MD, PhD - Weill Cornell Medical College Shirlene Sampson, MD - Mayo Clinic Daniel Maixner, MD - University of Michigan
10:45 am	11:00 am	*Break*
11:00 am	12:00 pm	**David Mrazek Memorial Lecture** Roy Perlis, MD - Massachusetts General Hospital
12:00 pm	1:00 pm	*Lunch*
1:00 pm	2:00 pm	**Judged Poster Session** *Best Poster Award Winners to be announced at dinner*
2:00 pm	3:00 pm	**Symposium: Disparities in Mental Health Care** George Rust, MD, MPH - Florida State University To be followed by audience conversation on equity
3:00 pm	4:30 pm	**Symposium: Child & Adolescent Mood Disorders** Cheryl King, PhD - University of Michigan Manpreet Singh, MD, MS - Stanford University
4:30 pm	4:45 pm	*Break*
4:45 pm	5:45 pm	**Keynote Lecture** Myrna Weissman, PhD - Columbia University
5:45 pm	6:30 pm	*Networking Happy Hour*
6:30 pm	8:00 pm	*Dinner* *Best Poster Award presentation*

WEDNESDAY, SEPTEMBER 25, 2019

Start	End	Session
8:00 am	8:45 am	**Breakfast**
8:45 am	9:00 am	**Opening Remarks**
9:00 am	10:00 am	**Symposium: Mobile Health Monitoring** Srijan Sen, MD, PhD - University of Michigan Dawn Sugarman, PhD - McLean Hospital
10:00 am	11:00 am	**Symposium: Computational Psychiatry** David Katzelnick, MD - Mayo Clinic Peter Zandi, PhD - Johns Hopkins University Paresh Patel, MD, PhD - University of Michigan
11:00 am	11:15 am	*Break*
11:15 am	12:15 pm	**Symposium: Funding Research Studies** Mi Hillefors, MD, PhD - National Institute of Mental Health Rob Vallentine - Dow Foundation
12:15 pm	12:30 pm	**Closing Remarks** *Boxed lunches provided*

Education Statement

SATISFACTORY COMPLETION

Learners must complete an evaluation form to receive a certificate of completion. You must attend the entire webinar as partial credit is not available. If you are seeking continuing education credit for a specialty not listed below, it is your responsibility to contact your licensing/certification board to determine course eligibility for your licensing/certification requirement.

PHYSICIANS

In support of improving patient care, this activity has been planned and implemented by Amedco LLC and National Network of Depression Centers. Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

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Credit Designation Statement – Amedco LLC designates this live activity for a maximum of 12.75 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

PSYCHOLOGISTS

This course is co-sponsored by Amedco and National Network of Depression Centers. Amedco is approved by the American Psychological Association to sponsor continuing education for psychologists. Amedco maintains responsibility for this program and its content. 12.75 hours.

The following state boards accept courses from APA providers for Counselors: AK, AL, AR, AZ, CA, CO, CT, DC, DE, FL, GA, HI, IA, ID, IL, IN, KS, MD, ME, MO, NC, ND, NH, NE, NJ, NM, NV, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, WI, WY
MI: No CE requirements
The following state boards accept courses from APA providers for MFTs: AK, AR, AZ, CA, CO, CT, DE, FL, GA, IA, ID, IN, KS, MD, ME, MO, NE, NC, NH, NJ, NM, NV, OK, OR, PA, RI, SC, SD, TN, TX, UT, VA, WA, WI, WY
The following state boards accept courses from APA providers for Addictions Professionals: AK, AR, CO, CT, DC, DE, GA, IA, IN, KS, LA, MD, MO, MT, NC, ND, NE, NJ, NM, NY (outstate held), OK, OR, SC, UT, WA, WI, WY
MA / MFTs: Participants can self-submit courses not approved by the MAMFT board for review.
The following state boards accept courses from APA providers for Social Workers: AK, AR, AZ, CA, CO, DE, FL, GA, ID, IN, KY, ME, MN, MO, NE, NH, NM, OR, PA, VT, WI, WY

SOCIAL WORKERS

As a Jointly Accredited Organization, Amedco is approved to offer social work continuing education by the Association of Social Work Boards (ASWB) Approved Continuing Education (ACE) program. Organizations, not individual courses, are approved under this program. State and provincial regulatory boards have the final authority to determine whether an individual course may be accepted for continuing education credit. Amedco maintains responsibility for this course. Social workers completing this course receive 12.75 clinical continuing education credits.

ASWB ACE approved continuing education

The following state boards accept courses from ASWB providers for Social Workers: AK, AL, AR, AZ, CA, CO, CT, DC, DE, FL, GA, ID, IL, IN, IA, KS, KY, LA, ME, MD, MA, MI, MN, MS, MO, NC, ND, NE, NH, NM, NV, OH, OK, OR, PA, RI, SC, SD, TN, TX, UT, VT, VA, WA, WI, WV, WY
The following state boards accept courses from ASWB providers for Counselors: AK, AR, AZ, CA, CO, CT, DC, FL, GA, IA, ID, IL, IN, KS, MA, MD, ME, MO, ND, NE, NM, NH, NV, OK, PA, TN, TX, UT, VA, WI, WY
AL / Counselors: Activities not providing NBCC approval may be approved by the Board for individual licensees upon receipt of acceptable documentation prior to the activity. Please send course details to your licensing board for approval BEFORE the event. No approvals afterward by the board.
The following state boards accept courses from ASWB providers for MFTs: AK, AR, AZ, CA, CO, FL, IA, ID, IN, KS, MD, ME, MO, NC, NE, NH, NM, NV, OK, PA, RI, TN, TX, UT, VA, WI, WY
MA / MFTs: Participants can self-submit courses not approved by the MAMFT board for review.
The following state boards accept courses from ASWB providers for Addictions Professionals: AK, CA, CO, CT, GA, IA, IN, KS, LA, MO, MT, ND, NM, NV, OK, OR, SC, WA, WI, WV, WY

TO CLAIM YOUR CREDITS

1. Go to http://nndc.cmecertificateonline.com
2. Click on the “National Network of Depression Centers Annual Meeting 2019”
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TUESDAY, SEPTEMBER 24, 2019

8:45a Advances in Neuromodulation

PROBING AND RESCUING DYSFUNCTIONAL BRAIN CIRCUITS IN DEPRESSION

PRESENTED BY

CONOR LISTON, MD, PHD

Associate Professor of Neuroscience and Psychiatry
Weill Cornell Medicine

LEARNING OBJECTIVES

1. To understand how neuroimaging (fMRI brain scans) can be used to understand diagnostic heterogeneity in depression and diagnose depression subtypes
2. To understand how neuroimaging (fMRI brain scans) can be used to predict antidepressant treatment response

ADVANCES IN THE USE OF TRANSCRANIAL MAGNETIC STIMULATION

PRESENTED BY

SHIRLENE SAMPSON, MD

Associate Professor
Mayo Clinic

LEARNING OBJECTIVES

1. Participants will be able to discuss the use of theta burst TMS in treating depression
2. Participants will be able to discuss new treatment protocols for providing TMS to treat depression

THE GEN-ECT PROJECT AND UPDATES FROM THE NNDC ECT TASK GROUP

PRESENTED BY

DANIEL MAIXNER, MD, MS

Associate Professor
ECT Program Director
University of Michigan

LEARNING OBJECTIVES

1. Learn of the background in ECT and genetics project
2. Understand the role of NNDC ECT Task Group's research efforts in the Gen-ECT project

11:00a David Mrazek Memorial Lecture

BEYOND ARTISANAL PRESCRIBING: CAN MACHINE LEARNING SAVE US FROM OURSELVES?

PRESENTED BY

ROY PERLIS, MD, MSC

Professor of Psychiatry
Director, Pharmacogenomics Research
Department of Psychiatry and Center for Human Genetic Research
Medical Director, Bipolar Clinic and Research Program
Massachusetts General Hospital

LEARNING OBJECTIVES

1. To examine the challenges in developing machine learning models to guide depression treatment
2. To summarize recent progress in developing decision support tools for depression treatment
3. To explore emerging directions for guiding next-generation treatment selection in depression

2:00p Disparities in Mental Health Care

PATHS TO MENTAL HEALTH EQUITY

PRESENTED BY

GEORGE RUST, MD, MPH, FAAFP, FACPM

Professor of Behavioral Sciences & Social Medicine
Director, Center for Medicine and Public Health
Florida State University College of Medicine

LEARNING OBJECTIVES

1. To review mental health disparities, including risk factors & determinants
2. To shift perspective to building assets and resiliency and equity
3. To identify practical steps for achieving collective impact on progress toward mental health equity, one community at a time.

PROGRAM NOTE

This presentation will be followed by an interactive audience conversation with Dr. Rust, facilitated by NNDC Medical Director and Conference Chair Dr. Sagar Parikh, on equity initiatives at academic medical centers. We invite all conference attendees to think about initiatives that are in place or being developed at your institutions to foster diversity, equity, and inclusion in the recruitment and training of researchers and clinicians. This is a unique opportunity to gain an understanding of these issues and initiatives across the Network, and will spark conversations that continue to highlight the successes and opportunities for growth at our Member Centers.

3:00p Child & Adolescent Mood Disorders

THE COMPUTERIZED ADAPTIVE SCREEN FOR SUICIDAL YOUTH (CASSY)

PRESENTED BY

CHERYL KING, PHD, ABPP

Professor
Director, Youth and Young Adult Depression and Suicide Prevention Research Program
University of Michigan

LEARNING OBJECTIVES

1. Attendees will be able to name three differences between classical and computerized adaptive screening tools for depression and suicide risk
2. Attendees will be able to describe three challenges inherent in screening youth for suicide risk
3. Attendees will be able to describe how the CASSY performs in predicting youth suicide attempts.

USING NEUROSCIENCE TO EVALUATE AND GUIDE TREATMENT FOR PEDIATRIC ONSET MOOD DISORDERS

PRESENTED BY

MANPREET K SINGH, MD, MS

Associate Professor
Director, Pediatric Mood Disorders Program
Stanford University

LEARNING OBJECTIVES

1. Recognize that youth with or at risk for mood disorders may show early signs of neurobiological dysfunction
2. Describe distinct neural trait and state markers of mood disorders
3. Consider candidate neurobiological targets for intervention.
4. Demonstrate brain indicators of treatment response in youth with and at risk for mood disorders.

4:45p Keynote Lecture

30 YEARS OF STUDYING FAMILIES AT RISK FOR DEPRESSION: WHAT'S BEEN LEARNED ALONG THE WAY

PRESENTED BY

MYRNA WEISSMAN, PHD

Diane Goldman Kemper Family Professor of Epidemiology and Psychiatry
Columbia University Vagelos College of Physicians and Surgeons
Chief, Division of Translational Epidemiology
New York State Psychiatric Institute

LEARNING OBJECTIVES

1. To understand the familial transmission of depression across generations
2. Be able to discuss opportunities for preventive interventions
3. To understand treatment of depression during pregnancy

WEDNESDAY, SEPTEMBER 25, 2019

9:00a Mobile Health Monitoring

PHYSICIAN TRAINING AS A MODEL TO IDENTIFY MOBILE TECHNOLOGY PREDICTORS AND PREVENTATIVE INTERVENTIONS FOR DEPRESSION UNDER STRESS

PRESENTED BY

SRIJAN SEN, MD, PHD

Frances and Kenneth Eisenberg Professor of Depression and Neuroscience
University of Michigan

LEARNING OBJECTIVES

1. To understand the promise of mobile technology in predicting depression

DEVELOPING A MOBILE APP FOR INDIVIDUALS WITH CO-OCCURRING SUBSTANCE USE AND MOOD DISORDERS

PRESENTED BY

SHIRLENE SAMPSON, MD

Assistant Professor
Harvard Medical School
Assistant Psychologist
McLean Hospital

LEARNING OBJECTIVES

1. Describe Integrated Group Therapy (IGT) for individuals with substance use and mood disorders
2. Identify ways that technology can enhance treatment for individuals with co-occurring disorders

10:00a Computational Psychiatry

THE NNDC MOOD OUTCOMES PROGRAM: UPDATE AND FUTURE DIRECTION

PRESENTED BY

DAVID KATZELNICK, MD
Former Professor of Psychiatry
Mayo Clinic
Mood Outcomes Program Clinical Champion
National Network of Depression Centers

PETER ZANDI, PHD
Professor
Johns Hopkins University
Mood Outcomes Program Research Champion
National Network of Depression Centers

LEARNING OBJECTIVES

1. To provide a status update on the goals of the Mood Outcomes Program
2. To present descriptive analyses of data from the Mood Outcomes Program
3. To discuss future directions of the Mood Outcomes Program

LEVERAGING THE ELECTRONIC HEALTH RECORD FOR COMPUTATIONAL MEDICINE: MOOD OUTCOMES PROGRAM AND BEYOND

PRESENTED BY

PARESH D PATEL, MD, PHD
Clinical Associate Professor
University of Michigan

LEARNING OBJECTIVES

1. Understand the strengths and pitfalls of implementation of the NNDC Mood Outcomes Program (MOP) within the clinical EHR workflow
2. Understand how big datasets leveraging the EHR, similar to that proposed for the NNDC MOP, have helped address challenging problems in medicine

11:15a Funding Research Studies

TIPS FOR PREPARING A SUCCESSFUL GRANT APPLICATION

PRESENTED BY

MI HILLEFORS, MD, PHD
Program Chief
National Institute of Mental Health

LEARNING OBJECTIVES

1. To undesrstand NIMH funding mechanisms
2. To understand the grants application process

A FUNDER'S TOP TEN LIST ON HOW TO SUCCESSFULLY SECURE PROGRAM SUPPORT

PRESENTED BY

ROBERT M VALLENTINE
President
The Dow Chemical Company Foundation

LEARNING OBJECTIVES

1. Participants will learn insight on how to obtain external funding, either research or program. Special focus on the junior faculty among the audience - regarding priorities and evaluation strategies used by both the Dow Foundation and other major US foundations in reviewing requests for funding.
2. Explain how Foundations evaluate proposals, and any insights into how this might differ from the way academics write grant applications to traditional funding agencies.
3. To make the audience feel more comfortable in approaching local foundations for program support.

Travel Award Recipients

Congratulations to the 2019 Emerging Scholar Travel Award Recipients! Check out their posters during the Annual Conference Poster Session at 1:00 pm on Tuesday, September 24.

ZIAD ALI, MD
University of Louisville
Poster # Abstract on p.#
DOPAMINE RECEPTOR SUPERSENSITIVITY OF TARDIVE DYSKINESIA MAY BE A PRESYNAPTIC MECHANISM

KATIE BESSETTE, MA
University of Illinois at Chicago
Poster # Abstract on p.#
NEUROTICISM AND RUMINATION ARE OVERLAPPING CONSTRUCTS, YET SHOW UNIQUE RELATIONSHIPS WITH RESTING STATE NETWORKS

COURTNEY FORBES
University of Toledo
Poster # Abstract on p.#
EMOTIONAL AVOIDANCE AND SOCIAL SUPPORT INTERACT TO PREDICT DEPRESSION SYMPTOM SEVERITY ONE YEAR AFTER TRAUMATIC EXPOSURE

JESSICA HARDER, MD
Brigham & Women's Hospital
Poster # Abstract on p.#
RILUZOLE AUGMENTATION PILOT IN DEPRESSION (RAPID) TRIAL

NADAV KLEIN, MD
The Ohio State University
Poster # Abstract on p.#
DOES AGE MODULATE RESPONSE TO KETAMINE INFUSION FOR TREATMENT-RESISTANT-DEPRESSION?

