

## **PSYCHIATRIC SUMMARY XXIII**

**Winter 2018**

*By Frederick Langheim, MD, PhD*

This issue marks the twenty-third installment consolidating recent clinical updates, mental health policy news, popular press news patients may be reading, and changes in the landscape of psychiatry in Wisconsin.

### **OF GENERAL INTEREST**

#### **Stimulants in Sports Supplements:**

A recent analysis of sport and weight loss supplements found multiple experimental stimulants present (Clinical Toxicology, Cohen et al., [LINK](#)).

#### **Burnout Departures at Stanford Cost \$7.75 Million a Year:**

As reported at the AMA Wire (11/17/2017, Sara Berg, [LINK](#)) Stanford university is making attempts to quantify the cost of physician burnout calculating a minimum replacement cost per departing physician of \$250,000 ranging up to a million dollars.

#### **Feds Tracking Opiate Prescribers:**

According to the Associated Press (Gurman, 1/1/2018, [LINK](#)) the Justice Department has an Opioid Fraud and Abuse Detection Unit, actively tracking which physicians “are prescribing the most, how far patients will travel to see them and whether any have died within 60 days of receiving one of their prescriptions, among other information.” According to the article, Deputy Attorney General Rod Rosenstein said the DOJ “will consider going after any law-breaker, even a pharmaceutical company, as it seeks to bring more cases and reduce the number of unwarranted prescriptions.”

### **CLINICAL PSYCHIATRY IN THE NEWS, IN BRIEF**

#### **Alzheimer’s May Start Anywhere in the Body?**

According to research published in Molecular Psychiatry (Bu et al., [LINK](#)) in a mouse model of Alzheimer’s disease, blood derived amyloid- $\beta$  can induce Alzheimer disease pathology in wild type mice.

#### **Sertraline no Better than Placebo in Advanced Kidney Disease:**

A multi-center randomized controlled study of sertraline versus placebo in chronic kidney disease (JAMA, Hedayati et al., [LINK](#)) found that sertraline was no better than placebo in managing depression and was prone to more side effects. For a review of the article, refer to Walther et al., ([LINK](#)) same issue.

#### **Debunking Adult Onset ADHD?**

According to the work of Sibley et al. (American Journal of Psychiatry, [LINK](#)), recent birth-cohort studies of late onset ADHD have been marred by incomplete psychiatric history and lack of consideration of alternative causes of dysfunction. In their longitudinal study of the normative comparison group in the Multimodal Treatment Study of ADHD, they studied 239 individuals without childhood ADHD using 8 (parent, teacher and self report) assessments from mean age just under 10 to mean age 24. They found:

Approximately 95% of individuals who initially screened positive on symptom checklists were excluded from late-onset ADHD diagnosis. Among individuals with impairing late-onset ADHD symptoms, the most common reason for diagnostic exclusion was symptoms or impairment occurring exclusively in the context of heavy substance use. Most late-onset cases displayed onset in adolescence and an adolescence-limited presentation. There was no evidence for adult-onset ADHD independent of a complex psychiatric history.

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### **Donepezil + Memantine Better than Monotherapy:**

According to a meta-analysis published in PLoS One (Chen et al., 8/21/2017 [LINK](#)) combining donepezil with memantine may be more effective in slowing cognitive decline than monotherapy.

### **Decline Requests and Decline Your Satisfaction Scores:**

Perhaps surprising to no one among our readers, a JAMA article (Jerant et al., 11/27/2018, [LINK](#)) indicated that physician denial of some requests resulted in lower patient satisfaction scores.

Specifically:

Compared with fulfillment of the respective request type, clinician denials of requests for referral, pain medication, other new medication, and laboratory test were associated with worse satisfaction

The article suggested that training with respect to providing denials involving increased patient education, may potentially ameliorate the struggle, noting that antibiotic refusal did not follow this pattern.

### **AVATAR Therapy May Benefit Those with Auditory Hallucinations:**

Published in the Lancet Psychiatry, Craig et al. ([LINK](#)) studied the use of therapy in which those who hear voices engage with a digital representation of their persecutor, voiced by the therapist, decreasing hostility and ceding control. This single location single-blind study of 150 eligible randomized subjects used a primary outcome of reduction in auditory verbal hallucinations at 12 weeks, measured by total score on the Psychotic Symptoms Rating Scales Auditory Hallucinations (PSYRATS–AH). They found that:

The reduction in PSYRATS–AH total score at 12 weeks was significantly greater for AVATAR therapy than for supportive counselling (mean difference  $-3.82$  [SE 1.47], 95% CI  $-6.70$  to  $-0.94$ ;  $p < 0.0093$ ). There was no evidence of any adverse events attributable to either therapy.

