

PSYCHIATRIC SUMMARY XVIII

Summer 2016

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This issue marks the eighteenth 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

FDA Releases Opioid Drug Safety Communication:

The FDA released the following communication ([LINK](#), 3/22/2016) adding warnings regarding serotonin syndrome ("Opioids can interact with antidepressants and migraine medicines to cause a serious central nervous system reaction called serotonin syndrome, in which high levels of the chemical serotonin build up in the brain and cause toxicity"), adrenal insufficiency, and sexual dysfunction.

Decriminalize All Drugs?

According to the Washington Post (Ingraham, 3/24/2016, [LINK](#)) a panel of medical experts convened by Johns Hopkins University and The Lancet called for the decriminalization of all nonviolent drug use and possession. Citing a growing scientific consensus on the failures of the global war on drugs, the experts further encourage countries and U.S. states to "move gradually toward regulated drug markets and apply the scientific method to their assessment."

Patient Satisfaction Contributing to Opiate Epidemic?

Time magazine (Sean Gregory, 4/13/2016, [LINK](#)) ran an article positing that the Patient Satisfaction component of the Affordable Care Act is incentivizing overprescribing of controlled substances and contributing to the opiate epidemic in the United States.

Medical Error Accounts is 3rd Leading Cause of Death:

According to a heavily publicized article by Makary and Daniel appearing in The British Medical Journal ([LINK](#)) medical error in the US accounted for approximately 251,000 deaths in 2013, third only behind heart disease (611,000) and cancer (585,000), followed by COPD (149,000), Suicide (41,000), Firearms (34,000) and motor vehicle accidents (34,000).

CLINICAL PSYCHIATRY IN THE NEWS, IN BRIEF

Healthy Heart = Healthy Brain:

According to research published in Journal of the American Heart Association (using a subsample of over 700 individuals in a population based study) the greater an individual's cardiovascular health, the less the decline in processing speed, executive function and episodic memory (Gardener et al., [LINK](#)).

Burning Calories = Healthy Brain:

Likewise, a neuroimaging evaluation of 876 individuals in the Cardiovascular Health Study (Raji et al., Journal of Alzheimer's Disease, [LINK](#)) found that "Increasing energy output from a variety of physical activities is related to larger gray matter volumes in the elderly, regardless of cognitive status."

Protozoa → Intermittent Explosive Disorder:

Adding to the literature on toxoplasmosis induced mental illness, a study publicized with this AAAS news release ([LINK](#), 3/23/2016) found that around 30 percent of those with intermittent explosive disorder were infected with toxoplasmosis.

Marijuana for PTSD:

The AP ran the following article (Finley, 3/22/2016, [LINK](#)) regarding veterans using marijuana to treat nightmares, anxiety and insomnia of PTSD.

Brintellix Not Approved for Cognition:

As reported at STAT (Robbins, 3/29/16, [LINK](#)), an advisory board to the FDA blocked a bid for vortioxetine (Brintellix) to be marketed to treat the impaired cognition of depression.

Poor Sleep and Teenage Frontal Lobes:

Appearing in the CDC's Morbidity and Mortality Weekly Report (MMWR), Wheaton et al ([LINK](#)) analyzed data from over 50,000 high school students and concluded that the likelihood of engaging in any one of "five risk behaviors was significantly higher for students who reported sleeping ≤ 7 hours on an average school night". They also found that "infrequent seatbelt use, riding with a drinking driver, and drinking and driving were also more likely for students who reported sleeping ≥ 10 hours compared with 9 hours on an average school night."

Anticholinergics and Brain Atrophy:

Appearing in JAMA Network, online ahead of print ([LINK](#)) Risacher et al. compared neuroimaging measures of atrophy as well as cognitive measures in over 50 individuals taking anticholinergic medications to over 300 matched controls who were not. They found that the use of anticholinergic medications "was associated with increased brain atrophy and dysfunction and clinical decline."