JIA-IN LEE, MD
Brigham & Women's Hospital
Poster # Abstract on p.#
ASSOCIATION BETWEEN OBESITY AND MAJOR DEPRESSIVE DISORDER ACROSS THE LIFESPAN: A REVIEW THROUGH A BIOPSYCHOSOCIAL LENS

CAITLIN MILLETT, PHD
Brigham & Women's Hospital
Poster # Abstract on p.#
TNF-α AND ITS RECEPTORS MEDIATE THE RELATIONSHIP BETWEEN PRIOR SEVERE MOOD EPISODES AND COGNITIVE DYSFUNCTION IN EUTHYMIC BIPOLAR DISORDER

JAMES MOLEY
The Ohio State University
Poster # Abstract on p.#
THE BEHAVIOR FORECAST: OPTIMIZING SITTER USAGE IN THE HOSPITALIZED PATIENT THROUGH IMPROVED COMMUNICATION

MICHAEL MORREALE, MPH
Johns Hopkins University
Poster # Abstract on p.#
THE GENETICS OF DEPRESSION TREATED BY ELECTROCONVULSIVE THERAPY (ECT): A PILOT STUDY AT JOHNS HOPKINS UNIVERSITY

KIMBERLY OROZCO
University of Illinois at Chicago
Poster # Abstract on p.#
UNDERSTANDING THE HISPANIC HEALTH PARADOX: PARENTAL DEPRESSION AS A MEDIATOR OF THE RELATIONSHIP BETWEEN CAREGIVER PLACE OF BIRTH AND CHILD ASTHMA CONTROL IN MEXICAN AMERICANS

HAITHAM SALEM, MD, PHD
University of Texas - Houston
Poster # Abstract on p.#
BORDERLINE PERSONALITY FEATURES IN BIPOLAR INPATIENTS: IMPACT ON COURSE AND MACHINE LEARNING MODEL USE TO PREDICT RAPID RE-ADMISSION

SARAH ROSE SLATE
Brigham & Women's Hospital
Poster # Abstract on p.#
AGE MODERATES THE RELATIONSHIP BETWEEN AFFECTIVE RESPONSE CONTROL AND BIPOLAR DISORDER IN ADULTS

CLAUDIA VESEL
University of Illinois at Chicago
Poster # Abstract on p.#
DIURNAL PATTERNS AS EVIDENCED BY OVER ELEVEN MILLION SMARTPHONE KEYSTROKES DURING DAILY USAGE: AN IOS BIAFFECT STUDY

Poster Abstracts

1. The correlation between inflammatory biomarkers and mood symptoms among patients with bipolar disorder

Ahmad Subhi Abu-Mohammad MD, Anastasia Yocum PhD, Steven Anderau BS, Melvin McInnis MD

Background: Bipolar Disorder is associated with an underlying inflammatory response during a mood state[1]. Peripheral inflammatory biomarkers such as Interleukins (ILs) 1,6, 10 and CRP have been associated with bipolar disorder[2].

Methods: We investigated the association of five inflammatory biomarkers, CRP, IL-1β, IL-6, IL-8, IL-10 with mood symptoms in 531 individuals. 364 have a current diagnosis of bipolar disorder (BP1, BP2, and BP NOS). 42 additional individuals have other psychiatric diagnoses included in the disease cohort. 125 are healthy controls for comparison. The biomarkers were analyzed using multiplex ELISA assays (V-PLEX.) On the same day of blood collection for ELISA, a 17 item Hamilton Rating Scale for Depression (HAM-D) and Young Mania Rating Scale (YMRS) were administered by trained clinicians to assess symptom severity for depression and mania, respectively. Data was analyzed using standard statistical methodologies.

Preliminary Results: All five biomarkers were measured successfully in all participants. Current evidence suggests that there may be an association, albeit non-statistically significant, between these inflammatory markers and bipolar disease. These results could possibly stratify different bipolar diagnosis.

Conclusions: Bipolar disorder may be associated with an underlying inflammatory state.

Limitations: Due to the cross sectional nature of the data, we may only infer that the differences in inflammatory biomarkers are due to psychiatric diagnosis.

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2. Dopamine Receptor Supersensitivity of Tardive Dyskinesia may be a Presynaptic Mechanism

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Introduction: Chronic treatment with dopamine D2 receptor antagonists for diseases such as schizophrenia has been proposed to lead to dopamine receptor supersensitivity. Frequently, this is conceptualized as upregulation or changes in the structure or function of the post-synaptic D2 receptor. However, the measured 1.4 fold increase in D2 receptor density is probably inadequate to explain outcomes such as tardive dyskinesia and dopamine supersensitivity psychosis.

Hypothesis: Recent data now suggest that what appears to be dopamine receptor supersensitivity may actually be related to presynaptic changes.

Discussion: It should be noted that there are many presynaptic changes that occur with chronic postsynaptic dopamine blockade. In this poster we argue that super-therapeutic blockade of postsynaptic D2 receptors results in excess synaptic dopamine which ultimately ends up being reuptaken by the presynaptic neuron through the dopamine transporter. The increased availability of recycled dopamine results in higher vesicular dopamine concentrations. Since the quantity of neurotransmitter release is determined by the number of presynaptic neurotransmitter vesicles, the increase in the number of dopamine molecules in the vesicles results in a higher concentration of synaptic dopamine with successive depolarization events. Supporting data for this hypothesis can be found in the observation that increased plasma phenylalanine concentrations can worsen pre-existing tardive dyskinesia. Additionally, medications that specifically reduce the concentration of intravesicular dopamine (vesicular monoamine 2 inhibitors) reduce symptoms of tardive dyskinesia. It is proposed that the combination of post-synaptic receptor upregulation, synaptic splitting, and elevated presynaptic vesicular dopamine levels conspire to produce the observed undesired consequences of chronic treatment with dopamine antagonists such as tardive dyskinesia and dopamine supersensitivity psychosis.

3. Neuroticism and Rumination are Overlapping Constructs, Yet Show Unique Relationships with Resting State Networks

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Background: Neuroticism (Neur) and rumination (Rum) are well-known traits that increase risk and recurrence for internalizing psychopathology (e.g., depression, anxiety), predict response to pharmacological and psychotherapeutic treatments, and are highly associated with increased self-referential and negative emotional processing. Yet, Neur is thought to be a stable, trait personality based upon temperament whereas Rum is conceptualized as a malleable habit. One way to parse the seeming contrast between these two constructs, which are highly correlated, is the use of functional connectivity (FC) associated with default mode network (DMN), salience-emotion network (SEN), and cognitive control network (CCN). Thus, this study examined the unique and overlapping FC relationships of Neur and Rum within and across these resting state networks. This was conducted in individuals who have or have never had a history of depressive episodes.

Methods: Adults (n=216) completed diagnostic interviews and self-reports on rumination (Rumination Response Scale) and neuroticism (NEO-PI). Of these, 117 were remitted from major depression (rMDD), 25 euthymic from bipolar disorder (eBD) and 74 were healthy controls (HC). Clinicians also completed depression and anxiety measures for each (Hamilton Depression and Anxiety Rating Scales). Linear regressions normed neuroticism and rumination, separately, by age and gender. Then a second set of linear regressions were conducted to obtained shared and residuals regressors, first of were conducted of Neur predicting Rum (leaving shared Neur / Rum and residual Rum regressors). For completeness, the opposite regression was also completed, resulting in shared Rum/Neur and residual Neur). One hundred forty-three individuals (rMDD=77, eBD=11, HC=55) had high quality 8 minute resting-state scans (n=10 removed for excessive movement), and were included in regressions of CCN, DMN and SEN seed-based FC conducted in SPM8, covarying for motion translations. CCN was probed using bilateral dorsolateral prefrontal cortex, inferior parietal lobule, and dorsomedial thalamus; DMN used bilateral posterior cingulate cortex, anterior hippocampal formation, and dorsomedial prefrontal cortex; SEN used bilateral amygdala, anterior insula, and subgenual anterior cingulate. Significant clusters (Alpha Sim corr p<.001, k>75) were identified.
Results: Rum and Neur were highly correlated after normalization across diagnoses (r=.72, p<.001). Residual Rum was negatively associated with FC from CCN seeds with: bilateral parahippocampal gyri, left inferior frontal gyrus; DMN seeds: bilateral middle frontal gyrus, left inferior parietal lobule; and SEN seeds: left postcentral and inferior parietal lobule. FC regressions found positive associations between residual Neur from CCN seeds with: right superior temporal gyrus, left inferior frontal gyrus, right precentral and bilateral postcentral gyri; DMN seeds: right putamen; and SEN seeds: left postcentral and inferior parietal lobule.
Conclusions: The current results confirm previous findings that trait Neur and Rum are highly correlated constructs, even across diagnostic categories. Additionally, important aspects of FC frequently associated with mood disorder diagnoses are associated positively with Neur and negatively with Rum. Specifically, higher residual Neur was associated with increased connectivity between traditional CCN and SEN networks, whereas higher residual Rum was more associated with decreased connectivity between traditional CCN and DMN regions. These findings suggest that personality variables can be correlated with habit tendencies yet still demonstrate unique aspects of functioning at the level of brain networks. There are implications for how and what we treat with technologies like transcranial magnetic stimulation.

4. Severe depression and suicidality in the post-partum is associated with inflammation, altered kynurenine pathway activity, and low serotonin

Amanda R Burmeister, Eric Achtyes, Sarah Keaton, LeAnn Smart, Patrick L Heilman, Stanislav Krzyzanowski, Gilles J Guillemin, Martha L Escobar Galvis, Chai K Lim, Maria Muzik, Teodor Postolache, Richard Leach, Lena Brundin

Background: Up to 20% of pregnant women suffer from depression, including some with suicidal ideation and behavior. There is an immediate need to identify the biological underpinnings of peri-partum depression (PPD) in order to develop novel therapies and biomarkers indicating risk for the disease. It has been suggested that PPD is triggered by the dynamic fluctuations of the inflammatory response during pregnancy and at delivery. Therefore, in this study, we targeted this understudied population to identify whether the pro-inflammatory profile in plasma, together with kynurenine pathway activity fluctuations, are associated with severe depression and suicidal behavior.
Methods: 165 women were enrolled post-partum and interviewed by DSM-IV SCID to diagnose PPD. Depression severity and suicidality were assessed using the Edinburgh Perinatal Depression Rating Scale and the Columbia Suicide Severity Rating Scale. Plasma was analyzed for interleukin (IL)-1β, IL-2, IL-6, IL-8, TNF-α, tryptophan, serotonin, kynurenine, nicotinamide, quinolinic- and kynurenic acids.
Results: Increased plasma levels of IL-6 and IL-8 and reductions of serotonin, IL-2 and quinolinic acid significantly predicted a diagnosis of PPD. Low serotonin specifically predicted suicidal behavior also when adjusting for depression depth. Our results remained after controlling for medication, psychosocial factors, age and body mass index.
Conclusion: We found that low serotonin, inflammation and altered kynurenine pathway activity predicted severe PPD. Suicidal behavior was specifically linked to low levels of serotonin. Inflammation and the kynurenine pathway may constitute treatment targets in PPD, which is important considering the limited number of tolerable treatments available during pregnancy and the post-partum.

5. Comparison of perceived barriers regarding psychiatric electroceutical interventions as treatment for clinical depression

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Background: Psychiatric electroceutical interventions (PEIs) are therapies that use electrical or magnetic stimulation to alter brain circuitry and function with the goal of treating neuropsychiatric conditions. A number of PEIs are currently used for treatment-resistant depression (TRD), while others are still undergoing clinical trials. Three such PEIs are electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS) and deep brain stimulation (DBS). Understanding barriers to treatment is important for planning mental health services, setting priorities in allocation of resources, and helping reduce the burden of TRD. However, little research has compared different stakeholders' perceived barriers to implementing these particular interventions.

Methods: As part of a larger project to assess different stakeholder views and attitudes towards PEIs, we conducted semi-structured interviews with 16 Michigan-based psychiatrists and 16 patients asking them about one or two of the PEIs mentioned above. We recruited psychiatrists directly via recommendation by a team member, and we recruited patients via flyers posted in various depression clinics. We performed content analysis on the 32 interview transcripts to examine patterns in major neuroethical considerations across the two stakeholder groups.
Results: Here we present results about barriers to the use of these therapies. In both groups, many of the barriers mentioned were related to TMS and ECT, which are both currently in clinical use. Availability of treatment was the most frequently mentioned barrier overall, with 12/16 psychiatrists and 13/16 patients describing this problem. In particular, participants noted that therapy, especially TMS, was not widely available. Another important theme was related to payment for the therapies. Psychiatrists mentioned insurance coverage (12/16), while patients talked more broadly about cost (13/16). Several participants in both groups mentioned insurance when referring to TMS. Stigma, particularly in relation to ECT, was viewed as a barrier for almost two thirds of participants in either group. The other barrier mentioned by at least half of participants was the time demands of these treatments (psychiatrists 11/16; patients 8/16). While only a few psychiatrists and patients were asked about DBS barriers in particular, they agreed that the cost and availability of treatment facilities were limiting.
Conclusion: Overall, our results suggest that psychiatrists and patients perceive similar barriers to implementation of PEI treatments. Structural barriers cut across all PEIs—including those that are still experimental—such as cost and availability of the treatments. Insurance coverage seems to be a barrier affecting TMS more than ECT. Both groups also acknowledged attitudinal barriers to ECT, such as stigma and lack of understanding. More research with a larger sample will help us better understand how to address these barriers to treatment for individuals with TRD.

6. Deep Brain Stimulation (DBS) for management of Parkinson's disease with Comorbid Major Depressive Disorder: Utilization and Impact on Inpatient Outcomes in United States

Amit Chopra MD FAPA

Aims and Hypothesis: To evaluate the utilization of deep brain stimulation (DBS) for the treatment of Parkinson's disease (PD) with comorbid Major Depressive Disorder (MDD), and to measure the impact of DBS on hospital outcomes in this population.
Background: DBS is an FDA approved treatment for management of medication-refractory PD. MDD is a common comorbidity in patients with PD and it adversely affects symptom burden with poor hospital outcomes. To our knowledge, there is no study that examines the rates of DBS utilization and its impact on hospital outcomes in PD+MDD patients.
Methods: A retrospective analysis was performed using the Nationwide Inpatient Sample (NIS) data (2012-2014). We identified 6840 PD+MDD inpatients (≥ 18 years) and sub-divided them in to DBS and non-DBS group, based on DBS procedure. Linear and logistic regression was used to evaluate the change in length of stay (LOS) and discharge, respectively with a P value < 0.05.
Results: Overall DBS utilization rate in PD+MDD patients was noted to be 25.3%. Higher rates of DBS utilization were evident for PD+MDD patients aged 36–50 years (56.1%), who were more likely to be Caucasian males, with private insurance (43.9%). DBS utilization was higher in large (31.8%), urban (26.6%) and teaching (33.8%) hospitals and in the Western US (37.2%). DBS was used mainly in PD+MDD patients with minor loss of body function (73.1%). After adjusting for demographic and hospital variables, length of stay (LOS) decreased by 3.5 days (95%CI -4.411 to -2.553, P<0.001) in the DBS group, as compared to the non-DBS group; however, the mean total charge ($85,435 vs $29,660) was higher in DBS group. As compared to non-DBS group, PD+MDD patients in the DBS group had a significantly higher likelihood of routine discharge (84.7% vs. 20.3%), and 2.4-fold less likelihood of transfer to skilled nursing facility (95% 0.075 to 0.118, P<0.001).
Methods: Higher rates of utilization of DBS in PD+MDD patients correlate with large academic centers in urban areas and also are influenced by geographic, demographic and insurance factors. DBS is associated with decreased LOS and significantly lower likelihood of transfer to skilled nursing facility in PD+MDD patients.

