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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

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Highlights

- CSF metabolite abnormalities were found in majority of individuals with treatment-refractory depression in a case-control study, with cerebral folate deficiency being the most common. (AJP)
- DSM-5 criteria for bipolar mania significantly reduces the prevalence of mania/hypomania compared to DSM-IV. (AJP)
- Prevalence of depression in mild cognitive impairment is reported to be 32%. (JAMA-P)
- Omega-3 fatty acids did not differ from placebo in preventing onset of psychosis in patients at ultra-high risk in a double-blind RCT. (JAMA-P)
- Montgomery-Asberg Depression Rating Scale with a 24-hour recall period (MADRS-24hr) has good psychometric properties and construct validity, and can be used to assess rapid onset of antidepressant efficacy. (JCP)
- Systematic review & meta-analysis suggests glutamatergic agents are effective as add-on treatment for OCD in general and especially for treatment-refractory OCD. (JCP)
- The association of depression with high levels of CRP and low levels of FeNO is confirmed in a large and representative sample of the US population. (JCP)
- In a multicenter, placebo-controlled, double-blind trial from South Korea, escitalopram failed to significantly reduce moderate or severe depressive symptoms in patients with acute stroke. (LP)
- In a case-control study 3% of first-episode psychosis patients were found to be serum positive for NMDAR antibodies, however these patients didn't differ in clinical characteristics or outcomes at 6 months. (LP)
- A therapist-guided, internet-delivered cognitive-behavioral therapy for adolescents with obsessive compulsive disorder was found to be effective at 3 month follow-up. (JAACAP)
- Prevalence rate of antipsychotic use in Medicaid-eligible youth decreased for all socio-demographic groups between 2008-2013. (JAACAP)

The American Journal of Psychiatry

Volume 174, Issue 1

Neurometabolic Disorders: Potentially Treatable Abnormalities in Patients With Treatment-Refractory Depression and Suicidal Behavior

Pan, et al.

This case-control study of 33 patients with treatment-refractory depression (at least 3 maximum-dose, adequate-duration medication trials) and 16 healthy controls utilized plasma, urine and CSF metabolic profiling and found CSF metabolite abnormalities in 21 of the 33 treatment-refractory participants and no abnormalities in the controls. The most common metabolic disorder was cerebral folate deficiency (N=12) with normal serum folate levels and then low CSF 5-methyltetrahydrofolate (5-MTHF) levels. All patients with a metabolic disorder showed improvement in depressive symptoms after the deficiencies were treated with folinic acid. The patient with low tetrahydrobiopterin responded to treatment with sapropterin.

Toward the Reliable Diagnosis of DSM-5 Premenstrual Dysphoric Disorder: The Carolina Premenstrual Assessment Scoring System (C-PASS)

Eisenlohr-Moul, et al.

This study evaluated the accuracy of The Carolina Premenstrual Assessment Scoring System (C-PASS) in diagnosing Premenstrual Dysphoric Disorder. Two hundred women were recruited to retrospectively report premenstrual emotional symptoms over the past 2 to 4 months via the Daily Record of Severity of Problems (DRSP.) Diagnoses were made by expert clinicians and C-PASS. The results were compared and showed that the overall correct classification by C-PASS was estimated to be at 98%. Consistent with previous research, retrospective reports of premenstrual symptom increases were a poor predictor of prospective C-PASS diagnosis.

Distinct Subcortical Volume Alterations in Pediatric and Adult OCD: A Worldwide Meta- and Mega-Analysis

Boedhoe, et al.

This meta- and mega-analysis of imaging studies evaluated a total of 1830 OCD patients and 1759 control subjects and found differing patterns of subcortical abnormalities in the pediatric and adult OCD population, implying neuroplasticity may play a role in OCD. Results found adult OCD patients had smaller hippocampal volumes and larger pallidum volumes compared to adult controls, whereas pediatric OCD patients demonstrated a larger thalamic volumes when compared to their age-matched controls.

Increased Activity or Energy as a Primary Criterion for the Diagnosis of Bipolar Mania in DSM-5: Findings From the STEP-BD Study

Zarate, et al.

In order to assess the diagnostic validity of the DSM-5 criteria for mania or hypomania, the authors analyzed point prevalence data from the Systematic Treatment Enhancement Program for Bipolar Disorder study (STEP-BD) at the initial visit and follow up. Utilizing data from 4,360 patients enrolled, they compared prevalence, clinical characteristics, validators, and clinical outcomes in the 310 subjects who met DSM-IV criteria for mania/hypomania at the time of study entry. Analysis was based upon symptoms reported on the Clinical Monitoring Form. With the new DSM-5 criterion of increased activity or energy as a core requirement for diagnosis, the prevalence of mania/hypomania decreased by 48%. However, only minor differences were noted in clinical and concurrent validators, and no changes were observed in longitudinal outcomes between those who did and those who did not meet the DSM-5 criteria.

JAMA Psychiatry

Volume 74, Issue 1

Altered Brain Activity in Unipolar Depression Revisited: Meta-analyses of Neuroimaging Studies

Müller, et al.

In this conceptual replication of meta-analyses of 99 neuroimaging experiments on cognitive and/or emotional processing, authors analyzed aberrant brain activation in adults with unipolar depression. Analyses were calculated across emotional and cognitive processing experiments, positive and negative emotion processing experiments, experiments with a sex discrimination task, those using facial stimuli, and memory processing. Results showed a lack of consistent group differences across studies and the absence of replicable effects with overall analyses across cognitive processing experiments ($p>0.29$) and emotional processing experiments ($p>0.47$) showing no significant results. A lack of convergence was noted also in analyses investigate positive, negative, or memory processes. Controlling for confounds did not change results.

