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Research Watch is an initiative by the residents of University Hospitals/ Case Western Reserve University; it aims to inform psychiatry residents and faculty of notable articles published in prominent research journals.

Journals covered in the issue:

- * American Journal of Psychiatry (AJP)
- * JAMA Psychiatry (JAMA-P)
- * The Journal of Clinical Psychiatry (JCP)
- * Lancet Psychiatry (LP)
- * Journal of the American Academy of Child & Adolescent Psychiatry (JAACAP)
- * Journal of the American Psychoanalytic Association
- * Translational Psychiatry (TP)

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Highlights

- DSM-5 criteria for depression with mixed features may be inadequately sensitive to detect patients with mixed depression. (AJP)
- Sertraline may be effective in preventing depressive disorders in patients following traumatic brain injury. (JAMA-P)
- The sweet-liking phenotype and a high craving for alcohol independently and particularly in combination are associated with a positive response to naltrexone. (JAMA-P)
- Greater raphe nuclei serotonin 1A binding potential predicts higher suicidal ideation and more lethal suicidal behavior over a 2-year prospective period. (JAMA-P)
- Early nonresponse in the antipsychotic treatment of acute mania in weeks 1 and 2 predicts nonresponse and nonremission in week 3. (JCP)
- SSRIs may decrease insulin secretion in older adults & increase the risk of insulin dependence in type 2 diabetics. (JCP)
- Observational study reports an incidental effect of buprenorphine in improving PTSD symptoms in veterans with co-occurring chronic pain and opioid use disorder. (JCP)
- Former regular users of cannabis who stop after onset of psychosis have the most favorable outcomes, while continued high-frequency users of high potency cannabis have the worst outcomes with regards to relapse. (LP)
- Meta-analysis suggests that clomipramine is associated with greater benefit than SSRIs for treatment of pediatric obsessive-compulsive disorder. (JAACAP)
- Dopamine partial agonist action of cannabidiol may account for its clinical antipsychotic effects. (TP)
- Downregulation of the SMAD pathway (involved in neurodevelopment) appears to be associated with cognitive deficits in schizophrenia. (TP)
- In first-episode psychosis, *AKT1* and *DICER1* gene expression may distinguish individuals with mania from schizophrenia spectrum. (TP)

The American Journal of Psychiatry

Volume 173, Issue 10

Mixed Depression in Bipolar Disorder: Prevalence Rate and Clinical Correlates during Naturalistic Follow-Up in the Stanley Bipolar Network

Miller, et al.

In a 7-year naturalistic study, 907 adult patients with Bipolar Disorder were followed to examine the prevalence and phenomenology of the newly introduced “with mixed features” specifier for major depressive episodes. Results showed that women were significantly more likely than men to experience subthreshold hypomania during visits with depression. Additionally, patients with one or more mixed depression visits had more symptomatic visits and less euthymic visits compared to patients without mixed features. DSM-5-based definitions of mixed depression yielded lower mixed depression prevalence rates compared to the definition of mixed depression used by the investigators Inventory of Depressive Symptomatology–Clinician-Rated Version (IDS-C) score ≥ 15 and a Young Mania Rating Scale (YMRS) score > 2 and < 12 at the same visit, suggesting that DSM-5 diagnostic criteria may be inadequately sensitive.

Offspring of Depressed Parents: 30 Years Later

Weissman, et al.

The authors report 30-year outcomes of 147 offspring of depressed (high-risk) and nondepressed (control) parents. Findings show approximately three times the rate for major depression in the high-risk group compared with the control group, and offspring at risk also had significantly higher rates of phobia, as well as elevated rates of substance use disorders that nearly reached significance. The study found that the period of highest risk for first onset is between the ages of 15 and 25 in both the high-risk and control offspring. In the uncommon case of prepubertal onset, there was a 10-fold increased risk in those with a positive family history compared to controls. The high-risk offspring also demonstrated poorer functioning and increased mortality (approximately 8-year difference in the mean age of death).

Hyperresponsiveness of the Neural Fear Network during Fear Conditioning and Extinction Learning in Male Cocaine Users

Kaag, et al.