7. Impact of Transcranial Magnetic Stimulation (TMS) on Sleep and Mood Outcomes in Patients with Treatment-Refractory Major Depressive Disorder (MDD): A Retrospective Study

Amit Chopra MD FAPA

Objectives: To assess the impact of transcranial magnetic stimulation (TMS) on sleep and mood outcomes in patients with treatment-refractory MDD.
Methods: We analyzed the sleep outcomes in patients with treatment-refractory MDD with > 3 failed antidepressant trials, who underwent TMS at our center. We utilized PHQ-9 scale, GAD-7 scale, Insomnia Severity Index (ISI) and Epworth Sleepiness Score (ESS) to assess the severity of depression, anxiety, insomnia and hypersomnia symptoms at baseline and after TMS.
Results: We present preliminary results of five patients with treatment-refractory MDD (2 males, 3 females) with a mean age of 49.4(range=23-69) and were given an average of 33.8 treatments. No medication changes were made to address sleep or mood issues during the TMS treatment period. TMS treatments was tolerated overall well without any significant adverse effects. Although reductions in anxiety symptoms and sleep difficulties were reported (see Table 1), a significant difference in mood was found when pre to post-TMS PHQ-9 scores were compared; t (4) =10.262, p < 0.001. These results suggest that TMS contributed to significant improvement in depressive symptoms.

Table 1: Descriptive Statistics (N=5)

	PHQ-9 Mean (SD)	ISI Mean (SD)	ESS Mean (SD)	GAD-7 Mean (SD)
BASELINE	19.40 (4.6)	10.60 (8.7)	6.20 (3.9)	13.60 (7.2)
ENDPOINT	7.00 (5.0)	7.60 (5.6)	4.20 (2.6)	7.40 (6.1)

Discussion: The impact of TMS on sleep outcomes in patients with treatment-refractory MDD is a topic of great interest due to two main clinical reasons. Firstly, if sleep disturbances, including insomnia and hypersomnia, predict the clinical outcomes in MDD patients receiving TMS treatment. Secondly, it needs to be determined that TMS is an effective treatment for comorbid sleep disturbance in patients with MDD. The data presented in our study is very preliminary since it is derived from only five patients who have completed TMS. Therefore, with a larger sample size, we anticipate more robust findings and that the improvements in sleep measures, that currently appear as trends, would develop into significant changes.
Results: TMS can be an effective treatment modality for management of comorbid sleep disturbances in patients with treatment refractory MDD. Objective tools such as actigraphy and EEG based sleep measures can be utilized to substantiate the subjective findings.

8. The effect of gender on facial emotion perception in major depressive disorder

Rebecca E Easter MA, Alexander P Demos PhD, Scott A Langenecker PhD

Background: Prior research has found consistent effects of gender on emotion perception, such that women are more accurate at identifying others' emotions than men. In addition, previous studies have found an effect of facial gender on emotion perception, generally finding gender stereotype-congruent effects, with better identification of sadness on female faces and anger on male faces. The current study aims to examine emotion perception in rMDD compared to HC and to investigate the effect of participant gender and facial gender on emotion perception in the diagnostic samples to examine whether the effects of gender persist in individuals with remitted depression.
Methods: 110 individuals diagnosed with rMDD and 73 HC completed the Facial Emotion Perception Test - a computerized test of facial perception of happiness, sadness, anger, and fear. Generalized linear mixed effects models were conducted, with diagnosis, participant gender, facial stimuli gender, and facial emotional valence included as predictors.
Results: Emotional valence was found to significantly predict accuracy, with individuals more accurately identifying happy faces than anger and fear faces. Additionally, the HC and rMDD samples exhibited different accuracy for female faces, such that individuals with rMDD demonstrated higher accuracy of emotions on female faces than HC. However, HC and rMDD individuals did not differ for male faces. Participant gender and diagnosis were significantly related, with HC men performing less accurately than rMDD men, HC men, and HC women. Finally, the relationship between participant gender and diagnosis was found to be emotion-specific. For happy faces, HC men performed worse than the other three gender-diagnosis subsamples. For negative faces, women with rMDD identified angry and fear more accurately than the other subsamples.
Conclusion: Emotion perception seems to be heightened in remitted depression compared to healthy controls. In addition, these findings suggest that major depression has an effect on emotion perception in both men and women. These findings have implications for future research on emotion perception across the course of depression and the examination of the effect of gender within this domain

9. Genomic prediction of objective sleep behavior in sleep-deprived and shift-work population

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Background: Medical internship is characterized of sleep deprivation and shift work. Our previous study (Kalmbach et al., 2018) discovered that longer sleep and less deviation from baseline sleep routine were associated with better mood of medical interns during internship year. Therefore, maintaining enough sleep and stable sleep pattern is crucial to medical interns' mental wellness and performance. Recent GWAS of morningness and sleep duration and derived polygenic score have elevated the perspective to study the biological basis of sleep behavior. Meanwhile, the emerging of wearable devices have provided inexpensive tools to objectively measure sleep in a more precise and convenient way than self-report. These progress have made it possible to conduct large-scale study on the relationship of biological basis and sleep behavior in sleep-deprived and shift-work populations like medical interns.
Methods: Intern Health Study is a longitudinal cohort study that assesses multiple aspects of medical interns around US. For 2017 cohort, whose medical internship lasted from July 2017 to June 2018, we followed 316 medical interns since baseline (one to two months prior to internship) until the end of internship by: 1) collected DNA samples and generated individual polygenic scores of morningness and sleep duration based on a recent GWAS from UK Biobank (Jones et al., 2016); 2) distributed Fitbit and collected daily measures of sleep schedule and duration.

Results: With linear regressions adjusted by age, gender and top 10 genetic principal components, we found that higher morningness polygenic score predicted smaller deviations in internship sleep timing, especially wake time, from baseline routine. One SD higher in morningness polygenic score was related to 13 less minutes in the change (p=0.007). Also, higher sleep duration polygenic score predicted longer average daily sleep time both at baseline (β=7 mins, p=0.019) and during internship (β=14 mins, p=2.35x10-4), and the association during internship was marginally stronger (interaction β=6 mins, p=0.055).
Conclusions: Our results indicated that genomically predisposed morning people were more prone to maintain a similar sleep schedule to baseline during internship. In addition, people who were genomically predisposed to sleep longer managed to have longer sleep both at baseline and during internship, and the differences became even wider during internship. Since sleep and mood are closely related, a deeper understanding of biological basis of sleep behavior may have potential to guide personalized intervention in improving sleep and mental health within medical interns and other sleep-disturbed professionals.

10. Preliminary Results of a Multidisciplinary Approach to Treating Patients with Comorbid Sickle Cell Disease and Opioid Use Disorder

Michael Finneran MD, Kirk Carruthers MD, and Julie Niedermier MD

Background: With more than 2 million people carrying the HbS gene and approximately 100,000 with Sickle Cell Disease, it is the most common inherited blood disorder in the US and is associated with significant morbidity and mortality.[1] As a result of the disease process, acute pain episodes and chronic pain are both common complications of the disease.[2] One notable study, found that in a group of adults with SCD, 29% reported pain on more than half of the days during a 6 month period.[3] As a result, many patients with SCD are prescribed opioids chronically and sometimes at high doses.[2] While there is limited data on this population, it is estimated that the risk of opioid use disorder in patients with SCD is between 0-9%.[4] Substance-related comorbidity in patients with SCD has historically been very difficult to identify and treat. We identified various potential factors including barriers to care, physician and patient considerations, and aspects of the SCD disease process as contributing to the difficulty in developing care plans for patients with sickle cell disease, opioid use disorder, and acute pain episodes. In an effort to improve quality of care, specialists within the academic medical center's departments of hematology and psychiatry collaborated to develop a multidisciplinary clinic.
Methods: In 2015, a multidisciplinary team was created consisting of a physician from the Department of Hematology, and a psychiatrist and psychologist from the division of addiction medicine within the Department of Psychiatry. The team meets to see patients once per month and accepts consults in which there is a concern for opioid addiction or other complications related to the mental health of patients with SCD. All three members of the team may see a new patient on the day of the clinic housed within the hematology division, and optimal care, potentially including medication assisted treatment, is provided. Preliminary estimates show that the team sees between 5-8 patients per month, and on average, 3 of these (35-60%) are specifically due to concerns of opioid use disorder. Currently a total of 10 patients are being seen longitudinally by the clinic for opioid use disorder. Of these, 4 are being seen for MAT (40%) and all 10 patients for psychotherapy. As a means of measuring the impact of the clinic, we looked at a case study of a patient that has benefited. The outcomes measured in this patient include the change in number of hospital admissions, ED visits for pain episodes, and change in daily dose of opioids in morphine milligram equivalents.
Results: In the 2 year period preceding transfer to the sickle cell multidisciplinary clinic, a patient had a total of 58 ED visits (29/ year average) and 28 hospital admissions (14/ year average) for acute pain episodes. In the last 2 years since transfer to the clinic, the patient has had a total of 3 ED visits and 1 hospital admission, amounting to a 94.8% reduction in ED visits and 96.4% reduction in hospital admissions. The patient had a progressive increase in dosage of their daily opioid regimen with a maximum dose of 1016 oral morphine milligram equivalents (MME) / day in the 6 months prior to transfer into the clinic. In the 6 months following transfer, the patient had a dose reduction to 721 MME /day, amounting to a 29.13% reduction. Some patients demonstrated less robust improvements, and limitations with the multidisciplinary approach include a relatively high dropout rate and frequent no-shows for visits.
Conclusions: The sickle cell multidisciplinary clinic constitutes a joint effort by addiction medicine and hematology professionals to address patients with comorbid opioid use disorder. The preliminary results of an index case are encouraging and suggest that this multidisciplinary approach can result in fewer hospitalizations and emergency visits, as well as lower overall daily opioid dosing for a patient with SCD. Potential areas for future improvement include methods to improve patient retention, increase access, reduce stigma, and to improve programming and dual diagnosis education for this population.

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11. Attenuated Reward Responsiveness Accounts for the Relation Between Depression and Suicide Outcomes in a Community Sample

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Background: Major depressive disorder (MDD) is associated with heightened risk for suicidal ideation (SI) and behavior[1]. This relation may be accounted for by anhedonia, which is a central feature of MDD and demonstrates robust relations with SI[2] and suicide attempts[3]. Anhedonia is characterized by alterations in reward responsiveness (RR), or the ability to seek out and respond to rewarding stimuli[4]. This study tested the hypothesis that (low) RR, assessed as a multidimensional construct, would account for the relation between depression and suicide outcomes.

Methods: Community adults (N = 365; mean age = 38.79) completed the General and Anhedonic Depression subscales of the Mood and Anxiety Symptom Questionnaire, the latter which assesses overall attenuated RR (e.g., reduced positive emotions and pursuit of pleasurable activities); the Temporal Experience of Pleasure Scale, which assesses anticipatory and consummatory components of RR; the Measure of Episodic Planning of Suicide, which assesses past suicide attempts; and the Depression Severity Index-Suicidality Subscale, which assesses SI.

Results: Anticipatory (but not consummatory or overall) RR accounted for the relation between general depression and SI when all were entered into the hierarchical linear regression model, Sobel z = 2.15, p = .031. Overall (but not anticipatory or consummatory) RR accounted for the relation between general depression and past suicide attempts when all were entered into the regression model, Sobel z = 1.97, p = .049.

Conclusions: Results highlight the specific RR deficits associated with suicide attempts and ideation, as well as suggest that low RR accounts for the relation between general depression and suicide outcomes. Whereas low anticipatory RR may be particularly relevant to SI, overall RR may be particularly relevant to suicide attempts. Strategies focused on targeting RR directly by increasing engagement with rewarding stimuli (e.g., behavioral activation) may be efficacious as an addition to current treatments for MDD and suicide risk.

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12. Emotional Avoidance and Social Support Interact to Predict Depression Symptom Severity One Year After Traumatic Exposure

Courtney N Forbes, Matthew T Tull, Hong Xie, Nicole M Christ, Kristopher Brickman, Mike Mattin, Elizabeth Gibson, Corion Jones, Sai Bhargav Ganga Vuppala, Nadin Rawan Mohamed, & Xin Wang

Background: Individuals exposed to a traumatic event commonly develop symptoms of depression[1][2]. Both intrapersonal and interpersonal risk factors have been associated with heightened risk for depression following traumatic exposure[3][4]; however, less is known about how these risk factors may interact to predict risk for the development of depression over time. The goal of this study was to examine the interactive influence of peritraumatic emotional avoidance (an intrapersonal risk factor) and social support (an interpersonal risk factor) on the severity of depression symptoms 12-months after traumatic exposure.

Methods: N = 46 individuals recruited shortly after visiting one of two urban hospital emergency departments for treatment following a traumatic event completed the Emotional Avoidance Questionnaire, the Multidimensional Measure of Perceived Social Support, and the Quick Inventory of Depressive Symptomatology shortly after the index trauma. Participants completed the QIDS again approximately 12-months later.

Results: Results revealed a significant main effect of emotional avoidance on 12-month depression, $\beta = .54$, $t = -2.59$, $p = .014$, $|95\%\ CI| = .1182\text{-}.9619$. The main effect was qualified by an interaction of emotional avoidance and social support, $\beta = -.02$, $t = -2.13$, $p = .040$, $|95\%\ CI| = .10011\text{-}.0419$. Follow-up analyses indicated that the relation of emotional avoidance to 12-month depression was positive and significant only for individuals with low levels of social support.

Conclusions: Results highlight the need to consider both intrapersonal and interpersonal risk factors, as well as their interaction, when predicting which individuals may be most at risk to develop depression following traumatic exposure. Brief interventions focused on increasing acceptance of distressing trauma-related emotions and increasing access to quality social support in the aftermath of a traumatic event may be efficacious in preventing the development of depression and associated negative outcomes.

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13. Trumped down? A prospective cohort study of political events and the mental health of young physicians

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Background: Increasing attention has been paid to systematic factors (e.g. heavy workloads, medical errors) that may contribute to the high rates of depression experienced by training physicians, yet the impact of exogenous factors – including politics - has remained largely unexplored. We sought to understand the effect of political events on the mood and mental health of young physicians during the Trump era.

Methods: We utilized longitudinal mood data provided by 2345 medical interns as part of the Intern Health Study, a prospective cohort study assessing stress and depression during the first year of residency training. We queried Google Trends to determine the date of peak public interest (value of 100) for 17 influential political and non-political events that occurred between 2016 and 2018. Mean mood score during the week following each event was compared to mean mood during the prior four-week control period.

