



The 25th Nevada Psychiatric Association National  
Psychopharmacology Update  
February 13-15, 2020  
Paris Hotel, Las Vegas

Brian Espinoza MD  
Interventional Psychiatry  
Electroconvulsive Therapy (ECT)—  
Adult & Adolescent  
IV Ketamine for Depression  
Genetic Testing  
Enhanced Medication Management

This annual conference continues to grow each year; this year, with attendance for 2020 in approximating 1,655 attendees. Some highlights from notes taken include:

**PREDICTION OF DISEASE VULNERABILITY & TREATMENT RESPONSE IN MOOD DISORDERS (Charles B. Nemeroff, MD, UT Austin)**

The speaker did a genetic analysis of patients from a previous study and looked at the genes which dictate 5-HT transporter binding. He found no differences in this genetic domain between non-responders, partial responders, and remitters (paper in submission).

Other areas of exploration; Genetic variants being fed into AI programs to find the magic combination of polygenetic diagnoses; EEGs with machine learning capabilities may become predictive tools.

**NEUROBIOLOGY & TREATMENT OF PTSD (Charles B. Nemeroff, MD, UT Austin)**

IV Ketamine (often advertised as effective for PTSD) has a recent study looking at reduction in PCL-5 scores (self-reported PTSD checklist). Participants had an average pre-Rx score of 55. Ketamine responders had a post-Rx average score of 12; however the control drug, a rapid and short acting Benzodiazepene, gave an average post-Rx score of 22.

An ECT study in Veterans with MDD & PTSD demonstrated drops in both Depression and PTSD scores.

A 2019 Stellate Ganglion Blockade Study had 113 patients with an average pre-Rx PCL of 50. Active Rx patients had an average 13 point drop, and Sham Rx patients had a 6 point drop; essentially no better than Psychotherapy.

A recent French Review found a 3.5 fold elevation of Bipolar Disorder in PTSD Patients with Childhood Trauma, along with an elevated suicide risk.

**MECHANISM OF ACTION & NEW ANTIDEPRESSANT DEVELOPMENT (Alan Schatzberg, MD, Stanford)**

5-HT hallucinatory agonists—the Psilocybins: Problematic to study as it is difficult to blind because of dissociative and hallucinatory experiences inherent in these compounds.

A new trial studying psilocybin assisted psychotherapy is underway.

NMDA antagonists:

S-Ketamine—1 of 3 blinded trials was positive. 1 maintenance study was positive, but treatment curves remained parallel after day 2. An S-Ketamine Discontinuation Trial showed a relapse rate twice that of coming off of an antidepressant alone, i.e. double the relapse rate for those coming off of S-Ketamine even though an antidepressant was left on board.

GABA system

Brexanolone, a Neurosteroid Progesterone derivative; no one in the audience had experience with the compound...likely not going to be used widely due to delivery and monitoring hurdles.  
SAGE-217; a minor separation from placebo up to day 12, but nothing clinically significant beyond that.  
The Cholinergic System; Botoxin injections: In one study the antidepressant effect preceded the cosmetic effect. A change in f-MRI response of prefrontal to amygdala activation was noted.  
The American Suicide Foundation has issued a grant to look at combining IV Ketamine with ultra-low dose Buprenorphine vs. IV Ketamine with placebo in hopes of potentiating the anti-suicidal effects of IV Ketamine. (This was based on a previous study demonstrating that Naltrexone blocks IV Ketamine anti-suicidal effects).

### **BRAIN STIMULATION STRATEGIES FOR TREATMENT RESISTANT DEPRESSION (Alan Schatzberg, MD, Stanford)**

TMS—A meta-analysis of routine TMS did not show high response and remission rates.

i-TBS is an accelerated and accentuated form of TMS which may reduce treatment periods from 4-6 weeks to 1-2 weeks.

r-TMS (shorter treatment sessions) will likely have future success with ongoing treatment and research.

VNS—A 2017 study followed implanted patients out to 5 year and observed clinical meaningful effects. A large scale multi-center trial is currently underway.

DBS—to date, there has been no real clear positive prospective data gathered. A recent study of Sub-genuate targets was cancelled due to lack of a positive signal.

### **UPDATE ON THE TREATMENT OF SCHIZOPHRENIA (Donald Guff, MD, NYU)**

A meta-analysis intimated that Second Generation Atypical have reduced the overall risk of Tardive Dyskinesia by 70%. A 2018 trial in the Lancet, suggest a 10 week trial of an antipsychotic in the treatment of Schizophrenia.

Cariprazine has notable D-3 partial agonism, showing a greater benefit for negative symptoms compared to Risperidone. One of the active metabolites has a half-life ranging from 1 to 3 weeks.

Lumateperone had just been released at around conference time. An atypical with the addition of glutamatergic modulation.

Cannabidiols; several large studies are ongoing.

Two new drugs not acting at the dopamine receptor;

TAARI-1(Trace Amine Associated Receptor); modulates dopamine transmission; a 4 week trial had initial positive results

Xanomeline (KarXT), an M-1/M-4 agonist shows promise

### **BIDIRECTIONAL RELATIONSHIPS OF SLEEP DISORDERS FOR PSYCHIATRISTS (John W. Winckelman, MD, PhD, Harvard)**

PTSD in Veterans; one study showed that a Pre-Deployment Sleep problem predicted Post-Deployment PTSD and insomnia.