Cannabidiol for Psychosis:

As reported in Medscape Psychiatry and Mental Health by Liam Davenport (4/21/16, [LINK](#)) promising research was presented at the Schizophrenia International Research Society (SIRS) 2016 Biennial Meeting. The work (lead investigator Philip McGuire, MD, PhD) showed results from the first randomized trial of cannabidiol as an adjunctive therapy for schizophrenia, and, compared with placebo, the compound significantly improved positive symptoms and symptom severity.

Psychiatric Sequelae of ICU Stays:

In a study at 41 hospitals of nearly 700 ICU patients, (Critical Care Medicine, Huang et al., [LINK](#)) approximately two thirds developed psychiatric symptoms:

During 12 months, a total of 416 of 629 patients (66%) with at least one psychiatric outcome measure had substantial symptoms in at least one domain. There was a high and almost identical prevalence of substantial symptoms (36%, 42%, and 24% for depression, anxiety, and posttraumatic stress disorder) at 6 and 12 months. The most common pattern of co-occurrence was having symptoms of all three psychiatric domains simultaneously. Younger age, female sex, unemployment, alcohol misuse, and greater opioid use in the ICU were significantly associated with psychiatric symptoms, whereas greater severity of illness and ICU length of stay were not associated.

Neuropsychiatric Side Effects of Quitting Smoking:

In a study appearing in The Lancet, Anthenelli et al. (funding from Pfizer and GlaxoSmithKline, [LINK](#)) authors conducted a triple blind andomised, double-blind, triple-dummy, placebo-controlled and active-

controlled (nicotine patch; 21 mg per day with taper) trial of varenicline (1 mg twice a day) and bupropion (150 mg twice a day) for 12 weeks with 12-week non-treatment follow-up study of 8144 participants. Their interpretation of results read:

The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo. Varenicline was more effective than placebo, nicotine patch, and bupropion in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.

Effects of Antepartum Depression:

In a study of 7267 antepartum mothers screened for depression, authors Vankatesh et al. (Obstetrics & Gynecology, [LINK](#)) found that:

Those with depressive symptoms had an increased likelihood of preterm and very preterm delivery as well having an SGA [small for gestational age] neonate. Such risk was not apparent among women who were treated with an antidepressant medication.

18+ Months of Sleep/Wake Disorder After TBI:

Appearing in Neurology (Imbach et al., [LINK](#)), prospectively studied 140 individuals who suffered from first ever acute traumatic brain injury. The authors found:

In the chronic state after traumatic brain injury, sleep need per 24 hours was persistently increased in trauma patients (8.1 ± 0.5 hours) as compared to healthy controls (7.1 ± 0.7 hours). The prevalence of chronic objective excessive daytime sleepiness was 67% in patients with brain trauma compared to 19% in controls. Patients significantly underestimated excessive daytime sleepiness and sleep need, emphasizing the unreliability of self-assessments on SWD in trauma patients.

Reptilian Sleep Architecture:

Recording from the Australian Dragon (Science, [LINK](#)), Shei-Idelson et al demonstrated electrophysiologic “features of slow-wave sleep and rapid eye movement (REM) sleep. These findings indicate that the brainstem circuits responsible for slow-wave and REM sleep are not only very ancient but were already involved in sleep dynamics in reptiles.”

FDA Approves Rx for Parkinson’s Hallucinations:

As reported in MedScape (Susan Jeffrey, 4/29/2016, [LINK](#)) “The US Food and Drug Administration (FDA) has approved pimavanserin tablets (Nuplazid, Acadia Pharmaceuticals) for the treatment of hallucinations and delusions associated with psychosis in Parkinson's disease (PD).” The article goes on to report that effectiveness was demonstrated in a clinical trial of 199 participants over 6 weeks, “where it was shown to be superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions without worsening the primary motor PD symptoms.”