Results: With the start of internship duties in July, the mean decline in mood for interns was -0.30 (95% confidence interval -0.33 to -0.27, t=-17.45, P<0.0001). The change in mood was of similar magnitude following the 2016 presidential election (mean mood change -0.32, 95% confidence interval -0.45 to -0.19, t=-4.73, P<0.0001) and subsequent inauguration (mean mood change -0.25, 95% confidence interval -0.37 to -0.12, t=-3.93, P=0.0001). Further, compared to men, women reported greater mood changes after both the 2016 election (t=2.33, p=0.020) and the inauguration (t=2.05, p=0.042). Overall, there were significant changes in mood following 66.7% (6/9) of political events assessed. In contrast, none of the non-political events included in the analysis were significantly associated with a change in mood.

Conclusions: In the contemporary era, politics has a measurable and repeated effect on the mood of young doctors. This finding adds to the growing list of factors involved in the mental health of training physicians, and signals the need for further evaluation of the risks and benefits of increasing entanglement between politics and medicine moving forward.

14. Adolescent Mood Monitoring a la NDDC: Does It Work? Will It Work?

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Background: The Child/Adolescent Mood Disorders Interest Group (CAMDIG) was tasked with revitalizing its membership and considering use of the Mood Outcomes Program (MOP). We received a Momentum grant to accomplish four aims: 1) Summarize clinician evaluations of the NNDC battery in the one current clinic where the adult battery is currently being administered to adolescents; 2) Determine patient and clinician level of interest in using the NNDC battery in clinics where the adult battery is not currently being administered to adolescent patients (n=14); 3) Measure change in evaluation 3 months post-implementation for any sites that begin administering the NNDC battery to adolescents; and 4) Generate potential new Child and Adolescent Mood Disorders Task Group (CAMD-TG) research protocols for future consideration. This presentation reports on our findings.

Experienced Consumer Evaluation: Six clinicians and 23 adolescents completed surveys. On a 16-item, 1-6 scale (6=desirable, potential range 16-96), patients' total scores ranged from 34-90 (M=68.4; SD=14.8); individual items ranged from 2.9 to 5.2 (M=4.3). Clinicians were more positive. On their 23-item, 1-6 scale (6=desirable, potential range 23-138), clinicians' total scores ranged from 99-127 (M=115.3; SD=10.8); individual items ranged from 2.3-5.7 (M=5.0).

Potential Consumer Evaluation: We hoped for 11 sites to definitely participate and extended invitations to an additional 4 sites with no active child/adolescent liaison. We were successful in obtaining data from 7 sites (JHU, NCH, UC-Denver, Stanford, U of M, Mayo, and UIC). IRB snafus were a larger problem than would seem warranted.

Attitudinal Change with Experience: None of the clinics began using the MOP during the course of our study.

New Study Collaboration: This project had two primary goals—to determine if the MOP will be deployed by NNDC CAMDIG clinics, and to "exercise our muscles" as an NNDC collaborative research group. We generated interest in assessing the attitudes, beliefs, and behaviors of adolescents, emerging adults, parents, and practitioners, and clinical practice of practitioners re: marijuana. We have been awarded a Momentum application to pursue this.

15. The Genetics of Depression Treated by Electroconvulsive Therapy (ECT): A Pilot Study at Johns Hopkins University

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Background: ECT is an effective treatment for severe depression that is refractory to first line therapies. However, between one-third to one-half of patients fail to achieve remission after acute ECT, and there is evidence that genetic factors may contribute to the clinical response. The Genetics of ECT Consortium (GenECT, a Psychiatric Genomics Consortium depression subgroup) has brought together ECT centers globally, including those in the National Network of Depression Centers (NNDC) in the US, to conduct a genetic study with one of the largest available samples to identify genetic variation that a) is associated with severe depression and indicates which patients are candidates for ECT, and b) influences response to ECT and predicts which patients may benefit from treatment. We conducted a pilot study at Johns Hopkins University to demonstrate the feasibility of carrying out this large-scale effort.

Methods: Participants 18 years or older with a mood disorder were approached during a course of outpatient ECT in the Johns Hopkins Brain Stimulation Program. After obtaining consent, a blood draw for a DNA sample was taken during the placing of the intravenous line for an ECT treatment. All clinical information for completing the GenECT data collection instrument was extracted from EPIC, Johns Hopkins' electronic medical record, in order to leverage the clinical data collected as part of routine care and minimize the burden on patients and providers.

Results: Over one month, 28 consecutive patients were approached and 25 (89.2%) consented to participate and provided a blood sample. Participants ranged in age from 29-78 years old, with a mean age of 52.8. A majority of the participants were female (68%) and Caucasian (92%). Clinical and genetic data are currently being analyzed.

Discussion: This pilot demonstrated our ability to flexibly embed study procedures and data collection into the existing ECT clinical workflow, which minimized the burden on the patients and providers and resulted in a high recruitment rate. It further supports the feasibility of successfully carrying out a larger genetic study with the goal of recruiting 25,000 patients with severe depression treated by ECT worldwide. A grant to the NIMH has been submitted to support the work of ECT centers in the NNDC to contribute to this effort in the US. The proposed study will motivate the development of new and more effective treatment strategies for this burdensome and difficult to treat condition. It will also identify genetic factors that can help distinguish which patients are good candidates for ECT before initiating treatment.

16. Development of a Residential Treatment Program for Adults with Severe Mood and Co-Morbid Disorders: Program Descriptions and Initial Outcomes

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Background: Accumulating evidence indicates that improved functioning is possible for adults with serious mental illness (SMI), which include severe depression and bipolar disorder[1]. Higher-level and intensive behavioral health service that includes multi-modal evidence-based interventions may be needed to support patients with severe mood disorders to reach functional and vocational recovery[2]. This study describes a newly developed residential treatment program that integrates Cognitive and Behavioral Therapy, psychopharmacotherapy, and a vocational program to support recovery for adults with SMI.

Program Description: Mayo Clinic John E. Herman Home and Treatment Facility is a 16-beds residential treatment with length of stay of three to six months. Interventions include: Behavioral Activation, Dialectical Behavioral Therapy, Acceptance and Commitment, Therapy group, weekly individual psychotherapy session; weekly medication management; Individual Placement and Support, and vocational programs.

Methods: Seven patients completed the program and self-report measures at admission and discharge to assess recovery from SMI (i.e., Maryland Assessment of Recovery in People with Serious Mental Illness (MARS-25)) and depressive symptoms (i.e., Patient Health Questionnaire 9-item (PHQ-9)).

Results: Among the first seven patients who completed the program, six reported improvement in their recovery from SMI. On average, MARS-25 total scores increased from 33.7 to 43.3. Mean total depression score decreased from 15.8 to 11.8. Five out of seven patients were able to gain competitive employment or education.

Conclusions: The development of a residential treatment that includes multi-modal behavioral health and vocation interventions to support adults with severe mood disorders to both manage psychiatric symptoms and achieve functional and vocational recovery is feasible. This is a very preliminary outcome and further study with larger sample size is needed to draw conclusion for the program effectiveness.

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17. Depressive symptoms and course are associated with early-relapse in opioid-dependent individuals treated with extended-release naltrexone but not buprenorphine-naloxone

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Background: Major Depressive Disorder (MDD) and depressive symptoms commonly co-occur with opioid use disorder (OUD) and have complex relationships with OUD treatment outcomes.[1,2] For example, co-occurring depression has been associated with both worse[1] and better[2] OUD treatment outcomes in opioid-dependent individuals. Some of the variance in this association may be due to individual differences in the response to medications for OUD treatment (MOU). In the present study, we examined differences in depression severity and in the associations between depression severity and opioid relapse in opioid-dependent adults randomized to receive one of two commonly prescribed, pharmacologically-distinct medications - extended-release naltrexone (XR-NTX), an opioid antagonist, and sublingual buprenorphine-naloxone (BUP-NAL), a partial opioid agonist.

Methods: Effects of depression and treatment condition on opioid relapse were examined using data from a 24-week open-label, randomized controlled, comparative effectiveness study comparing XR-NTX versus BUP-NAL for opioid relapse prevention (NIDA CTN-0051).[3] In the study, 570 opioid-dependent adults (169 females, mean age = 33.9 years) were randomly assigned to 24-weeks of XR-NTX (4ml, 380 mg naltrexone base IM every 4 weeks) or Bup/Nal (SL, daily dose range = 8-24 mg), with both treatment arms offered weekly behavioral therapy. Depressive symptoms were assessed via the 17-item Hamilton Depression Scale (HAM-D). XR-NTX and BUP-NAL groups did not differ in age, sex, education, or on HAM-D scores at baseline (bsl). Logistic regression models examined whether depressive symptoms (continuous variable) or MDD diagnosis (categorical, based on HAM-D cutoff scores at bsl) were predictive of early-relapse secondary to medication induction failure and opioid-relapse events by week-24.

Results: 26% of participants met criteria for moderate-to-severe MDD at bsl. 204 [72%] of 283 participants in the XR-NTX group and 270 [94%] of 287 in the BUP-NAL group were early-relapsers. In the total sample, HAM-D scores at week-24 ($\beta = 0.07$, $p < 0.001$) were associated with early-relapse and a number of depression x treatment condition interactions were identified [txt con x HAM-D_{bsl} ($\beta = 0.03$, $p < 0.001$); txt con x $\text{MDD diagnosis}_{bsl}$ ($\beta = 0.33$, $p = 0.02$); and txt con x $\text{HAM-D scores}_{week\text{-}24}$ ($\beta = 0.05$, $p < 0.001$)]. Post-hoc analyses showed a general pattern of increased depression severity being associated with early-relapse in the XR-NTX but not the BUP-NAL group.

Conclusions: Depressive symptoms and disorders represent an important treatment target in individuals with OUD. We found that depression severity was associated with early-relapse and that in opioid-dependent individuals with co-occurring depressive symptoms or MDD that the type of medication received influenced the likelihood of early-relapse. The presence of moderate-to-severe MDD at bsl and increased depressive symptoms during OUD treatment were predictive of induction failure with XR-NTX but not BUP-NAL. Individual differences in the severity of depression during XR-NTX treatment could be due to differences in risk genes (e.g. ORPM1) or childhood adversity, both of which influence inter-individual response to naltrexone. While preliminary and requiring replication, our results suggest that MOU with BUP-NAL may be the treatment of choice in individuals with OUD who have co-occurring depression.

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18. Riluzole Augmentation Pilot in Depression (RAPID) Trial

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Background: Intravenous ketamine administration produces rapid antidepressant effects, supporting a role for the glutamatergic system in depression. Riluzole is another glutamatergic drug that has shown promise as a potential treatment for depression. We examined whether augmenting standard SSRI therapy with riluzole produced a greater antidepressant response than stand-alone SSRI treatment.

Methods: Subjects with untreated depression were randomly assigned to either sertraline + riluzole or sertraline + placebo for 8 weeks. Subjects were monitored for changes in Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HAM-A), and Clinical Global Impression (CGI) scores. Response and remission rates were assessed via change in HDRS scores.

Results: Thirteen subjects completed the study. There was no significant between-group differences in response or remission rate [$X2(1, N=13)=1.04$, $p = 0.31$] and [$X2(1, N=13)=0.93$, $p = 0.34$], respectively. There was a trend toward a significant reduction in average HDRS score in placebo compared to riluzole patients [$F(1, 11)=4.22$, $p=0.06$]. The placebo group showed a greater reduction in average CGI score compared to the riluzole group [$F(1, 12)=5.57$, $p=0.04$].

Background: Discordant with our hypothesis, riluzole was not more effective than placebo at reducing depression symptoms and was associated with reduced global clinical status relative to placebo.
The purpose of this study was to investigate whether taking riluzole along with a standard antidepressant (sertraline, also known as Zoloft) can help improve symptoms in people with major depression. To investigate this, we looked at how the severity of depression symptoms changed after 8 weeks in patients taking riluzole + sertraline compared to patients taking placebo + sertraline. The placebo pills looked exactly like riluzole but did not contain any actual medication. The purpose of using placebo pills was to see if the study results were due to the riluzole or due to other reasons. We hypothesized that patients taking riluzole + sertraline would experience a greater reduction in depression symptoms, in less time, than those taking placebo + sertraline. Our findings revealed that riluzole was not more effective than placebo at reducing the severity of depression symptoms. In fact, riluzole + sertraline was associated with worse depression symptoms overall than placebo + sertraline.
Clinical Implications: Our findings suggest that riluzole is less effective at treating symptoms of major depression than a placebo pill is when taken in combination with sertraline.

19. Role of the Kynurenine Pathway and the Endocannabinoid System as Modulators of Inflammation and Personality Traits

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Background: Kynurenine pathway metabolites and endocannabinoids both exert potent regulatory effects on the immune system, but the relationship between these molecules is unknown. The role of these immunobiological mediators in emotionality and personality traits is not previously characterized.
Methods: Interleukin-6 (IL-6), 2-arachidonoylglycerol (2-AG) and picolinic acid were measured in the plasma of physically healthy individuals who had history of mood, anxiety, and personality disorders (n=96) or who had no history of any psychiatric disorder (n = 56) by DSM-5 Criteria. Dimensional assessments of personality were performed using the Eysenck Personality Questionnaire (EPQ) and the Tridimensional Personality Questionnaire (TPQ).
Results: Plasma IL-6 levels were significantly associated with plasma 2-AG levels and plasma PIC levels across all subjects. PIC levels were also negatively associated with 2-AG levels across all subjects, independent of IL-6 levels. In our analysis of the biological determinants of personality factors, we identified significant associations between IL-6 and novelty seeking assessment, and between PIC and neuroticism assessment.
Conclusions: These data provide evidence of a biological link between metabolites of the kynurenine pathway, the endocannabinoid system and IL-6 and suggest that these factors may influence personality traits.

20. Effectiveness of Ultrabrief Right Unilateral Electroconvulsive therapy for the Treatment of Primary and Secondary Psychotic disorders

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Background: The efficacy of electroconvulsive therapy (ECT) in the treatment of severe depression is well documented and ECT is likely more effective than conventional drug therapy in many cases. Evidence, in fact, indicates that patients with psychotic depression have a better response to ECT than patients with nonpsychotic depression. According to a report from the CORE study, patients with psychotic features were found to have earlier and more favorable response rates compared to patients with non-psychotic depression. Additionally, remission rates have been found to be higher in patients with delusional depression versus non-delusional depression. Traditionally patients with psychotic presentations are treated with bilateral (BL) lead placement with the assumption that BL lead placement is more effective for this population than any other ECT modality. There are no randomized trials comparing different electrode placements in patients presenting with psychotic features. Usually patients with psychotic features are not treated with right unilateral (RUL) ECT despite of the significant decreased risk for cognitive adverse effects.
Methods: A retrospective chart review of 250 patients undergoing UB (ultrabrief) RUL ECT during a 5-year period was completed. This review identifies 106 patients with primary or secondary psychotic disorders who received UB RUL (mean age 63, 66% female). 84.9% (n=90) were Caucasian. This patient group consisted of MDD with psychotic features (64.2%), bipolar disorder with psychotic features (17.9%), primary psychotic disorder (6.6%), catatonia (11.3%). Quick Inventory of Depressive Symptomatology (QIDS) was completed both pre-ECT and post-ECT, while the Clinical Global Impression–Improvement (CGI-I) scale was performed post-ECT. Response defined by a decrease of QIDS by 50% and CGI-I ≤2.

Results: Mean baseline QIDS was 19.4 (SD 6.8). Post-treatment QIDS was 6.6 (SD 5.5). Post-ECT response rate was 81.25%. Post-ECT CGI-I response rate was 74.15 %. Montreal Cognitive Assessment (MOCA) pre-ECT was 21.2 and post-ECT was 26. Electroconvulsive Cognitive Assessment ECCA (n=23) was 19.8 (pre-ECT), 21.3 (mid-ECT), and 24 (post-ECT).