A 2019 European review and meta-analysis showed the following;

Sleep disturbance predated over one year the onset of Childhood Bipolar Disorder.

Hypersomnia precedes Depressive Episodes. Sleep Deprivation preceded Manic

Episodes. Insomnia was bidirectional, precedes either mania or depression.

#### RLS (Restless Legs Syndrome)

A longitudinal study showed a 50% increased risk of depression at 6 year follow-up.

“Bidirectional”; a German study showed that a diagnosis of Depression led to an increased risk of RLS.

Suicidal Ideation is more common in RLS, and Suicide Attempts were increased in a prospective study.

Zolpidem; a 2019 study published in the AJP showed a decreased risk of suicidality compared to Placebo in the treatment of Sleep Disturbances.

SSRI's—a common cause of disrupted sleep; a high association with PLMS (Periodic Limb

Movements of Sleep), and, the most common cause of RBD (REM Sleep Behavioral Disorder).

RBD—looks like a potential 5- to 10-year predictor of Parkinson's Disease

The British Journal of Psychiatry Paper suggesting an association between Benzodiazepenes and Dementia—"a confounding by indication"—we know that patients with Mood and Sleep Disorders have a higher risk of Dementia Disorders.

The speaker reviewed all of the medications that we all use for sleep; at the end of the talk, the emphasis was for online CBT-I (Insomnia) programs available.

### **AUTISM (Eric Hollander MD, Montefiore)**

Oxytocin—a centrally acting hormone implicated in social cognition and trust; missed the window for drug development; can be obtained at compounding pharmacy's, but at a high cost; mixed results

TSO (Trichuris Suis Ova)—pig whipworm eggs; ingested into our gut microbiome; a pilot study showed decreases in the rigidity domain vs. placebo

Cannabidivarin—no THC content; no "high"; has anticonvulsant and anti-inflammatory effects; no side effects like atypical and anticonvulsants; a controlled study with an N = 100 currently underway.

Medical Marijuana—legal for use in ASD in Rhode Island and Pennsylvania

### **PHARMACOTHERAPY OF ADHD ACROSS THE LIFESPAN (Jeffrey H. Newcorn, MD, Mt. Sinai)**

Jornay PM—given at night

Adhanasia XR—"super" long acting

Stimulants in ADHD and Bipolar Disorder—a Swedish National Registry review showed a 10 times greater risk of inducing mania if mood not stabilized first

### **TREATMENT OF BIPOLAR DISORDER (Bruce J. Schwartz, MD, Montefiore)**

A 2016 UK review of 5,000 records showed that Lithium was superior to Depakote, Olanzapine and Quetiapine for Maintenance Treatment. In numerous non-U.S. countries, Lithium is the standard of care for Maintenance Treatment. The speaker opined that once a day dosing of Lithium, with levels of 0.5-0.6 seemed to mitigate any adverse renal effects.

In many European countries, Quetiapine is used first line for Bipolar Depression.

Topiramate "has no effect on mood states in Bipolar Disorder"; a pharmaceutical firm was fined \$180 million for making claims of effectiveness.

Gabapentin "not effective" in Bipolar Disorder.

Tamoxifen seems to have anti-manic properties.

Pramipexole—the speaker suggested the following dosing paradigm; start at 0.5 mg hs; increase by 0.5 mg q 3 days; mean dose = 2.5 mg; dose range = 1-5 mg

### **RISKS & BENEFITS OF BENZODIAZEPENES (David V. Sheehan, MD, USF)**

An NIDA study—morbidity and mortality with Benzodiazepenes had remained at a flat line for decades, until the addition of Opioids came into play

Diazepam, it was suggested, has the fastest onset of action due to its lipophilicity

Based on a reported 1/2 life of 7 hours, the speaker suggested dosing Clonazepam tid, as opposed to the traditional bid dosing

### **POTENTIALLY RAPID ACTING TREATMENTS FOR INDIVIDUALS WITH SUICIDAL IDEATION AND BEHAVIOR (Gerard Sanacora, MD, PhD, Yale)**

A 2020 meta-analysis of all Ketamine Trials—25 reports, more than 500 patients; "IV Ketamine has a role for the rapid reduction of Suicidal Ideation, though it appears to be a short-term response"

S-Ketamine—the study which showed a rapid overall improvement, and led to FDA approval, was conducted under a "Super Standard of Care"; the ASPIRE studies (Phase 3; to be published at time of conference) demonstrated a 50% Remission Rate, 10% better than standard of care for MDD

The speaker noted the challenges of these studies, citing a European study published in the JCP, 2009, with 50% of subjects committing a serious suicide attempt, initiating that suicidal thought within 10 minutes of attempting.