This fMRI study showed hyperresponsiveness of the amygdala and insula during fear condition and hyporesponsiveness of the dorsomedial prefrontal cortex during extinction learning in cocaine users compared to control subjects. In cocaine users, skin conductance responses were positively correlated with responsiveness of the insula, amygdala, and dorsomedial prefrontal cortex during fear conditioning but negatively correlated with responsiveness of the ventromedial prefrontal cortex during extinction learning. This suggests that cocaine users have increased sensitivity to aversive conditioned cues, which might be a risk factor for stress-relief craving in cocaine use disorder.

JAMA Psychiatry
Volume 73, Issue 10

Parental Psychiatric Disease and Risks of Attempting Suicide and Violent Criminal Offending in Offspring: A Population-Based Cohort Study

Mok, et al.

This population-based cohort study of over 1.7 million individuals examined the associations between full spectrum of parental psychiatric disease and risks of attempted suicide and violent offending in offspring. Results showed elevated risk in offspring in virtually the full spectrum of parent psychiatric disease with the greatest elevations in incidence rate ratios for parental diagnoses of antisocial personality disorder (3.96 suicide attempt and 3.62 violent offending), cannabis misuse (3.57 suicide attempt and 3.31 violent offending), and parental suicide (3.42 suicide attempt and 3.31 violent offending). A history of mental illness or suicide attempt in both parents was associated with a double risk compared to having just one affected parent. The association was strongest for female than male offspring for violent offending.

Incidence of Depression After Stroke, and Associated Risk Factors and Mortality Outcomes in a Large Cohort of Danish Patients

Jorgensen, et al.

This register-based Danish cohort study examined whether the incidence of and risk factors for depression differ between patients with stroke and a reference population without stroke; study occurred within 2 years post stroke. Compared with the reference population, patients with stroke had a higher incidence of depression during first 3 months of hospitalization (HR 8.99), which declined during the second year follow-up. Significant risk factors included older age, female gender, single cohabitation, basic educational attainment, diabetes, high level of somatic comorbidity, history of depression, and stroke severity. In both stroke and reference populations, depressed individuals, especially those with new onset, had increased all-cause mortality. In most models, depression-related mortality was approximately twice as high in the reference population versus the stroke population.

Sertraline for Preventing Mood Disorders Following Traumatic Brain Injury: A Randomized Clinical Trial

Jorge, et al.

A double-blind, placebo-controlled, parallel group RCT was conducted at a university hospital with 24 week follow-up to assess the efficacy of sertraline treatment in preventing depressive disorders following TBI. Enrolled patients included age range of 18-85 years with mild, moderate, or severe TBI. Placebo or sertraline (100mg/d) were given for 24 weeks or until development of a mood disorder. Of 94 patients enrolled in the study, the NNT to prevent depression after TBI at 24 weeks was 5.9.

Association of the Sweet-Liking Phenotype and Craving for Alcohol With the Response to Naltrexone Treatment in Alcohol Dependence: A Randomized Clinical Trial

Garbutt, et al.

This double-blind, randomized, placebo-controlled trial evaluated eighty actively drinking patients randomized by sweet-liking (SL) or sweet-disliking (SDL) phenotypes and by pre-treatment high or low craving for alcohol for response to naltrexone treatment. Results showed that the SL phenotype and a high craving for alcohol were independently associated with a positive response to oral naltrexone (50 mg/d). The combination of the SL phenotype and high craving was associated with a strong response to naltrexone, with 17.1 fewer heavy drinking days and 28.8 more abstinent days compared with placebo.

Positron Emission Tomographic Imaging of the Serotonergic System and Prediction of Risk and Lethality of Future Suicidal Behavior

Oquendo, et al.

Previous cross-sectional studies have shown that individuals with depression who attempt suicide have lower midbrain serotonin transporter binding potential and that higher serotonin 1A binding potential in the raphe nuclei (RN) is associated with greater lethality of past suicide attempts and suicidal intent and ideation. This prospective study showed that greater RN serotonin 1A binding potential predicted higher suicidal ideation and more lethal suicidal behavior during a 2-year period. The authors concluded that this effect may be mediated through less serotonin neuron firing and release, which affects mood and suicidal ideation and thereby decision making.