Conclusions: UB RUL ECT is a safe and effective treatment modality for patients presenting with psychotic features. RUL treatment modality could be considered as an option prior to BL ECT in order to decrease risks of cognitive adverse effects. Further studies are warranted to establish further treatment guidelines.

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21. Monitoring cognitive function in patients receiving ECT: ECCA a promising tool

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Background: Electroconvulsive therapy (ECT) is one of the most effective treatment modalities for severe depressive disorders. Memory deficit is the most common side effect from ECT. The cognitive deficits encountered in ECT are very unique and specific to certain domains. The majority of tools that are widely available and extensively used in the ECT field such as the Montreal Cognitive Assessment (MoCA) or the Mini-Mental Status Exam (MMSE) were developed specifically to assess mild cognitive impairment and Alzheimer's disease and do not effectively evaluate the deficits presented in the context of ECT. One of the current challenges in evaluating memory issues in ECT is the lack of a brief and sensitive tool to evaluate the cognitive deficits during and after ECT. Based on these limitations, the ElectroConvulsive Cognitive Assessment (ECCA) was developed as a simple, stand-alone cognitive screening tool to assess the specific memory domains compromised in ECT.

Methods: One hundred and thirty six subjects were enrolled. The ECCA and the MoCA were administered prospectively to fifty-five patients with major depressive disorder (MDD) (age 57.8±17.06) using a within-subject study design at three time points: pre-treatment, before the sixth treatment, and one week post-treatment. The psychometric properties of the total and domain scores of both instruments were examined at all three time points. To examine construct validity, forty demographically comparable patients with MDD who did not receive ECT (age 60.3±12.35 years), and forty-one healthy, age-matched healthy controls (age 59.4±14.94 years) were evaluated.

Results: At baseline ECCA and MoCA scores were not statistically different ($p=0.11$). Prior to the sixth ($p<0.001$) and final ECT session ($p<0.001$), total ECCA scores in the ECT group were significantly lower than the MoCA total scores. The ECCA domains of subjective memory ($p<0.05$), informant-assessed memory ($p<0.0001$), attention ($p=0.03$), autobiographical memory ($p<0.001$), and delayed verbal recall ($p<0.05$) were significantly lower post-ECT compared to pre-ECT. Construct validity was modest to high (Kappa coefficients of 0.68 with 95% confidence interval (CI), [0.35, 1]). Inter-rater reliability was found to be moderate to high (Lin's concordance correlation coefficient=0.84 with 95% CI [0.71, 0.92]).

Conclusions: The ECCA is a brief, reliable, cognitive screening assessment tool that may be useful to assess global cognitive function in patients with MDD treated with ECT.

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22. Attempted suicides in elderly with existing DNRs: An emerging geriatric ethical dilemma

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Background: Cases of suicide attempts by elderly with existing Do Not Resuscitate (DNR) documentation presents several clinical and ethical issues, including whether to proceed with treating the individual involved, or to yield to family expectations. The case presented here raised further complications because of the suicide pact made by the couple involved, the advanced age of the couple, and their family's perception of mental illness and confusion regarding the validity of DNR.

Case Report: An elderly couple aged 93 and 92, both living in an assisted living facility (ALF) attempted double suicide by overdose and cutting their wrist. The husband with advanced dementia (aged 93) convinced his reluctant wife to carry on with suicide attempt and was admitted to the inpatient psychiatric unit after medical stabilization. Based on his existing DNR, his family requested no services including withholding food and water, as he wanted to die. The treatment team felt deeply conflicted on the ethics of following the family's wishes as the patient had no terminal illness and with proper medical and psychiatric treatment, was likely to return to his ALF without significant complications. After lengthy discussions between the treatment team and the family regarding the nature of depression and treatment choices, the proxy consented to start antidepressant medication. The patient's symptoms improved and was discharged to the ALF within the next few weeks.
Discussion: The incidence of suicide attempts among elderly are becoming more frequent. When presented with an existing DNR and family involvement, the treatment decisions for suicide attempts among elderly becomes very challenging for the mental health providers. Systematic case-by-case, medical-ethical psychiatric team discussions guided by ethical and legal guidelines, are needed to resolve these predicaments.

23. Relationship between burden of psychotropic medications and cognitive performance in a large sample of individuals with bipolar illness

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Background: The contribution of medication to cognitive impairment in bipolar illness is complicated to control for and results in mixed findings. There seems to be an increase in risk for medication-associated cognitive side effects with polypharmacy and higher dosages (Balanzá-Martínez et al., 2010). We used an adopted protocol often seen in the literature to assess the influence of total psychotropic medication use on cognition (Sackeim, 2001). We predicted that those with greater medication usage (greater burden of psychotropic medications) would show poorer performance on cognitive tasks, notably in speed-related tasks.
Methods: Individuals with bipolar illness (n=397) from the Prechter Longitudinal Study were administered a neuropsychological test battery and medications were recorded. A single medication variable was created reflecting the quantity, duration, and dosage of psychotropic medication (e.g., antidepressant, antipsychotic, mood stabilizer, etc.) for each individual. This resulted in a summed composite score: medication load.
Results: Correlational analyses between medication load and neuropsychological test performance showed statistically significant correlations for the Purdue Pegboard trials, the Rey Osterrieth Complex Figure learning and recall trials, and the Trail Making Test Part B. However, partial correlations between medication load and neuropsychological performance, controlling for current depressive symptoms, were not significant.
Conclusions: In sum, findings show a significant negative effect of medication burden on fine motor dexterity, timed visuomotor sequencing, and visual memory, but effects may be better accounted for by current depressive symptoms. Depressive symptoms, therefore, may have a greater contribution to cognitive performance than polypharmacy.

24. Does Age Modulate Response to Ketamine Infusion for Treatment-Resistant-Depression?

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Background: Ketamine can provide rapid improvement of symptoms in patients with treatment resistant depression (TRD). Despite the long history of ketamine's use in experimental and clinical medicine, the exact mechanism of action for its antidepressant activity remains elusive. While it is still undetermined, there is evidence that moderating factors like sex, age, psychiatric comorbidities, and disease chronicity may impact ketamine's efficacy in treatment of depression. In some studies, dissociative side effects, which mostly occur through the NMDA receptor antagonism, positively correlate with treatment response. Notably, younger adults seem to experience more dissociative symptoms after ketamine, and NMDA receptors tend to decline with age to a greater extent than other neurotransmitter receptors. Both of these findings suggest that ketamine may display age-related differences in effectiveness with less robust response to repeated infusions of ketamine in elderly individuals.
Methods: This is a prospective study of patients undergoing ketamine treatment for psychiatric indication. Patients with TRD who qualified for ketamine infusion as standard of care were eligible to participate. The study was approved by the IRB and participants signed informed consent. Patients received up to 10 continuous intravenous infusion of ketamine added to their ongoing antidepressants. Treatment response was measured using the clinician-rated Montgomery Asberg Depression Rating Scale (MADRS) and the self-report PHQ-9 at each visit. Demographics, diagnoses and concomitant treatments were obtained from the medical records. sequencing, and visual memory, but effects may be better accounted for by current depressive symptoms. Depressive symptoms, therefore, may have a greater contribution to cognitive performance than polypharmacy.

Results: Patients age averaged 50.0±17.1 (mean ±SD), ranging from 21 to 75, with 20% ≤30 year old, 44% >30-<60 year old and 36% ≥60 year old. Severity of depression did no differ between groups. Baseline MADRS average scores were 36.0 ± 8.3, 32.9±6.9 and 33.6± 13.3 (p=0.758), respectively. Correlation between age and response was analyzed after one infusion and at the end of the infusion course as well as time to response for responders. Correlation of age with changes in scores of individual symptoms on the PHQ-9 was also measured.
Limitations: The small number of patients may limit the detection of differences between age groups.

25. A Computational Approach to Examining the Mechanisms of Risk Propensity in Euthymic Bipolar Disorder

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Introduction: Bipolar disorder (BD) is associated with excessive pleasure-seeking behaviors that often characterize its clinical presentation, contributing to high substance use comorbidities among those with BD. This study used a computational approach to investigate the role of altered reward processing in risky decision-making during the euthymic phase of BD and its relationship to history of substance use disorder (SUD).
Methods: This study included 33 participants with BD and 33 healthy controls (HC). Eighteen of the BD participants had no history of SUD (BD-nSUD), and 15 had a history of SUD (BD-SUD). Participants completed the Balloon Analogue Risk Task (BART), self-ratings of behavioral activation/inhibition, and executive function tasks. We applied a previously validated computational model (Wallsten et al., 2005, Psychological Review, 112:862-880) to the BART data of each participant to estimate 4 parameters: behavioral consistency, value of rewards, magnitude of initial risk propensity, and certainty of initial risk propensity. These parameters were then compared between the groups and correlated with the executive function and psychological measures.
Results: The BD-SUD group over-valued rewards relative to BD-nSUD and HC groups (H), and increased valuation of rewards was significantly correlated with reduced executive function and reduced behavioral inhibition. In addition, the magnitude of initial risk propensity was significantly lower in the BD-SUD group than in the HC and BD-nSUD groups, suggesting a more conservative approach to risk-taking in the euthymic phase, which could represent a potential protective mechanism for this particular sub-group.
Conclusions: The results highlight the value of computational methods in deconstructing the cognitive processes contributing to bipolar disorder and related vulnerabilities, informing personalized treatment strategies.

26. Association between obesity and major depressive disorder across the lifespan: a review through a biopsychosocial lens

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Background: Increasing evidence supports a bidirectional relationship between major depressive disorder (MDD) and obesity. Here we update the existing literature by examining this relationship in terms of biomarkers, sex differences, and aging.
Methods: Using Pubmed, we conducted a literature review including all English publications from January 2016 to January 2019 using the following keywords: MDD, obesity, body mass index, adipose tissue, waist circumference, and body fat distribution.
Results: Converging biological evidence suggests a significant relationship between obesity and MDD including genetic determinants, adipokines, and other inflammatory factors. Childhood trauma also plays a significant role. In adulthood, obesity with or without biopsychosocial stressors, was associated with an increased risk for depression, especially in pregnant women (including pre-, during, and post-pregnancy). In older adults, sarcopenia, visceral fat, and metabolic factors significantly mediated the relationship between obesity and depression risk. Emerging data also point toward clinically-relevant sex differences in this area.
Conclusions: Predicting risk factors and elucidating pathophysiological mechanisms associated with increased rates of depression in obese individuals will be crucial for the future development of treatment strategies that target this population. Identifying age-specific risk factors may contribute to a personalized medicine approach, which may ultimately provide meaningful improvements to the quality of clinical care.

27. Impact of Religious Coping on Treatment Outcome: A Systematic Literature Review

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Background: Religion/spirituality (R/S) has been largely associated with salutary effects on mental health. At the same time, R/S can sometimes contribute to mental illness or otherwise interfere with treatment. *Positive religious coping* (PRC) involves responding to life stressors in adaptive ways related to the sacred (e.g., prayer, reading scripture, etc.). N*egative religious coping* (NRC) is a form of internal struggle or conflict in the spiritual realm in relation to oneself, others, or the divine (e.g., feeling distant from God, believing that life has no meaning, etc.). The present study is a systematic literature review examining the association between religious coping and outcomes in psychological treatment for psychiatric disorders and symptom clusters.

Methods: PsychInfo and PubMed databases were searched for relevant peer-reviewed journal articles and doctoral dissertations published/indexed through March 2019. A total of 2,338 articles were independently screened for relevance by two reviewers. After applying exclusion criteria, removing duplicates, and conducting a quality assessment, 20 articles based on 19 original studies were included in the data synthesis.
Results: Most articles included in the review focused on treatments for either depressed mood (6 studies) or substance abuse (7 studies). Despite some inconsistency of the results across the studies, more studies than not indicated that PRC positively impacts treatment outcomes, while NRC negatively impacts treatment outcomes. However, in studies of treatments that included manipulation of religious coping, decreases in NRC, but not increases in PRC, were shown to improve treatment outcomes.
Conclusions: Results indicate that religious coping is an important psychosocial factor that should be considered in psychological treatment of psychiatric disorders and symptoms. When addressing religious coping directly in order to improve outcomes, it may be more efficacious to direct treatment efforts at decreasing NRC rather than increasing PRC. More original studies using gold standard measures of NRC/PRC are needed.

28. Public views about treating depression across four treatment modalities

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Background: Americans' views about mental health treatments are influenced by values, beliefs, and ethical concerns that are not fully understood. Uninformed beliefs, biases, and perceptions of the functioning, impact, and side effects of a variety of mental health treatments may inhibit help-seeking behavior and the adoption of effective therapies. Psychiatric Electroceutical Interventions (PEIs)—therapies that aim to treat psychiatric conditions with electrical stimuli—may be especially prone to misunderstandings.
Methods: To explore these dynamics, we conducted an experiment with video vignettes to examine how views about treating depression vary across four treatment modalities: two non-PEIs therapies: psychotherapy and selective serotonin reuptake inhibitors (SSRIs); and two PEIs: transcranial magnetic stimulation (TMS), and deep brain stimulation (DBS). Among other issues, we investigated the perceived risks and negative affect towards these treatments by subjects.We administered a between-subjects, four-group, post-test only experiment via Qualtrics to 284 US adults recruited from the crowdsourcing website Amazon Mechanical Turk. Each subject was randomly assigned to watch a brief video describing one of the four treatments described above, before answering some questions on their views about their assigned treatment. We employed principal components analysis and reliability analysis to inform the construction of a 7-item Perceived Risk Scale (Cronbach's $\alpha = 0.75$) and a 7-item Affect Scale ($\alpha = 0.88$). Additionally, we analyzed our experimental data with a series of one-way ANOVAs with a post-hoc Tukey HSD test.
Results: Overall, perceived risk [$F(3, 280)=9.17$, $p<0.001$] and affect [$F(3, 280)=36.78$, $p<0.001$] varied significantly across the experimental groups. In particular, post hoc comparisons using the Tukey HSD test indicated that subjects in both the TMS and the DBS group perceived their treatment more negatively ($p<0.001$) and riskier ($p<0.001$) and than did subjects in the psychotherapy group. TMS and DBS were also perceived as more negatively than SSRIs ($p<0.001$) but no significant difference was found in terms of risk. Further, subjects in the DBS group perceived their treatment more negatively ($p=0.042$) than did subjects in the TMS group. There was no statistically significant difference in how TMS and DBS subjects perceived the riskiness of their respective therapies.
Conclusions: Taken together, our survey results highlight the complexity of public views about risk and negative affect towards PEIs. Further research with a larger sample is needed to better understand additional factors that may be contributing to divergent views across these different treatment modalities.

29. Social and clinical variables that influence longitudinal depression outcomes after brain stimulation

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Background: Clinical trials of antidepressant treatments typically measure short-term effects over 6-12 weeks. Less is known about long-term outcomes over a time frame of months to years. The clinical effects of time-limited neurostimulation interventions such as electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and intravenous ketamine can be durable for some individuals, but many patients subsequently relapse. The underlying causes of this individual variation remain unknown. This study aimed to identify sociodemographic and clinical predictors of short- and long-term depression outcomes following ECT.