### **Stimulants and Pregnancy:**

Appearing in JAMA Psychiatry, (Huybrechts et al., [LINK](#)) authors findings included:

Results from this cohort study including 1.8 million pregnancies nested in US Medicaid Analytic eXtract (2000-2013), with replication of initial safety signals in 2.5 million singleton pregnancies in the Nordic Health registries (2003-2013), suggest a potential small increased risk of cardiac malformations associated with methylphenidate use (pooled relative risk, 1.28; 95% CI, 1.00-1.64); an increase in the risk of this malformation type was not found for amphetamines. Neither methylphenidate nor amphetamines were associated with an increased risk for malformations overall.

### **Spindle Decoupling and Age Related Memory Loss:**

According to research published in Neuron ([LINK](#)) Helfrich et al. sought to explore whether coupled interaction between slow-wave oscillations and sleep spindles correlated with memory retention and reduced coupling with cognitive aging.

Combining electroencephalography (EEG), structural MRI, and sleep-dependent memory assessment, we addressed these questions in cognitively normal young and older adults. Directional cross-frequency coupling analyses demonstrated that the slow wave governs a precise temporal coordination of sleep spindles, the quality of which predicts overnight memory retention. Moreover, selective atrophy within the medial frontal cortex in older adults predicted a temporal dispersion of this slow wave-spindle coupling, impairing overnight memory consolidation and leading to forgetting. Prefrontal-dependent deficits in the spatiotemporal coordination of NREM sleep oscillations therefore represent one pathway explaining age-related memory decline.

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### **Esketamine in Phase II Success:**

Published in JAMA Psychiatry ([LINK](#)) Daly et al used a double-blind, doubly randomized, delayed-start, placebo-controlled study to test the safety and efficacy of intranasal esketamine in treatment resistant depression.

Sixty-seven participants (38 women, mean [SD] age, 44.7 [10.0] years) were included in the efficacy and safety analyses. Change (least squares mean [SE] difference vs placebo) in MADRS total score (both periods combined) in all 3 esketamine groups was superior to placebo (esketamine 28 mg: -4.2 [2.09],  $P = .02$ ; 56 mg: -6.3 [2.07],  $P = .001$ ; 84 mg: -9.0 [2.13],  $P < .001$ ), with a significant ascending dose-response relationship ( $P < .001$ ). Improvement in depressive symptoms appeared to be sustained (-7.2 [1.84]) despite reduced dosing frequency in the open-label phase. Three of 56 (5%) esketamine-treated participants during the double-blind phase vs none receiving placebo and 1 of 57 participants (2%) during the open-label phase had adverse events that led to study discontinuation (1 event each of syncope, headache, dissociative syndrome, and ectopic pregnancy).

## **MENTAL HEALTH IN THE POPULAR PRESS**

### **AI IDs SI?**

In a heavily publicized study published in Nature Human Behavior ([LINK](#)) Just et al., used machine learning algorithms to differentiate those who had attempted suicide from those who had not. The study used Gaussian Naive Bayes machine learning to:

identify such individuals (17 suicidal ideators versus 17 controls) with high (91%) accuracy, based on their altered functional magnetic resonance imaging neural signatures of death-related and life-related concepts. The most discriminating concepts were 'death', 'cruelty', 'trouble', 'carefree', 'good' and 'praise'. A similar classification accurately (94%) discriminated nine suicidal ideators who had made a suicide attempt from eight who had not. Moreover, a major facet of the concept alterations was the evoked emotion, whose neural signature served as an alternative basis for accurate (85%) group classification.

### **Mental Health Access Delays:**

The Boston Globe (Fryer, 10/31/2017, [LINK](#)) ran an article on the sometimes months long delays in accessing mental health care in the Boston area.

### **FDA Approves Opiate Treatment Device:**

In a release 11/15/2017 ([LINK](#)) the FDA approved marketing of a transdermal cranial nerve stimulating device purported to reduce clinical opiate withdrawal rating scale scores.