### **THE IMPACT OF RESEARCH FINDINGS ON OUR UNDERSTANDING AND TREATMENT OF SUICIDAL BEHAVIOR (John G. Keilp, PhD; Columbia)**

A 2017 Journal of Affective Disorders study by the speaker showed that during treatment of depression, decreases in subjective symptoms are linear, and possibly driving decreases in Suicidal Ideation, while somatic symptoms were disparate and/or lagged behind improvements in suicidality.

Cognitive problems do not track along with depression severity, but certain domains may be markers In preparation ideators versus attempters, differences in Neuropsychological testing were noted;

- Past attempters showed more deficits in attention, cognitive control, and memory

- Violent attempts were associated with deficits in decision making

- Executive functioning may be more intact in those attempters who make more carefully planned attempts, especially using non-violent means

The speaker discussed 2 studies using Cellphone based applications for suicide monitoring in Adolescents;

- EMA (Ecological Momentary Assessment); requires responses to cued sets of questions asked throughout the day; difficult to correlate mood and affective symptoms with onset of Suicidality, but graphs showed “terrible and rapid” fluctuations in Suicidal Ideation.

- Passive Monitoring; uses text and call data, geolocation, accelerometer info, etc.; TBD

### **ADDING A SPECTRUM APPROACH TO BIPOLAR DIAGNOSIS (James Phelps; [PsychEducation.org](http://PsychEducation.org))**

The speaker discussed screening instruments;

- The Bipolarity Index; used in the STEP-BD studies

- The Bipolar Spectrum Diagnostic Scale

- Mood Check; Bipolar Spectrum Diagnostic Scale plus a screen for non-manic Bipolar

- Markers (available on speakers website; see above)

It is noted in the FDA package insert for antidepressants that patients should be adequately screened to determine if they are at risk for Bipolar Disorder

An International Society of Bipolar Disorder 2013 Report indicated that Anxiety is a Bipolar symptom, accurately described as “frantically anxious”

E-Couch “Mood Gym”; promoted by the Australian National Health Service; a free on-line CBT driven program for depression and anxiety

### **TREATING THE BIPOLAR MAJORITY (James Phelps; [PsychEducation.org](http://PsychEducation.org))**

CBT-IB (Cognitive Behavioral Therapy for Insomnia, Bipolar Version)— 2016; well validated; available on speaker’s website (see above); the manual is 4 pages and downloadable for free

Regular Sleep Rhythm—involves a “Wind Down Routine” and a “Start Up Routine

Dark Therapy—validated by a RCT published in The Journal of Bipolar Disorder, 2016; involves the use of Amber Lens (special glasses) which filter out blue light, and helps reset circadian rhythms; all info available on speaker’s website (speaker does not profit from Amber lens purchases); can be done with Amber light bulbs also, if one does not want to purchase/wear lenses

#### Lithium

- 2018 Journal of Crisis Intervention and Suicide Prevention—Alabama Counties; positive correlation between concentration of Lithium in water supply and Suicide Rates

- 2019 British Journal of Psychiatry—N = 60; 3 year progression from MCI to Alzheimer’s; Control Group = 30%; Lithium Group (levels 0.25-0.5) 16%

- 2017 JAMA-Psychiatry—small signal for Lithium prevention of Dementia

- To Be Published; Lithium Collaborative Care Study—N = 641; doses of 150 to 600 mg daily with an average level of 0.32; anti-dementia signal and lower PHQ-9 scores

2016 Amsterdam Study—the more Antidepressants a Bipolar patient has been exposed to, the less likely they are to respond to indicated Bipolar treatments  
<https://www.survivingantidepressants.org>; a website that may be helpful for patients needing to taper off of antidepressants

**A CAUTIONARY TALE ABOUT INTEGRATIVE MEDICINE: DON'T BELIEVE EVERYTHING YOU HEAR (Phillip R. Muskin, MD; Columbia)**

CBD is a potent inhibitor of CYP-3A4 and CYP-2D6; potentially effective metabolism of TCA's, Clozapine, Tamoxifen et al.

CBD + Divalproex; reports of elevated liver enzymes and injury

CBD and Dementia; not a “big effect”, but “maybe”

[ConsumerLab.com](http://ConsumerLab.com); a prescription website suggested by the speaker that analyzes prescription medications and the various Integrated Medicine compounds that are not subjected to FDA scrutiny. This organization uncovered the issues with bioavailability of generic medications such as Bupropion LA, Venlafaxine LA, et al.

ArginMax & Maca; 2 compounds available for low libido (for women) and erectile dysfunction; contraindicated in patients with estrogen sensitive tumors, endometriosis, prostate CA, contain Vitamin K which may interfere with anticoagulants

**ETHICS IN THE DIGITAL AGE AND SOME CONSTANT STUFF (Colleen Coyle, JD; General Counsel, American Psychiatric Association)**

70% of Google queries are health-related

Goldwater Rule—basically, we can not speak out about an individual, however, we can speak out about a policy; only applicable to APA members

ESA (Emotional Support Animal) Letters—the speaker suggested that we document that we have “no knowledge of animal status, e.g. vaccinations, viciousness,” etc.

Apps—it was suggested that if we were to utilize apps in our practice, that we review Privacy Standards, i.e. selling data to 3rd parties for direct marketing

Law Enforcement Agencies have access to Prescription Monitoring Programs