Methods: We conducted a prospective observational study of participants with treatment-resistant unipolar or bipolar depression (n=114) at the University of Michigan. Depressive symptoms were measured at baseline, acutely after ECT (n=105), and then every 6 months for up to 24 months during naturalistic treatment (n=68). Sociodemographic and clinical features were examined as predictors using generalized linear models and linear mixed models.
Results: Two-thirds of those who completed the ECT series were classified as responders. Individuals with fewer medication failures and those without a maternal history of depression were more likely to respond acutely. Following the ECT series, depression trajectories varied widely, and longer-term outcomes were predicted by distinct features. After controlling for baseline depression and acute ECT response, better long-term depression outcomes were predicted by generalized anxiety, being married, and high-quality relationships and social support.
Conclusions: Short- and long-term depression outcomes after ECT are predicted by distinct social and clinical variables. Social relationships and supports, in particular, may strongly influence longer-term depression outcomes. Assessments and interventions in the social domain might be targeted to improve longitudinal depression outcomes after brain stimulation.

30. TNF-α and its receptors mediate the relationship between prior severe mood episodes and cognitive dysfunction in euthymic bipolar disorder

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Background: It is known that 40-60% of patients with bipolar disorder (BD) have neurocognitive deficits. It is increasingly accepted that functioning in BD is negatively impacted by these deficits, yet they have not been a successful target for treatment. The hypothesis of neuroprogression in BD postulates that cognitive deficits develop over the course of the illness and are influenced by prior severe mood episodes, leading to wear-and-tear on the brain. The biomarkers that predict cognitive deficits in BD are largely unknown, however recent evidence suggests that inflammation may be associated with poorer cognitive outcomes in BD.
Methods: We measured tumor necrosis factor alpha (TNF-α), and TNF receptors one and two (TNF-R1 and TNF-R2) in 219 euthymic BD patients. Structural equation modeling was used for the primary purpose of assessing whether TNF markers measured by the multiple indicators TNF-α, TNF-R1 and TNF-R2, mediate the effect of number of prior severe mood episodes (number of psychiatric hospitalizations) on the latent variable "Executive Function" assessed by a set of observed variables, namely, the neurocognitive tests: Controlled Oral Word Association Test (COWAT), Wisconsin Card Sorting Test (WCST) and Stroop.
Results: The Chi-Square value of 49.6 had a non-significant p-value of 0.23, which indicated that the model fits the data acceptably. Further, the Root Mean Squared Error Approximation (RMSEA) of 0.027 and PCLOSE of 0.9 further supported that the model had a 'close fit'. Holding covariates constant (age, sex, premorbid IQ, education, and race), the direct effect of prior severe mood episodes on executive function (EF) was -0.14, whereas the indirect effect of severe mood episodes on EF mediated by TNF was -0.03, and thus the total effect of severe mood episodes on EF was -0.17. The path coefficients above were individually significant, and by inference the direct, indirect, and total effects were also statistically significant. The direct effect of TNF markers on EF in this model is -0.2. Thus, this estimated model was consistent with peripheral TNF markers partially mediating a causal effect of severe mood episodes on executive cognitive function.
Conclusions: Our results indicate that TNF variables partially mediated the relationship between prior severe mood episodes and executive function in BD. These results may implicate TNF variables in the neuroprogressive course of BD.

31. The Behavior Forecast: Optimizing Sitter Usage in the Hospitalized Patient Through Improved Communication

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Background: The use of sitters for constant observation (CO) of hospitalized patients is a topic of great importance to health systems, staff, and patients given implications on care quality, patient safety, and resource utilization. While most research has been conducted to evaluate the role of sitters in fall prevention[1], patients with delirium[2], and suicidal patients[3], it is also clear that sitters represent a significant cost to the organizations that employ them[4]. Relatively little work has been done, however, to examine the efficiency with which sitters are ordered, removed, and managed within systems.
Methods: Preliminary data for this study indicated that lack of real-time communication is a common culprit when sitters are not utilized efficiently, with providers often relying on dated assessments when deciding whether to continue sitter orders for patients. This quality improvement project was designed and conducted at a large, academic medical center with the aim to develop a novel handoff communication tool that will allow staff to more effectively summarize and relay the status of patients with sitters for specific indications to other providers.

Results: The tool created is called the Behavior Forecast, which is an electronic medical record (EMR) template form that assigns a categorical short-term risk classification ("sunny, cloudy, or stormy") to patients based on sets of established criteria for each disposition.
Conclusions: The aim of the intervention is to provide more consistent and accurate information to providers who can then make more informed decisions based upon behavioral trends when placing daily sitter orders and cancellations. Further directions of this project include implementation of the Behavior Forecast and statistical analysis to determine its efficacy.

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32. Clinical, Cognitive, and Brain-Based Markers of Late Life Mood Disorders: A Multi-Site Registry Project

National Network of Depression Centers Geriatric Mood Disorders Task Group

Background: Most studies of late-life depression and bipolar disorder are limited by small, demographically homogenous sample sizes, reducing the ability to generalize findings to a broader population of older adults experiencing mood disorders. Multi-site studies can overcome some of the limitations inherent in single-site designs by including larger sample sizes and increased participant diversity.
Methods: The Geriatric Mood Disorders Task Group has been developing a multi-site data registry that capitalizes on existing data collected by members of the Task Group at different institutions. This project combines clinical, neuropsychological, and resting state fMRI data collected among older adults with depression, bipolar disorder, and no history of mental illness.
Results: To date, we have pooled data from four different institutions- Harvard-McLean, University of Illinois at Chicago, University of Michigan, and University of Utah. This includes 206 with depression, 238 with bipolar disorder, and 243 healthy controls. Our analysis plan entails examination of between-group differences and identification of clinical predictors of neuropsychological and brain network functioning. We will also examine heterogeneous data sources (clinical, neuropsychological, neuroimaging) across geriatric mood disorders for transdiagnostic characterization of the population to capture "biotypes" consistent with the RDoC framework.
Conclusions: We describe some of the challenges in creating a multi-site registry and how such a project can lead to NIH funding.

33. Understanding the Hispanic Health Paradox: Parental Depression as a Mediator of the Relationship between Caregiver Place of Birth and Child Asthma Control in Mexican Americans

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Background: The Hispanic Health Paradox describes the phenomenon that Hispanics in the US, especially foreign-born, have better health outcomes compared to other ethnic-racial groups with similar socioeconomic profiles.[1,2] Previous research has offered partial explanations on how caregiver place of birth is linked to better asthma outcomes for their children.[4,5] Additionally, many studies have analyzed the relationships between caregiver mental health and their child's asthma control.[6] However, little research has examined the interconnected relationships of all three; caregiver country of origin, child asthma outcomes, and caregiver mental health.
Methods: Data were obtained from the Asthma Action at Erie trial, a randomized control trial designed to assess the community health worker intervention of 223 caregiver/child dyad participants. For this paper, the sample was restricted to only Mexican American caregivers (N=165). Caregiver depression was measured by the 9 item Patient Health Questionnaire(PHQ-9), and child asthma control was assessed through the Asthma Control Test (ACT).[8] Multivariable linear model was used to examine relationships among caregiver place of birth, caregiver depression, and child asthma control, controlling for demographic and site characteristics (child age, gender, body mass index and caregiver age, education). Mediation analyses explored whether caregiver depression mediated associations between caregiver place of birth and child ACT.
Results: Children of caregivers born in Mexico (n=95) had better asthma control (higher ACT), while conversely children of Mexican American caregivers born in the US (n=70) had worse asthma control (lower ACT), Estimate of difference = 1.82 (SE=0.86), p = .034. US-born caregivers had higher depression versus Mexican-born caregivers (Estimate = 1.59; SE =0.41, p < .001). Mediation analyses indicated that caregiver depression mediated the relationship between caregiver place of birth and the child's asthma control.

Conclusions: Caregiver depression may explain the link between caregiver place of birth and child asthma control, furthering our understanding of the Hispanic Health paradox. Results suggest that when developing pediatric asthma interventions, providing screening and supports for caregiver depression are paramount, especially for Mexican American families born in the United States.

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34. Using IV Ketamine More Effectively: Safety and Efficacy of 100-minute versus 40-minute infusions for Refractory Depression

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Meta-analytic data demonstrate that IV ketamine is effective for treatment-refractory depression (TRD), usually using 40-minute infusions. Biological or clinical predictors of response have not been identified. The mammalian target of rapamycin (mTOR) signaling pathway serves as a central regulator of cell metabolism, growth, proliferation and survival, and is implicated in ketamine treatment. To examine mTOR response and evaluate other biomarkers, we are conducting a multi-site clinical trial of IV ketamine for TRD, administering 3 acute infusions. We use remission (MADRS < 9) to define remitters and non-remitters to ketamine. Both 100-minute and 40-minute infusions have been administered, providing an opportunity to compare side effects, safety, and tolerability. In addition, preliminary comparison of efficacy between the infusions is also possible. To date, 55 of a proposed 100 subjects have completed the 3 acute phase infusions and some have had additional maintenance infusions, yielding 153 individual infusions of 100-minutes and 90 individual infusions of 40 minutes. Participants have a mean age of 44.12 years (SD 13.42) and most are female (69%). Comparison of side effects between the two infusion types reveals noted differences, with the 100-minute infusion appearing more tolerable. In a subsample of 30 infusions, rates of cardiac and psychotomimetic side effects were 8% and 13.8%, respectively. Preliminary efficacy data suggests lower response after a single 100-minute infusion compared to a single 40-minute infusion, but similar response after 3 infusions. These unique data on side effects and overall safety and tolerability, along with preliminary efficacy data, provide an opportunity to consider the merits of 100-minute infusions as an alternative treatment which is safer and easier to use by psychiatrists.

35. Depression During Pregnancy is Associated with Altered Gut Microbiome and Immune System

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One in ten women experience depression during their pregnancy or antenatal depression (AND). AND confers significant risks to mother (e.g., suicide) and child (e.g., preterm birth, low birth weight, infant neurodevelopmental disorders), yet only 5% of women with AND receive adequate care. Despite increasing evidence linking depression to the gut microbiome, this research has not been extended to the perinatal period. Our aim was to examine gut microbial structure and composition and the activity of the immune system in pregnant women with and without AND. Sixty-four pregnant women provided fecal and blood samples at their first (<16 gestational weeks) and second trimesters (24-28 gestational weeks) and completed the Computerized Adaptive Diagnostic Test for Major Depression Disorder (MDD) diagnostic screening tool (CAD-MDD). Using DADA2, 16S rRNA amplicon sequence analysis of fecal DNA, DADA2 identified exact sequence variants (ESVs) that were correlated against AND using Generalized Linear Models (GLM). GLM were adjusted by age, gestational weeks and BMI and all multiple comparisons were corrected for false discovery rate. AND rates were 15.6% (T1) and 10.6% (T2). While Shannon index was not associated with AND, the average Bray-Curtis distance was inversely associated with AND ($p=0.02$). Several ESV were significantly different in women with AND compared with those without. For instance, Paraprevotella and Faecalibacterium were enriched and depleted respectively in women with AND overall, while Lactobacillus was only depleted at their first trimester. Additionally, TNF-alpha was negatively associated with AND during the first trimester (p-value<0.1), and IL-6 and IL-12(p70) were increased in mothers with AND in the second trimester (p-value<0.05). In summary, we provide new evidence that AND is associated with altered gut microbial and immune systems that vary with gestational age and could serve as a future assay to detect AND in clinical settings. The current work is funded by the Arnold O. Beckman Postdoctoral Fellowship Award and the NIH R03HD095056.

36. Epidural Steroid Injection-induced Brief Reactive Psychosis and Mania in a Geriatric Patient

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Background: The psychiatric risks of oral and intravenous steroid treatments are well-documented. However, impacts of epidural steroid injections for chronic pain on the mental status of geriatric patients, are seldom discussed.

Clinical History and Interventions: A 76-year-old female with no prior psychiatric history was presented to the emergency department by her family for inability to sleep, confusion, and behavioral outbursts. The mood instability and psychosis were reported as having started a week after her third epidural steroid injection for pain associated with a prior fall. Despite initial treatments for hyponatremia, sepsis, and possible localized seizure, her increasing paranoia and impulsivity responded only for brief periods to urgently administered lorazepam and haloperidol. Additional IV steroids were given for suspected meningitis, although lumbar puncture demonstrated no abnormalities. Phenytoin was given for EEG signs of localized right temporoparietal seizure, yet paranoia increased, and mental status continued to deteriorate. After ten days without explanatory neurological findings, at therapeutic phenytoin level for seizure prevention, with lorazepam and haloperidol as needed, the patient was transferred to the geriatric psychiatry unit. Upon admission to the inpatient unit, she was loud, grandiose, verbally aggressive, unable to sleep, hyper-religious, paranoid, non-redirectable, and identified her husband and daughter as demons. Phenytoin was discontinued and risperidone and valproic acid were restarted. Hyper-religiosity and paranoia greatly improved within a week, though the patient remained very talkative and tangential, with disorganized thought process. Valproic acid was titrated to 1000 mg per day, yielding level of 56.2, accompanied by improvement to mild talkativeness and circumstantiality. She was able to interact appropriately, with minimal lorazepam requirement, and was discharged three days later with linear thought process and free of psychosis. On outpatient follow-up, there was minimal residual hypomania and no recurrence of psychosis, allowing wean of valproic acid and discontinuation of risperidone. Two months later, symptoms resolved completely.

Discussion: The persistence of this patient's psychosis for nearly 1 month, and hypomania for about 3 months, underscores the importance of careful risk-benefit analysis before initiating epidural steroids. This is particularly important in elderly patients who are more susceptible to psychiatric adverse effects lasting as long as analgesic benefits.

37. How a History of Childhood Trauma affects Cognition in Adult Patients with Bipolar Disorder

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Background: Exposure to childhood trauma has been associated with a more severe course of illness for patients with bipolar disorder; it includes earlier age of onset, more mood episodes, and more suicidal behaviors, amongst other traits. Cognitive impairment has emerged as a core feature of bipolar disorder that predicts functional disability. We compared neurocognitive performance in bipolar patients who report a history of severe childhood Emotional Abuse (EA), Emotional Neglect (EN), Physical Abuse (PA), Physical Neglect (PN), and Sexual Abuse (SA) with bipolar patients without trauma histories.

Methods: 237 adult bipolar patients were given the Childhood Trauma Questionnaire (CTQ) and completed a comprehensive cognitive battery. CTQ scores were used to categorize patients based upon the presence/absence of severe trauma on each of the CTQ subscales (EA, EN, PA, PN and SA). An ANOVA and regression model were used to determine whether childhood trauma type moderated performance on a series of cognitive tasks. The tasks included Matrics Consensus Cognitive Battery (MCCB), 4 subtests of the WAIS, Color Stroop Test, Controlled Oral Word Association (COWAT), and Reading the Mind in the Eyes.

Results: When controlling for age and education, total CTQ score was associated with an impaired global performance on the MCCB ($p=0.035$). A history of PN was significantly associated with a worse composite score on the MCCB ($p<0.01$), particularly in the domains of working memory ($p<0.01$) and visual learning ($p<0.04$). Patients who reported PN also performed significantly worse on WAIS vocabulary ($p<0.04$), and the Stroop ($p<0.03$), than those without PN. Patients with a history of PA were impaired on the visual learning ($p<0.02$) and speed of processing ($p<0.04$) tasks ($p<0.02$), social cognition (Reading the Mind in the Eyes; $p<0.02$), the Stroop ($p<0.01$), and WAIS vocabulary ($p<0.01$) relative to patients without PA.