The Journal of Clinical Psychiatry

Volume 3, Issue 9

Early Nonresponse in the Antipsychotic Treatment of Acute Mania: A Criterion for Reconsidering Treatment? Results From an Individual Patient Data Meta-Analysis

Welten, et al.

This meta-analysis of 1,243 patients over an 11 year period attempted to uncover if early lack of response to antipsychotic medication for acute mania predicts treatment failure. The study also aimed to define what is the criterion for an early nonresponse. The data was collected from 10 double-blind, randomized, placebo-controlled trials assessing the efficacy of antipsychotics for acute manic episodes. Early nonresponse in weeks 1 and 2, defined by cutoff scores ranging from a $\leq 10\%$ to a $\leq 50\%$ reduction in symptoms compared to baseline on the Young Mania Rating Scale, significantly predicted nonresponse ($\leq 0\%$ symptom reduction) and nonremission (YMRS score higher than 8) in week 3.

Selective Serotonin Reuptake Inhibitors Decrease Pancreatic Insulin Secretion in Older Adults and Increase the Risk of Insulin Dependence in Type 2 Diabetes Patients

Noordam, et al.

The authors investigated whether there was a link between the use of SSRIs and insulin secretion as part of the prospective population-based Rotterdam Study cohort from 1991-2012. This was done by evaluating markers for glucose-insulin homeostasis in a nondiabetic older population as well as the association between SSRI use and insulin dependence in a diabetic population of older adults. Results showed that the participants who were using an SSRI compared to the participants who were not using a SSRI had lower levels of insulin, lower degree of insulin resistance, and less insulin secretion, though similar glucose levels. It was also shown that >90 days of consecutive use of SSRIs in diabetic patients was associated with 2.17 times higher risk of starting insulin treatment than that of participants not using antidepressants.

Observational Evidence for Buprenorphine's Impact on Posttraumatic Stress Symptoms in Veterans With Chronic Pain and Opioid Use Disorder

Seal, et al.

This retrospective cohort of 382 Iraq and Afghanistan veterans from 2007 to 2013 assessed the effectiveness of Buprenorphine in treating PTSD in patients with co-occurring chronic pain and opioid use disorder. The authors used time-varying general estimating equation models to evaluate change in PTSD symptoms among the veterans started on buprenorphine versus those maintained on moderately high-dose opioid therapy. This was measured using the PTSD Checklist and the Primary Care PTSD Screen. The results showed twice as many veterans in the buprenorphine group (23.7%) compared to those in the opioid therapy group (11.7%) experienced improvement in PTSD symptoms ($P = .001$). Compared to veterans in the opioid therapy group, veterans receiving buprenorphine showed significant improvement in PTSD symptoms after 8 months, with increasing improvement up to 24 months.

The Lancet Psychiatry

Volume 3, Issue 10

Effects of continuation, frequency, and type of cannabis use on relapse in the first 2 years after onset of psychosis: an observational study

Schoeler, et al.

Cannabis use after first episode of psychosis has been associated with relapse. This prospective observational study aimed to study whether the effects on outcome varied depending on the type of cannabis consumed and usage pattern. The study recruited and followed up patients aged 18-65 years who presented with their first episode of psychosis. Relapse of psychosis within 2 years after onset of psychosis was defined as risk of subsequent admission to hospital. Analysis revealed that former regular users of cannabis who stopped after onset of psychosis had the most favorable illness course with regards to relapse, while continued high-frequency users (i.e. daily use in all 24 months) of high-potency (Skunk-like) cannabis had the worst outcome, with more relapses, reduced time to relapse, and more intense psychiatric care after the onset of psychosis.

Journal of the American Psychoanalytic Association
Volume 64, Issue 4

Unavoidable Satisfaction: The Analyst's Pleasure

Shulman M

Shulman considers the satisfying elements of practicing psychoanalysis while reconciling them with concerns for boundary violations.

Can Babies Remember Trauma? Symbolic Forms of Representation in Traumatized Infants

Coates SW

Through clinical examples, Coates focuses on three aspects of early event trauma in young children: the roles of fantasy/reality, age-related capacity for symbolic representation, and the child's attachment. She comes to three conclusions: children as young as neonates can experience extreme psychological suffering, these same children can experience events as life-threatening, and the way that trauma is resolved for a young child can have profound consequences in its attachment.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 55, Issue 10

Long Term Outcomes of Attention-Deficit /Hyperactivity Disorder and Conduct Disorder: A Systematic Review and Meta-Analysis

Erskine, et al.