Ketamine Metabolite for Depression:

A team of researchers has published in Nature (Zanos et al., [LINK](#)) on the antidepressant qualities of a metabolite of ketamine, suggesting benefit without ketamine related side effects. They wrote that:

The metabolism of (R,S)-ketamine to (2S,6S;2R,6R)-hydroxynorketamine (HNK) is essential for its antidepressant effects, and that the (2R,6R)-HNK enantiomer exerts behavioural, electroencephalographic, electrophysiological and cellular antidepressant-related actions in mice. These antidepressant actions are independent of NMDAR inhibition but involve early and sustained activation of AMPARs (α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors).

Depression as Dementia Prodrome?

Published in The Lancet Psychiatry (Mirza et al., [LINK](#)) researchers explored the link between longitudinal course and severity of depression in conjunction with development of a dementing disorder looking at 3325 participants from 1993 to 2004. They found that:

During 26 330 person-years, 434 participants developed incident dementia. Only the trajectory with increasing depressive symptoms was associated with a higher risk of dementia compared with the low depressive symptom trajectory . . .

Reaching the conclusion that:

Risk of dementia differed with different courses of depression, which could not be captured by a single assessment of depressive symptoms. The higher risk of dementia only in the increasing trajectory suggests depression might be a prodrome of dementia.

CBT-I is Recommended First Line Treatment for Insomnia:

Appearing in the Annals of Internal Medicine, Qaseem et al. ([LINK](#)) recommend that cognitive behavioral therapy for insomnia be first line treatment ahead of pharmaceutical sleep aids.

Aripiprazole and Impulse Control Problems:

Many sources reported recent FDA warning ([LINK](#)) that aripiprazole has been linked to impulse control disorders including eating, shopping, gambling and sexual behaviors.

Magic Mushrooms and Mental Health:

According to a small study appearing in The Lancet Psychiatry, Carhart-Harris et al. ([LINK](#)) performed an open label study of 12 individuals (6 male, 6 female) with moderate to severe treatment resistant depression. They evaluated dosing and side effects of psilocybin hallucinogenic mushrooms, finding:

The adverse reactions we noted were transient anxiety during drug onset (all patients), transient confusion or thought disorder (nine patients), mild and transient nausea (four patients), and transient headache (four patients). Relative to baseline, depressive symptoms were markedly reduced 1 week (mean QIDS difference -11.8 , 95% CI -9.15 to -14.35 , $p=0.002$, Hedges' $g=3.1$) and 3 months (-9.2 , 95% CI -5.69 to -12.71 , $p=0.003$, Hedges' $g=2$) after high-dose treatment. Marked and sustained improvements in anxiety and anhedonia were also noted.

Prenatal Nicotine → Schizophrenia?

In a national birth cohort study involving nearly 10,000 individuals who developed schizophrenia, Niemelä et al., (The American Journal of Psychiatry, [LINK](#)) found that:

A higher maternal cotinine level, measured as a continuous variable, was associated with an increased odds of schizophrenia (odds ratio=3.41, 95% confidence interval, 1.86–6.24).

Categorically defined heavy maternal nicotine exposure was related to a 38% increased odds of schizophrenia. These findings were not accounted for by maternal age, maternal or parental psychiatric disorders, socioeconomic status, and other covariates. There was no clear evidence that weight for gestational age mediated the associations.

SSRIs → Dementia?

In a retrospective cohort study of over 3500 individuals, Wang et al., (Alzheimer Disease & Associated Disorders, [LINK](#)) reported:

A retrospective cohort study was conducted including 3688 patients age 60 years or older without dementia enrolled in a depression screening study in primary care clinics. Information on antidepressant use and incident dementia during follow-up was retrieved from electronic

medical records. The Cox proportional hazard models were used to compare the risk for incident dementia among 5 participant groups: selective serotonin re-uptake inhibitors (SSRI) only, non-SSRI only (non-SSRI), mixed group of SSRI and non-SSRI, not on antidepressants but depressed, and not on antidepressants and not depressed. SSRI and non-SSRI users had significantly higher dementia risk than the nondepressed nonusers (hazard ratio [HR]=1.83, P=0.0025 for SSRI users and HR=1.50, P=0.004 for non-SSRI users). In addition, SSRIs users had significantly higher dementia risk than non-users with severe depression (HR=2.26, P=0.0005). Future research is needed to confirm our results in other populations and to explore potential mechanism underlying the observed association.