Conclusions: A history of childhood trauma is associated with impaired cognitive performance in patients with bipolar. This is consistent with prior reports and suggest that early life risk factors contribute significantly to adult outcomes in bipolar patients.

38. Borderline Personality Features in Bipolar Inpatients: Impact on Course and Machine Learning Model use to Predict Rapid Re-Admission

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Background: Prior research indicated that nearly 20% of patients diagnosed with either BD or BPD also met criteria for the other diagnosis. Yet limited data is available concerning the potential impact of co-occurring BPD and/or BPD features on the course or outcome in BD patients. With this in mind, the current study examined this co-morbidity utilizing the standardized Borderline Personality Questionnaire (BPQ).

Methods: 714 adult patients with a primary diagnosis of BD per DSM-IV admitted to the psychiatric unit at an academic hospital in Houston, TX between 7/13 and 7/18. All patients completed BPQ within 72 hours of admission. Statistical analysis was used to detect correlations between BD severity, length of stay (LOS), and the BPQ scores. A machine learning model was constructed to predict the parameters affecting patients' readmission rates within 30 days.
Results: Analysis revealed that, the severity of certain BPD traits at baseline was associated with mood state and the outcome measured by LOS. BD inpatients admitted during acute depressive episodes had significantly higher mean scores on 7 of the 9 BPQ subscales ($p<0.05$) compared to those admitted during acute manic episodes. BD inpatients with greater BPQ scores on 4 out of the 9 BPQ subscales had significantly shorter LOS than those with lower BPQ scores ($p<0.05$). The machine learning model identified six variables as predictors for likelihood of 30 day re- admission with a high sensitivity (83%), specificity (77%), and area under the receiver operating characteristic curve (ROC) of 86%.
Conclusions: While preliminary, these results suggest that BD inpatients with greater levels of BPD features were more likely to have depressive rather than manic symptoms, less psychotic symptoms, and a shorter LOS. Moreover, machine learning models may be particularly valuable in identifying BD patients at highest risk for adverse consequences including rapid re-admission.

39. Comorbid anxiety disorders and quality of life among patients with bipolar disorder

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Background: Anxiety disorders are highly prevalent among patients with bipolar disorder (BD), and seem to be associated with serious functional impairment and higher rates of morbidity. We carried out a study analyzing the impact of comorbid anxiety disorders on the quality of life of BD patients.
Methods: The sample consisted of 81 adult outpatients (30 males/51 females, mean age+ SD=35.98 ± 13.88 years) who met DSM-IV-R criteria for BD (52 BD type I, 17 BD type II, and 12 BD NOS). The diagnosis of BD and the presence of comorbid anxiety disorders was established through the administration of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Quality of Life was measured through the World Health Organization Quality of Life scale (WHOQOL-100). Initially, a two-step cluster analysis was performed, utilizing the different domains of the (WHOQOL-100). The resulting clusters were compared as for the rates of comorbid anxiety disorder. In addition, we utilized analysis of covariance to compare bipolar patients with and without anxiety disorders in regard to their quality of life scores, with age, gender, and mood state as covariates.
Results: 40 BD patients met criteria for comorbid anxiety disorders, and 27 met criteria for more than one disorder. The most prevalent anxiety disorders identified were PTSD (n=19), GAD (n=13), panic disorder (n=13), agoraphobia (n=10), and social anxiety disorder (n=10). The two-step cluster analysis revealed two different clusters of patients, respectively, with high and low quality of life scores. Anxiety Disorders were significantly more prevalent in the low quality of life group (63.8% versus 36.9%, $p=0.015$). Moreover, the comparison between patients with and without comorbid anxiety disorders through ANCOVA revealed lower quality of life scores among patients with an associated diagnosis of anxiety disorder with respect to the physical health (40.95 ± 14.78 vs 51.71 ± 13.27; $F=8.93$, d.f. 1/71, $p<0.01$), psychological health (44.60 ± 24.02 vs 55.02 ± 15.53; $F=8.68$, d.f. 1/71, $p<0.01$), and environment (57.93 ± 20.19 vs. 73.19 ± 14.69; $F=18.5$, d.f. 1/71, $p<0.01$) domains of the WHOQOL scale, even when mood state was included as a covariate.
Conclusions: Our results suggest that comorbid anxiety disorders are associated with substantial impairment in quality of life among patients with BD. The systematic assessment and management of anxiety in BD patients represent a promising and important area for clinical interventions and research.
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40. Age moderates the relationship between affective response control and bipolar disorder in adults

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Background: Bipolar disorder (BD) patients have impairments in neurocognition, including affective processing and affective response control. While studies suggest that cognitive control may decline with age in BD, less is known about age-related changes in affective response control.
Methods: 258 BD participants and 54 healthy controls (HC), ages 18-70, completed the Cambridge Neuropsychological Test Automated Battery Affective Go/No-Go task (CANTAB AGN) to assess affective response control. We examined the relationship between BD and affective response control (number of commission errors and response time), as well as a potential moderating effect of age, using mixed effects linear regression models.
Results: BD participants made more commission errors overall than HC ($p<0.001$), while all participants had slower reaction times on negative than positive target words ($p=0.026$). We found a 3-way group-by-age-by-valence interaction on response time ($p=0.018$), indicating that the relationship between diagnosis and age differed by target valence. For negative target words, older BD participants exhibited a slower response time than either younger BD participants or HC participants. No significant moderating effect of age was observed for positive target words.
Conclusions: These cross-sectional findings suggest an effect of emotional stimuli on response control in adults with BD and that the relationship between BD and affective response control to negative targets may be age-dependent. Longitudinal studies are needed to examine patterns of within-individual changes in affective response control with aging in BD.

41. Treatment Decisions and Course of Illness for Pregnant Women with Bipolar Disorder

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Background: For women with bipolar disorder, the risk of recurrence of an episode of depression, mania, or mixed can be as high as 70% during pregnancy and 40-70% postpartum (Viguera et al., 2007). Many women discontinue medication due to perceived risk to fetal health, such as birth defects or future developmental delays. Discontinuing treatment of bipolar disorder can put both mother and child at risk during and following pregnancy. However, those who continue psychotropic medication during pregnancy still have a risk of recurrence. Some women may add complementary treatments such as yoga, exercise, or mindfulness to assist in mood regulation throughout pregnancy.

Purpose: This survey research examined the rate of recurrences among women who continued medication and those who discontinued medication during the perinatal and postpartum periods. Complementary treatments and associated recurrence rates were explored.

Methods: Retrospective self-report survey data were collected from 108 women. 46 women reported having been diagnosed with bipolar disorder prior to pregnancy and were taking medication at that time. Three were excluded from postpartum outcomes because their pregnancies were not completed. 28/46 (61%) women reported discontinuing medication during pregnancy and 18/46 (39%) women continued taking psychotropic medication. 28/46 (61%) women reported not trying complementary treatment during pregnancy and 18/46 (39%) reported trying one. Data were collected on recurrences of depressive, manic, or mixed episodes during pregnancy, 3-months postpartum, and 4-15 months postpartum.

Results: 12 of the 46 women reported depression during pregnancy. 21 reported depression in the 3-month postpartum period. 19 reported depression during the 4- to 15-month postpartum period. Of the 12 participants who reported a depressive episode during pregnancy, 6 had continued medication and 6 had discontinued; of those 12, 3 had tried complementary treatment during pregnancy and 9 had not. Of the 21 women who reported a depressive episode in the 3-month postpartum period, 5 had continued medication during pregnancy and 16 had discontinued; of those 21, 7 had tried complementary treatment during pregnancy and 14 had not tried one. Of the 19 women who reported having had a depressive episode in the 4-15 months postpartum, 5 had continued medication during pregnancy and 14 had discontinued; of those 19, 7 had tried complementary treatment during pregnancy and 12 had not. Recurrences of mania were also analyzed.

Discussion: These findings further elucidate the challenging decisions faced by pregnant women with bipolar disorder. These data suggest that stopping medication prior to pregnancy may be associated with an increased likelihood for depression in the postpartum period amongst these women. These data also suggest that adding complementary treatments may be associated with decreased depression during perinatal and postpartum periods. Future research will supply data to obstetricians, psychiatrists, physicians, and women with this disorder. Informed decision-making for pregnant women with bipolar disorder is critical for the health of two generations.

42. Spatial Working Memory in Individuals with Bipolar Disorder & Substance Misuse

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Objective: Individuals with bipolar disorder demonstrate significant cognitive impairments (Martínez-Arán et al., 2004). Performance on spatial working memory tasks among individuals with bipolar is mixed (Barret, Kelly, Bell, & King, 2008; Pirkola et al., 2005). Additionally, literature examining the impact of comorbid bipolar and alcohol or cannabis use disorders is mixed (Braga, Burdick, DeRosse, & Malhotra, 2012; Marshall et al., 2012). We examined performance on the Spatial Working Memory (SWM) subtest of the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Participants and Methods: We compared 81 individuals with Bipolar 1 disorder (BP1) (age: 27.84±6.69) to 89 neurotypical individuals (NT) with no history of psychiatric illnesses (age: 27.36±7.05) on SWM. A subset of 50 BP1 individuals with no substance use were compared to 31 BP1 with cannabis use disorder, 35 BP1 with alcohol use disorder, and 20 BP1 with both cannabis and alcohol use disorder.

Results: BP1 committed significantly more errors (22.79±18.57) compared to NT (15.67±14.03) on the SWM task (p=.005) and demonstrated significantly slower first (BP1: 1.29±0.52, NT: 1.11±0.38) and last response times (BP1: 13.81±3.34, NT: 12.43±1.20) (p=.008, p=.001, respectively). There was no significant difference in performance between the BP1 individuals compared to the BP1 with cannabis use/dependence or alcohol use/dependence on either errors (p=.475 and p=.289, respectively) or response times (first: p=.912 and p=.988, respectively; last: p=.655 and p=.380, respectively). Similarly, there was no significant difference in performance between the BP1 compared to the BP1 with alcohol and cannabis use/dependence on errors (p=.867) or response times (first: p=.956 and last: p=.518).

Discussion: Individuals with Bipolar 1 disorder were more prone to error on a measure of SWM compared to NTs. BP1 individuals also demonstrated slower response times throughout the task and appeared less efficient. Use or dependence of either cannabis and/or alcohol did not significantly affect performance. Further research is needed on the mechanisms underlying SWM difficulties among those with Bipolar disorder.

43. The relationship between temperament factors and mood chronicity in bipolar disorder

Caley J Terry, Elise E Trim, Elena M Lamping, David M Marshall, Melvin G McInnis, Kelly A Ryan

Certain personality and temperament factors have been shown to be elevated among individuals with BD, when compared to healthy controls. Previous research shows that individuals with bipolar disorder (BD) have higher scores on neuroticism and openness, but lower scores on agreeableness, conscientiousness, and extraversion (Barnett, et. al., 2011) compared to those without BD. Also, research has shown that there is increased impulsivity in individuals with BD compared to those without BD, but these studies are limited in number. We aimed to compare at our two sub-groups of BD in a longitudinal research cohort of individuals with BD, those with chronic mood course vs remitting mood course, on certain temperament factors. We hypothesized that individuals with a chronic mood course would have higher neuroticism scores and higher ratings of impulsivity than those in the remitting mood course group. Our sample was comprised of those from the Prechter Longitudinal Study of BD, including individuals deemed to have a remitting mood course by study clinicians and a best estimate process (n=253), and those with a chronic mood course (n=475). We compared the means of these two groups on the NEO Personality Inventory, Revised (NEO PI-R) and on the Barratt Impulsiveness Scale (BIS). When looking at impulsivity scores, those with a chronic mood course scored higher on all 1st order factors,): attention ($p < .001$), cognitive instability ($p= .009$), motor ($p= .001$), and self-control ($p= .020$). There were no group differences on cognitive complexity ($p= .059$) and perseverance ($p= .287$).The chronic group scored higher on neuroticism ($p < .001$) and several other facets of the NEO PI-R. However, there were no group differences on overall scores on extraversion ($p= .573$), openness ($p= 1.000$), agreeableness ($p= .116$), or conscientiousness ($p= .305$) domain scores overall. The remitting group had higher scores on several extraversion, agreeableness, and conscientiousness subfacets and this will be discussed further. These findings tell us that individuals with a chronic mood course are more impulsive, anxious, and hostile; while the remitting group shows higher traits of gregariousness, compliance, discipline, and deliberation. It also tells us that while the chronic group scores higher on the neuroticism factor, there are not any differences between chronic and remitting individuals on all other personality domains, suggesting that that chronicity of mood symptoms over the lifetime does not seem to impact many other personality factors outside of those in the neuroticism area.

44. Childhood trauma and other life experiences and their role in mood chronicity of bipolar disorder

Elise E Trim, Caley J Terry, Elena M Lamping, David M Marshall, Melvin G McInnis, Kelly A Ryan

Previous findings from this sample have shown that when compared to those with a remitting mood course of bipolar disorder (BD), individuals with a chronic mood course show no differences across age, education, neuropsychological functioning, or significant clinical illness features. Given these and findings from other research that individuals with BD are more likely to have experienced trauma than healthy controls without BD (Watson, et. al., 2014), we examined the influence of trauma history on chronicity of bipolar illness symptomatology. We aimed to examine how our two mood course samples (e.g., chronic symptoms vs remitting symptoms) differed in terms of childhood trauma and other significant life experiences. We specifically looked at childhood trauma, stressful life events, and relationship experiences with their mother and father. We hypothesized that those with higher reports of trauma and poorer parental relationships would have a more chronic mood course. The sample was selected from Prechter Longitudinal Study of BD, including individuals deemed to have a remitting mood course by study clinicians and a best estimate process (n=253), and those with a chronic course of mood symptoms (n=475). We compared the means of those chronically ill with those with remitting mood symptoms on the childhood trauma questionnaire (CTQ), life events checklist (LEC), and experiences in close relationships (ECR) with their mother and father. We found that those with a more chronic mood course had higher endorsement of childhood trauma, specifically with emotional abuse ($p= .013$, $M= 12.4$, $SD= 5.59$) and emotional neglect ($p= .020$, $M =13.1$, $SD= 5.65$) compare to the remitting group ($M= 10.3$, $SD= 5.26$ and $M=11.3$, $SD= 5.17$), controlling for current mood. No significant group differences were found when measuring the presence of other stressful life events or parental relationship experiences. These findings indicate that the influence of childhood emotional neglect and/or abuse may contribute to the individuals having a more chronic course of bipolar symptoms, and that other later significant life experiences or quality of parental relationships may not be as influential. Previous Prechter research into the Seven-Factor model of BD demonstrates the strong connection between BD and seven key features, including temperament and personality, and life story factors (McInnis, et. al., 2018). Future research should examine these other important factors, such as temperament, personality, and measures of current social support and their influence on the chronicity mood symptoms in BD.

45. Diurnal Patterns as Evidenced by over Eleven Million Smartphone Keystrokes During Daily Usage: An iOS BiAffect Study

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Background: Our group has previously demonstrated that keyboard dynamics, unobtrusively collected on Android smartphones, are associated with cognition and mood outcomes in bipolar disorder (Stange et al., 2018; Zulueta et al., 2018). Here, we report the initial results from a much larger ongoing open-science iOS study on mood and cognition using keyboard dynamics. Through an academia-industry partnership with Sage Bionetworks, our iOS BiAffect project leverages Apple's ResearchKit framework to enroll and study eligible U.S. adults directly via their personal iPhones.