### **Army Rebuked for Lowering Mental Health Standards:**

Appearing in USA Today (Tom Vanden Brook, 11/14/2017, [LINK](#)) the Army received criticism for considering allowing admission to individuals who have engaged in non-suicidal self-mutilating behavior.

### **Rises in Suicide and Social Media Use Linked?**

The AP (Lindsey Tanner, 11/14/2017, [LINK](#)) reported on a study published in Clinical Psychological Science correlating teen social media use increases with increases in suicide rates.

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### **Rise in Young Female Self Harm:**

As reported in AMA Morning Rounds 11/24/17:

In "Science Now," the Los Angeles Times (11/21, Healy) reports that from "2009 to 2015," US emergency departments "saw a sharp rise in treatment of girls 10 to 24 who intentionally injured themselves." What's more, "among girls 10 to 14 years old, rates of" ED "visits for treatment of self-harm surged 18.8% yearly between 2009 and 2015," research revealed. These "data on non-fatal self-injury," which "were gathered by the Centers for Disease Control and Prevention's National Center for Injury Prevention and Control," were published Nov. 21 as a research letter in the Journal of the American Medical Association.

In "To Your Health," the Washington Post (11/21, Eltagouri) reports, "Self-harming behaviors like ingesting poisons, cutting and overdosing on drugs are strong indicators of suicide – the second-leading cause of death among people between 10 and 24 years old in 2015, according to data gathered by the Centers for Disease Control and Prevention's National Center for Injury Prevention and Control."

The AP (11/21, Tanner) reports that reasons for the increase are not clear, "but some mental health experts think cyberbullying, substance abuse and economic stress from the recent recession might be contributing."

### **Projected Marked Increases in Deaths from Drugs, Alcohol and Suicide:**

Appearing in multiple news outlets, a report from Trust for America's Health (TFAH) and Well Being Trust (WBT) titled Pain in the Nation ([LINK](#)) suggested that if current trends continue, death rates from these causes will double by 2025.

### **Monthly Depot Buprenorphine Approved:**

As reported in AMA Morning Rounds 12/4/2017:

[The Wall Street Journal](#) (12/1, Al-Muslim, Whalen, Subscription Publication) reported the Food and Drug Administration approved a monthly injection of buprenorphine (Sublocade) for the treatment of opioid addiction. FDA Commissioner Scott Gottlieb said, "With the approval today of a monthly formulation of the drug buprenorphine for the treatment of opioid use disorder, patients have access to a new and longer-acting option for the treatment of opioid addiction."

### **As reported in 12/11/2017 AMA Morning Rounds:**

The [NBC News](#) (12/10, Snow, McFadden) website reported that "one in five American children, ages three through 17 – some 15 million – have a diagnosable mental, emotional or behavioral disorder in a given year," CDC research has found. Just "20 percent of these children," however, "are ever diagnosed and receive treatment; 80 percent – some 12 million – are not receiving" any treatment at all. The piece also points out, "Some 50 percent of cases of mental illness begin by age 14, according to the American Psychiatric Association."

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### MENTAL HEALTH POLICY

#### **1/3 of Wisconsin Counties Sue Drug Makers for Opioid Crisis:**

As reported in AMA Morning Rounds:

The [AP](#) (11/7, Moreno) reports nearly two dozen Wisconsin counties are suing opioid makers, “alleging in a federal lawsuit Tuesday that the companies’ ‘nefarious and deceptive’ marketing campaigns precipitated the nation’s opioid overdose epidemic.” Drug companies knew their “products were addictive, subject to abuse, and not safe or efficacious for long-term use,” the lawsuit says, naming Purdue Pharma, Johnson & Johnson, Endo Health Solutions, Inc. and subsidiaries of the companies as well as three doctors in California and Utah. The AP notes that “more than 52,000 Americans died in 2015 from drug overdoses, most of them involving prescription opioids or related illicit drugs such as fentanyl and heroin, according to the U.S. Centers for Disease Control and Prevention.”

The [Milwaukee Journal Sentinel](#) (11/7, Behm) reports that more than one-third of Wisconsin counties sued drug makers and physicians, joining a “growing number of more than two dozen states, cities and counties around the U.S. that already have filed lawsuits.” The Journal-Sentinel counts 28 separate lawsuits.