Veteran Risk Factors for Suicide:

In an extensive longitudinal retrospective cohort study of Army-enlisted soldiers from 2004 to 2009, Ursano et al. (JAMA Psychiatry, [LINK](#)) explored timing and risk factors for suicide attempts in a manner which could prove valuable to those treating former and current soldiers..

Accidental Deaths Including Overdoses on the Rise:

Appearing in the AMA Morning Rounds of 6/10/2016:

The [AP](#) (6/9, Borenstein) reports over 136,000 Americans died from accidents in 2014, an increase of 15.5% from a decade earlier, according to a new report from the National Safety Council. The report also found that deaths from accidental poisonings, including drug overdoses, increased 78% during the same time period, making them more common than fatal car crashes. Opioid overdoses alone killed 13,486 people in 2014, according to the report.

Protein in Exercise Mediated Neurogenesis:

According to research published in Cell Metabolism (Hyo Yool Moon et al., [LINK](#)) running induced the production of cathepsin B (CTSB) secretion, also associated with adult neurogenesis. In mice with CTSB knock-out, running no longer memory or adult neurogenesis. In humans, plasma CTSB levels are correlated with both fitness and memory.

Church Attendance Reduces Suicide in Women?

VanderWeele et al. (appearing in JAMA Psychiatry, [LINK](#)) published research from a long-term cohort study (Nurses' Health Study) using Cox proportional hazard regression, among just under 90,000 women ages 30 to 55, finding that: "frequent religious service attendance was associated with a significantly lower rate of suicide."

MENTAL HEALTH IN THE POPULAR PRESS:

Boutique Eating Disorder Clinics:

The New York Times (Goode, 3/14/2016, [LINK](#)) ran a lengthy article on the challenges of treating eating disorders and how investors appear to have seized an opportunity to develop private, out-of-pocket residential treatment centers focusing on amenities, suggested by the tone, at the expense of outcomes.

\$1 for Depression/Anxiety = \$3-\$5 for the Economy:

Many news outlets ran stories on a study appearing in The Lancet (Chisholm et al., [LINK](#)) which was a global return on investment analysis. Researchers concluded that, based on improved life-years and impact on productivity, the return on investment for treatment of depression and anxiety is quite good.

Suicide on the Rise:

According to the AMA Morning Report of 4/22:

In "Health & Science," the [Washington Post](#) (4/22, Keating, Bernstein) reports [research](#) (pdf) released Friday by the CDC's National Center for Health Statistics found the suicide rate in the US rose 24 percent between 1999 and 2014 to 13 per 100,000 people, led by an even greater rise among middle-aged white people, particularly women. The overall rise in part can be attributed to substance addiction, "gray divorce," and the rise of the Internet and social media. In addition, economic distress in wake of the recent recession appears to underpin some of the increase for middle-aged Caucasians.

The suicide rate among young girls is also increasing, the [Los Angeles Times](#) (4/21, Healy) reports in "Science Now." For example, "among girls five to 15 years old – a segment of the population among whom suicide was a rare phenomenon in 1999, rates of suicide tripled between 1999 and 2014, with one suicide yearly for every 6,660 such girls."

[USA Today](#) (4/22, Asrar) reports that CDC behavioral scientist Kristin Holland, PhD, MPH, "believes there are multiple factors contributing towards the increase in suicide rate, and mental health is only one of them." She stated, "Many people view suicide as a mental health problem, but many people who die of suicide do not have a mental health problem. It's a public health problem."