The core technology behind BiAffect is a custom virtual keyboard that replaces the native iOS keyboard and thus allows for the collection of keyboard dynamics and typing kinematics metadata (i.e., not what is typed but how one types). The aims of this study were to establish how typing dynamics may change over the course of the day (i.e., diurnal patterns) and in relation to user demographics (gender and age), while controlling for the way each user interacts with their phone (e.g., one vs. two-handed typing, the number of autocorrects and backspaces [as a proxy of typing errors], and the total number of keypresses for that session).

Methods: We report analyses of our current iOS sample that have successfully undergone data quality control, cleaning and all preprocessing steps, a dataset comprising most active 365 users who collectively contributed more than 16 million keypresses. Of those, 249 participants reported their age and gender. The active users span ages between 18 and 82 with a mean age of 37.7 (71% females 27% males and 2% non-binary). To briefly outline our preprocessing pipeline, all inter-key delay times (i.e., the time between two consecutive keypresses) are calculated within a typing session (i.e., when the keyboard is deactivated or there is a pause between typing for more than 8 secs). Next, each inter-key delay is tagged by the specific keypress categories of the two keypresses involved (here we present only the categories that include character to character inter-key delays). To distinguish between one- vs. two-handed typing (i.e., typing mode), inter-key delay is linearly regressed to the distance between the center of the two touch events-of-interest on a per session basis. The slope of this linear regression and its corresponding p-value are used to classify one-handed (positive slope, $p < 0.05$) and two-handed (negative slope, $p > 0.05$) sessions. This method was validated via test data collected on internal testing phones. The slope and median inter-key delay for each test session were also classified via a Gaussian mixture model with a 99% accuracy. As long inter-key delay times encode events other than word-level typing behaviors (e.g., pauses or being distracted in the middle of typing), to better infer pure typing speed we examined 11,446,443 character-to-character keypresses in ~115k sessions with inter-key delays between 0.1 and 2 seconds to capture general cognitive-motor processes in daily smartphone communication. Then, we conducted hierarchical growth-curve mixed-effects models relating typing speed to other variables of interest. For our 2-level mixed-effects model, we set the dependent variable to be the median inter-key delay on the session-level. Random effects of the models included the user as the cluster (ICC = .81) and allowed each user to have their own slopes of the time of day (both linear and quadratic) and different intercepts for their typing mode. Fixed effects were tested hierarchically adding the time of day, age of the user, typing mode, gender, number of backspaces, autocorrects and characters per session. Model improvement was assessed via deviance testing.

Results: Results supported a second-order polynomial effect of diurnal patterns (first order, $b = 1.10$, $t = 4.83$, $p < .0001$; second-order, $b = 2.66$, $t = 13.40$, $p < .0001$). People typed more slowly in the middle of the night (midnight to 6am) as compared to during midday (noon to 6pm). There was a positive linear effect for age ($b = .070$, $t = 14.60$, $p < .0001$), such that older people typed slower. While there was no significant gender effect ($F = .385$, $p = .819$), a higher number of autocorrects ($b = -.008$, $t = -34.69$, $p < .0001$) and backspaces ($b = -0.0004$, $t = -2.20$, $p < .03$) both resulted in shorter inter-key delays (i.e., faster typing) within the sessions. There was an interaction between diurnal patterns and age, such that older people exhibited a more pronounced slowing in the typing speed at the end of the day/early hours of the morning (first order, $b = .48$, $t = 2.06$, $p < .04$; second-order, $b = .55$, $t = -2.72$, $p < .007$). Furthermore, we observed an interaction between age and the number of autocorrects ($b = -.001$, $t = -5.79$, $p < .0001$). This is likely because faster typing leads to more typos/errors, which then trigger more backspaces/autocorrects and that might be amplified in older users.

Discussion and Conclusion: Our main findings established 1) the utility of collecting keyboard dynamics in the wild to examine the association between typing performance and aging in the context of diurnal patterns, and 2) supports the feasibility of BiAffect in successfully recruiting participants using a crowd-sourced open-science research paradigm. Future analyses will further explore the relationship between keyboard dynamics and mood symptoms, diagnoses, as well as major domains of cognition.

46. Early response to ketamine infusion for depression: comparison between genders

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Background: Ketamine, a non-competitive NMDA receptor antagonist, has been used for treatment-resistant depression (TRD) and is characterized by a rapid onset of action. Several studies have shown that a single-dose infusion of ketamine can rapidly decrease suicidal ideation and provide antidepressant effects. Although gender seems to affect response to other antidepressants, its role in ketamine response has not been fully studied in the clinical setting. In animal studies, ketamine was found to be metabolized differently between sexes with females having greater concentrations of ketamine over the first 30 minutes in the brain and plasma than males, due to slower clearance rates and longer half-lives. In addition, estrogen and progesterone may modulate the effects of ketamine on synaptic plasticity.

Methods: The study was approved by the Institutional Review Board and participants signed consent. Patients (n=22, 12 male, 10 females) with TRD received their first 0.5 mg/kg continuous intravenous infusion of ketamine over 40 minutes for treatment-resistant depression as standard of care. Treatment response was measured using the clinician-rated Montgomery Asberg Depression Rating Scale (MADRS) and the self-report PHQ-9. Scores at the 2nd visit (2-5 days after the 1st injection) were compared to scores at baseline. Assessments were performed before the injections.

Results: There was no difference in age between the two groups (52.5±17.6 for men; 52.7±12.7 for women, p = 0.971). Patients presented with moderate to severe depression with average MADRS score of 34.3±8.6 at Baseline and no difference between genders (p = 0.55). The average MADRS scores decreased 8% for men (from 33.5±9.5 to 30.7±9.4) and 27% for women (from 35.2±.4 to 25.6.0±7.8, p <0.05 Kruslal-Wallis test) between the 1st and 2nd assessments. After one ketamine injection, 30% of women and 0% men had a decreased in MADRS score ≥50%, defined as response to treatment.
Conclusion: Data from this small sample suggest that females may have a higher rate of early response to a low-dose ketamine infusion than men. However, other variables may account for the results. A recent study (Freeman et al, 2019) using HAMD-6 scores did not detect difference between men and women. Different scales and study design may explain the discrepancy. Since early response to one dose of ketamine has been suggested as a good predictor for long term response, determining if there is a gender difference in early response will be important to validate this index for all patients.

47. Screening for Perinatal Depression using the CAT-MHTM in Urban-Dwelling African American and Hispanic Women

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Background: Ketamine, a non-competitive NMDA receptor antagonist, has been used for treatment-resistant depression (TRD) and is characterized by a rapid onset of action. Several studies have shown that a single-dose infusion of ketamine can rapidly decrease suicidal ideation and provide antidepressant effects. Although gender seems to affect response to other antidepressants, its role in ketamine response has not been fully studied in the clinical setting. In animal studies, ketamine was found to be metabolized differently between sexes with females having greater concentrations of ketamine over the first 30 minutes in the brain and plasma than males, due to slower clearance rates and longer half-lives. In addition, estrogen and progesterone may modulate the effects of ketamine on synaptic plasticity.
Methods: The study was approved by the Institutional Review Board and participants signed consent. Patients (n=22, 12 male, 10 females) with TRD received their first 0.5 mg/kg continuous intravenous infusion of ketamine over 40 minutes for treatment-resistant depression as standard of care. Treatment response was measured using the clinician-rated Montgomery Asberg Depression Rating Scale (MADRS) and the self-report PHQ-9. Scores at the 2nd visit (2-5 days after the 1st injection) were compared to scores at baseline. Assessments were performed before the injections.
Results: The average overall PND rate per visit on CAD-MDD™ was 14.95% (17.9% in African-Americans and Latinas), with 4% in the moderate/severe categories on CAT-DI. The rate per visit on average of PND on the PHQ-9 was 10.8% (9.9% in African-Americans and Latinas). There was a trend toward an association between screening measure and PND outcome, with CAD-MDD™ detecting higher incidence of PND compared to PHQ-9 (p=.09). CAT-DI and PHQ-9 scores significantly correlated (r=0.70, p<.001). Results were similar in minority women.
Conclusions: CAD-MDD™ detected higher rates of PND than the PHQ-9, particularly for minority women. Psychiatric diagnostic interviews are underway to compare the sensitivity of the two measures. These data support the continued future use of the CAT-MHTM in screening for perinatal mental health.

48. A Phase 3, Double-Blind, Placebo-Controlled Trial of SAGE-217 in Postpartum Depression: Assessment of Depressive Symptoms Across Multiple Measures (Sage Therapeutics, Inc)

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Background: An estimated 10-20% of new mothers globally experience postpartum depression (PPD) each year, making PPD one of the most common medical complications during and after pregnancy. GABAergic dysfunction has been implicated in the etiology of both PPD and major depressive disorder (MDD). SAGE-217, an investigational oral GABAA receptor PAM demonstrated rapid (by Day 2) and statistically significant improvement of symptoms of depression in subjects with MDD in a double-blind, randomized, placebo-controlled trial. This Phase 3 study (NCT02978326) is the first double-blind, randomized, placebo-controlled trial of SAGE-217 in women with PPD.
Methods: Women (n=151), ages 18-45, ≤6 months postpartum, diagnosed with PPD (defined here as a major depressive episode with onset in the 3rd trimester or ≤4 weeks postpartum), and a Hamilton Rating Scale for Depression (HAM-D) total score ≥26 at baseline were enrolled. Randomization was 1:1 to receive either SAGE-217 30 mg or placebo capsules for 14 days, with follow-up through Day 45. The Day 15 change from baseline in HAM-D total score was the primary endpoint. The change from baseline in HAM-D total score at all other time points, HAM-D response (total score reduction ≥50%), HAM-D remission (total score ≤7), and the change from baseline in the Montgomery-Åsberg Depression Rating Scale (MADRS) were secondary endpoints. Adverse event (AE) reports and standard clinical measures were used to assess safety and tolerability.

Results: SAGE-217 achieved the primary endpoint of a significant reduction in least-squares (LS) mean HAM-D total score versus placebo (-17.8 vs. -13.6, p=0.0028) at Day 15. Significant differences favoring SAGE-217 vs. placebo were observed at Day 3 (p=0.0252) and were sustained through Day 45 (p=0.0027). HAM-D response (72% vs. 48%, p=0.0049) and remission rates (45% vs. 23%, p=0.0110) were significantly greater in the SAGE-217 group compared to the placebo group at Day 15, and these clinically and statistically significant improvements were maintained through Day 45 (response p=0.0216; remission p=0.0091). At Day 15, SAGE-217 was associated with a significant decrease from baseline in LS mean MADRS score (-22.1 vs. -17.6, p=0.0180). The most common (≥5%) AEs in the SAGE-217 group were somnolence, headache, dizziness, upper respiratory tract infection, diarrhea, and sedation.
Conclusions: In this Phase 3, double-blind, randomized, placebo-controlled trial, SAGE-217 treatment resulted in rapid (by Day 3), statistically significant, and sustained (over the study period) reductions in depressive symptoms in women with PPD. SAGE-217 was generally well-tolerated supporting the further development of SAGE-217 as a potential treatment for PPD.

49. GUIDED HAM-D6 (Assurex Health/Myriad Genetics)

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Background: The Genomics Used to Improve DEpresssion Decisions (GUIDED) trial assessed outcomes associated with combinatorial pharmacogenomic (PGx) testing in patients with major depressive disorder (MDD). Analyses used the 17-item Hamilton Depression (HAM-D17) rating scale; however, studies demonstrate that the abbreviated, core depression symptom-focused HAM-D6 rating scale may have greater sensitivity toward detecting differences between treatment and placebo. However, the sensitivity of HAM-D6 has not been tested for two active treatment arms. Here, we evaluated the sensitivity of the HAM-D6 scale, relative to the HAM-D17 scale, when assessing outcomes for actively treated patients in the GUIDED trial.
Methods: Outpatients (N=1,298) diagnosed with MDD and an inadequate treatment response to >1 psychotropic medication were randomized into treatment as usual (TAU) or combinatorial PGx-guided (guided-care) arms. Combinatorial PGx testing was performed on all patients, though test reports were only available to the guided-care arm. All patients and raters were blinded to study arm until after week 8. Medications on the combinatorial PGx test report were categorized based on the level of predicted gene-drug interactions: 'use as directed', 'moderate gene-drug interactions', or 'significant gene-drug interactions.' Patient outcomes were assessed by arm at week 8 using HAM-D6 and HAM-D17 rating scales, including symptom improvement (percent change in scale), response (≥50% decrease in scale), and remission (HAM-D6 ≤4 and HAM-D17 ≤7).
Results: At week 8, the guided-care arm demonstrated statistically significant symptom improvement over TAU using the HAM-D6 scale (Δ=4.4%, p=0.023), but not using the HAM-D17 scale (Δ=3.2%, p=0.069). The response rate increased significantly for guided-care compared with TAU using both HAM-D6 (Δ=7.0%, p=0.004) and HAM-D17 (Δ=6.3%, p=0.007). Remission rates were also significantly greater for guided-care versus TAU using both scales (HAM-D6 Δ=4.6%, p=0.031; HAM-D17 Δ=5.5%, p=0.005). Patients taking medication(s) predicted to have gene-drug interactions at baseline showed further increased benefit over TAU at week 8 using HAM-D6 for symptom improvement (Δ=7.3%, p=0.004) response (Δ=10.0%, p=0.001) and remission (Δ=7.9%, p=0.005). Comparatively, the magnitude of the differences in outcomes between arms at week 8 was lower using HAM-D17 (symptom improvement Δ=5.0%, p=0.029; response Δ=8.0%, p=0.008; remission Δ=7.5%, p=0.003).
Conclusions: Combinatorial PGx-guided care achieved significantly better patient outcomes compared with TAU when assessed using the HAM-D6 scale. These findings suggest that the HAM-D6 scale is better suited than is the HAM-D17 for evaluating change in randomized, controlled trials comparing active treatment arms.

Notes

LOCAL RESOURCES

Urgent Care & Pharmacies

Concentra Urgent Care
8am - 6pm (Mo-Fr)
3131 S State St
Ann Arbor, MI
(734) 213-6482

CVS Pharmacy
9am - 9pm (Mo-Fr)
10am - 6pm (Sa-Su)
1700 S Industrial Hwy
Ann Arbor, MI
(734) 827-7980

University of Michigan Hospital Emergency Room
1500 E Medical Center Dr
Ann Arbor, MI
(734) 936-6666

Shopping & Convenience

Briarwood Mall
10am - 9pm (Mo-Sa)
11am - 6pm (Su)
100 Briarwood Cir
Ann Arbor, MI
(734) 769-9610

Meijer
Open 24 hrs
3145 Ann Arbor-Saline Rd
Ann Arbor, MI
(734) 769-7800

Speedway
Open 24 hrs
4001 S State St
Ann Arbor, MI
(734) 665-0513

Target
8am - 11pm (Mo-Sa)
8am - 10pm (Su)
2000 Waters Rd
Ann Arbor, MI
(734) 996-0700

NNDC 2020

The NNDC Annual Conference is going on the road - to Rochester, Minnesota! Join us September 30-October 2, 2020 as we host the 2020 NNDC Annual Conference together with the Mayo Clinic Department of Psychiatry and Psychology!