This meta-analysis looked at all current evidence linking ADHD and Conduct Disorder (CD) with a range of health and psychosocial outcomes. Published cohort and case-control studies from 1980 to March 2015 that reported a longitudinal association between ADHD or CD and adverse outcomes with a minimal follow-up of 2 years were included. In total, 114 out of 278 studies met inclusion criteria and 98 were used in subsequent meta-analyses. ADHD was associated with adverse outcomes including academic achievement, other mental and substance use disorders, and employment. CD was associated with outcomes relating to academic achievement, other mental and substance use disorders, and criminality. Overall implications suggest long-term disability without appropriate intervention.

Systematic Review and Meta-Analysis: Early Treatment Responses of Selective Serotonin Reuptake Inhibitors and Clomipramine in Pediatric Obsessive-Compulsive Disorder

Varigonda, et al.

The purpose of this meta-analysis was to examine the time course of response to selective serotonin reuptake inhibitors (SSRIs) and clomipramine in pediatric obsessive-compulsive disorder (OCD); whether higher doses of SSRIs were associated with an improved response, differences in efficacy among SSRI

agents, differences in efficacy between SSRIs and clomipramine, and whether any differences existed between pediatric OCD and adult OCD in terms of time course and magnitude of response. A total of nine trials were included. The greatest benefits occurred early in treatment for both clomipramine and SSRIs. Clomipramine was associated with a greater measured benefit compared to placebo than SSRIs. There was no evidence for a relationship between SSRI dosing and treatment effect. Adults and children with OCD demonstrated a similar degree and time course of response to SSRIs in OCD.

Randomized, Controlled Trial of Intravenous Immunoglobulin for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections

Williams, et al.

This study was a randomized-entry, double-blind, placebo-controlled 6 week trial including 35 children meeting criteria for Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and obsessive-compulsive disorder (OCD). An optional open-label treatment course was available for non-responders. Individuals were assessed at 12 and 24 weeks and primary outcome measures were the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) and the Clinical Global Impressions-Improvement (CGI-I) rating. During the double-blind phase, the mean decrease in the CY-BOCS score was 24% in the IVIG group and 12% in the placebo group with six responders in the IVIG group versus four in the placebo group. Although IVIG was safe and well-tolerated, the differences between IVIG and placebo were not statistically significant.

Translational Psychiatry

Volume 6, Oct 2016 issue

Cannabidiol is a partial agonist at dopamine D2High receptors, predicting its antipsychotic clinical dose

Seeman P

It had recently been reported that 800 to 1000 mg of cannabidiol per day improves psychotic symptoms of schizophrenia, although cannabidiol is not known to act on dopamine receptors. The present study conducted on rat brain found that cannabidiol acts on D2 receptors as a dopamine partial agonist. This dopamine partial agonist action of cannabidiol may account for its clinical antipsychotic effects.

Molecular signatures associated with cognitive deficits in schizophrenia: a study of biopsied olfactory neural epithelium

Horiuchi, et al.

Investigators obtained olfactory epithelium from patients with schizophrenia and control subjects using nasal biopsy. Further analysis identified association of cognitive deficits with *SMAD 5* gene and downregulation of the *SMAD* pathway in schizophrenia. The *SMAD* pathway has been important in multiple tissues, including the role for neurodevelopment and bone formation, and offers a potential novel target in addressing cognitive deficits of schizophrenia.

Gene expression alterations related to mania and psychosis in peripheral blood of patients with a first episode of psychosis

Gouvea, et al.

Authors investigated gene expression differences between patients with first episode psychosis–schizophrenia spectrum or first episode psychosis–Mania and healthy controls. Blood samples were collected and the expression of 12 psychotic-disorder-related genes was evaluated by quantitative PCR. *AKT1* and *DICER1* expression levels were higher in bipolar disorder patients compared with that in schizophrenia patients and healthy controls. *MBP* and *NDEL1* expression levels were higher in schizophrenia and bipolar patients than in healthy controls, indicating that these genes are psychosis related (independent of diagnosis). There was no correlation between gene expression and symptoms severity.