Omega-3 as Augmentation for Depression:

Time magazine (Sifferlin, 4/26/16, [LINK](#)) reported on a recent American Journal of Psychiatry paper reviewing nutraceuticals, finding some augmentation benefit to antidepressants through supplementation with omega-3 fatty acids.

Spanking Similar to Physical Abuse:

Many news sources reported on a study which ran in the Journal of Family Psychology (Gershoff and Grogan-Kaylor, 4/7/2016, [LINK](#)), which included:

Whether spanking is helpful or harmful to children continues to be the source of considerable debate among both researchers and the public. This article addresses 2 persistent issues, namely whether effect sizes for spanking are distinct from those for physical abuse, and whether effect sizes for spanking are robust to study design differences. Meta-analyses focused specifically on spanking were conducted on a total of 111 unique effect sizes representing 160,927 children. Thirteen of 17 mean effect sizes were significantly different from zero and all indicated a link between spanking and increased risk for detrimental child outcomes. Effect sizes did not substantially differ between spanking and physical abuse or by study design characteristics. (PsycINFO Database Record (c) 2016 APA, all rights reserved)

Costs of Mental Illness:

According to the Washington Post (Amy Ellis Nut, 5/19/2016, [LINK](#)) mental illness was associated with "\$201 billion in estimated costs in 2013. Trailing far behind in second place are heart conditions, at \$147 billion, then trauma, at \$143 billion. Cancer costs come in fourth and diabetes a distant eighth."

Elite Soldiers More Likely to Suicide at Home:

In an article appearing in the New York Times (Carey, 5/29/2016, [LINK](#)) it is noted that elite servicemen are less likely to suicide while deployed and more likely to do so when home.

Destigmatizing Mental Illness:

Much has been reported on efforts of the mentally ill, particularly among celebrities, in reducing the stigma of mental illness. The Washington Post (Itkowitz, 6/1/2016, [LINK](#)) ran an article profiling several individuals who are playing their part in helping to institute this change.

FDA Approves Forehead Cooling Device for Insomnia:

Appearing at Medscape (Pauline Anderson, 6/8/2016, [LINK](#)) this article reviews the work of Eric Nofzinger MD on 230 patients over 3800 research nights demonstrating the safety and efficacy of the Cerève Sleep System, a prescription device that helps reduce latency to stage 1 and stage 2 sleep by keeping the forehead cool

Shortage of Child/Adolescent Psychiatrists:

NBC (Brown, Zhang and Schuppe, 6/18) ran an article at their website ([LINK](#)) reporting on the growing shortage of child and adolescent psychiatrists in the nation.

Google Glass for Autism?

A research project at Stanford, reported on by the Associated Press (Chea, 6/23, [LINK](#)) uses facial recognition software with Googles eyeglass like wearable computer to provide individuals with autism real-time interpretation of facial emotions during everyday interactions. If successful, the researchers believe they could have a commercial product available in a few years.

Marijuana for Alzheimer's?

Appearing in the Washington Times (Shepperd, 6/29, [LINK](#)), researchers at the Salk Institute have found that some chemicals in cannabis, including THC, "can promote the cellular removal of amyloid beta, a toxic protein associated with Alzheimer's disease."

MENTAL HEALTH POLICY

CDC Opiate Guidelines:

Reported in multiple news sources, the CDC released guidelines stemmed at curbing iatrogenic opiate addiction. As per the AMA Morning Rounds of 3/16/2016:

[USA Today](#) (3/15, Szabo) reports that the Centers for Disease Control and Prevention is urging physicians "to avoid prescribing powerful opiate" pain medications "for patients with chronic pain, saying the risks from such drugs far outweigh the benefits for most people." USA Today points out that "the CDC directed the guidelines to primary care physicians, who prescribe nearly half of opiates."

The [AP](#) (3/15, Perrone) reports, "Under the new [guidelines](#) [pdf]," physicians "would prescribe" pain medications "only after considering non-addictive pain relievers, behavioral changes and other options." Additionally, "the CDC...wants" physicians "to prescribe the lowest effective dose possible." Meanwhile, "for short-term pain, the CDC recommends limiting opioids to three days of treatment, when possible."

In a front-page story, the [New York Times](#) (3/16, A1, Tavernise, Subscription Publication) reports, "The guidelines do not apply to prescriptions for patients who are receiving cancer or end-of-life treatment."

The [Los Angeles Times](#) (3/15, Ryan, Karlamangla) reports that the American Medical Association "said that it was 'largely supportive' of the guidelines but on alert for 'possible unintended

consequences.” Dr. Patrice A. Harris, chair of the AMA Task Force to Reduce Opioid Abuse, said, “We know this is a difficult issue and doesn’t have easy solutions and if these guidelines help reduce the deaths resulting from opioids, they will prove to be valuable.”

Senate Mental Health Reform Bill:

Reported in the 3/17/2016 AMA Morning rounds:

[The Hill \(DC\)](#) (3/16, Sullivan) reports that yesterday by voice vote, the Senate Health, Education, Labor and Pensions Committee “advanced a bipartisan mental health bill,” the Mental Health Reform Act of 2016 ([S 2680](#) (3/17, Subscription Publication)), “to the full Senate as part of a difficult push to achieve mental health reform in an election year.”

[Congressional Quarterly](#) (3/16, Siddons, Subscription Publication) reports the committee also approved “four other bills to combat drug abuse.” Even though S 2680 “would provide block grants to strengthen state-provided mental health care” and “moved through the committee without objection,” both Republicans and Democrats “were concerned about Medicaid’s prohibition against reimbursements to hospitals and facilities larger than 16 beds for mental health and substance abuse treatment.” Legislators hope to address that issue on the Senate floor.

[Modern Healthcare](#) (3/16, Muchmore, Subscription Publication) points out that “funding for implementing the programs” covered by the bills “remains elusive,” however.

FDA Considers ECT Reclassification:

Many of you may be aware of the push to reclassify electroconvulsive therapy. A draft report being considered is available at this [LINK](#).

Tennessee Governor Signs Bill Allowing Counselors to Refuse to Treat:

In a story publicized across a broad swath of national news outlets, the governor of Tennessee has signed a bill allowing mental health counselors the legal ability to refuse to see a patient based on the counselor’s religious beliefs. As reported in the AMA Morning Rounds of 4/28/16:

The [Wall Street Journal](#) (4/27, Kamp, Subscription Publication) reports that yesterday, Gov. Bill Haslam (R-TN) signed into law [Senate Bill 1556](#) (pdf), legislation allowing mental health counselors the right to refuse patients based on the counselors’ personal or religious beliefs.

The [AP](#) (4/28, Burke, Schelzig) reports that in response, “the American Counseling Association called the legislation an ‘unprecedented attack’ on the counseling profession and said Tennessee was the only state to ever pass such a law.” Those who oppose the law “say the legislation is part of a wave of bills around the nation that legalizes discrimination against gays, lesbians, bisexuals and transgender people.”

According to [CNN](#) (4/27, Almasy), “in a written statement to the media,” the governor “said two of his concerns had been addressed by this most recent version of the bill.” The current version now “requires therapists and counselors to treat people who are an imminent danger to themselves or others.” In addition, the law “mandates the mental health professional arrange a referral to another counselor or therapist.”

The [Tennessean](#) (4/27) points out that the bill’s provisions “go into effect immediately.”

Medical Marijuana for VA?

The house reportedly passed a bill (Litvan and Dennis, Bloomberg Politics, 5/19/16, [LINK](#)) to ease access to medical marijuana for United States veterans within the VA system.

Violations of ACA Parity for AODA:

Appearing in the AMA Morning Rounds of 6/8, and published at Modern Healthcare (Steven Ross, 6/7/2016, [LINK](#)), Steven Ross wrote on the National Center on Addiction and Substance Abuse survey which found that nearly two-thirds of health plans violate ACA rules on addiction treatment coverage.