Prevalence of Depression in Patients with Mild Cognitive Impairment: A Systematic Review and Meta-analysis

Ismail, et al.

Authors sought to provide estimate of prevalence of depression in patients with mild cognitive impairment (MCI) and identify reasons for heterogeneity as depression is common in individuals with MCI and may confer a higher likelihood of progression to dementia. A literature search identified 57 studies comprising 20,892 patients that met their inclusions criteria. The overall prevalence of depression in patients with MCI was 32%. Interestingly, there was a significant difference ($p<0.001$) in prevalence of depression in community samples (25%) compared to clinic samples (40%).

Estimating the Heritability of Structural and Functional Brain Connectivity in Families Affected by Attention-Deficit/Hyperactivity Disorder

Sudre, et al.

Structural connectivity as defined by diffusion tensor imaging of white matter and resting-state fMRI were used to evaluate ADHD similarities in extended multigenerational families with ADHD. The majority of participants were males over 20 years old. Heritable patterns were found in white matter tracts connecting the ipsilateral cortical regions and the corpus callosum. Heritable patterns of functional connectivity were found in the default mode, cognitive control, and ventral attention networks. Specifically, more symptoms of hyperactivity/impulsivity and inattention were associated with decreased functional connectivity in the default mode network.

Effect of ω -3 Polyunsaturated Fatty Acids in Young People at Ultrahigh Risk for Psychotic Disorders - The NEURAPRO Randomized Clinical Trial

McGorry, et al.

NEURAPRO was a double-blind, placebo-controlled, randomized clinical trial which determined that treatment with ω -3 polyunsaturated fatty acids in combination with a high-quality psychosocial intervention, cognitive behavioral case management (CBCM), was no more effective than placebo plus CBCM in preventing onset and improving outcomes in patients at ultrahigh risk for psychosis. These findings differed from the findings of an earlier original single-center trial with promising results.

Effect of Group vs Individual Cognitive Processing Therapy in Active-Duty Military Seeking Treatment for Posttraumatic Stress Disorder - A Randomized Clinical Trial

Resick, et al.

This randomized control trial of 268 active-duty military service members with PTSD aimed to determine the effects of cognitive processing therapy on PTSD and co-occurring symptoms and whether they differ when administered in an individual or a group format. Those treated in individual or group cognitive processing therapy formats improved significantly with large effect sizes, but individual cognitive processing therapy produced significantly greater improvement. Symptoms of depression and suicidal ideation did not differ significantly between formats.

The Journal of Clinical Psychiatry

Volume 3, Issue 12

Depression Is Associated With High Levels of C-Reactive Protein and Low Levels of Fractional Exhaled Nitric Oxide: Results from the 2007-2012 National Health and Nutrition Examination Surveys

Cepeda, et al.

This population-based, cross-sectional study sought to investigate the relationship between major depressive disorder and psychoneuroimmunological dysfunction utilizing data from the National Health and Nutrition Examination Survey (NHANES). The authors assessed the association between two established inflammatory markers, C-reactive protein (CRP) and the neurotransmitter nitric oxide, and

depression as measured by the PHQ-9 questionnaire. Among 14,276 subjects, 7.73% had depressive symptoms, 10,036 subjects had CRP values, and 12,513 subjects with ≥ 2 reproducible fractional exhaled nitric oxide (FeNO) measurements. After adjustment, CRP levels were 31% higher and FeNO levels 10.7% lower in individuals with depressive symptoms than in those without in a large and representative US population.

Glutamatergic Agents as Add-On Medication for the Treatment of Obsessive-Compulsive Disorder: A Systemic Review and Meta-Analysis

Laoutidis, et al.

This meta-analysis of eight double-blind, randomized controlled trials of glutamatergic agents as add-on treatment in adults with obsessive-compulsive (OCD) showed an overall ratio for response of 3.71. When limited to studies of treatment-resistant patients, the effect size remained significant. Substances were notably well-tolerated with mild and benign adverse effects. Thus, augmentation strategies with glutamatergic substances were effective in OCD, and especially so for treatment-refractory OCD with limited side effects relative to antipsychotics.

Evidence to Support Montgomery-Asberg Depression Rating Scale Administration Every 24 Hours to Assess Rapid Onset of Treatment Response

Johnson, et al.

This study investigated the suitability of the Montgomery-Asberg Depression Rating Scale (MADRS), with a 24-hour recall period (MADRS-24hr), to assess the rapid onset of the antidepressant effect in treatment-resistant depression (TRD). Content validity was evaluated qualitatively through semi-structured interviews with patients with MDD and health care professionals (HCPs) well-versed in MDD and the use of the MADRS. Psychometric analysis was conducted on data from two randomized clinical studies of patients with TRD. Among 23 patients with TRD and 11 HCPs, the majority reported that the items captured in the MADRS can fluctuate in a 24 hour period and that a meaningful change in symptoms could be assessed in a 24-hour period, except for reduced sleep and appetite. Psychometric property evaluation showed that the instrument had high internal consistency reliability, test-retest reliability, construct validity, and post-intervention responsiveness to change.

Lurasidone Dose Escalation in Early Nonresponding Patients With Schizophrenia: A Randomized, Placebo-Controlled Study

Loebel, et al.

This multiregional, 6-week, randomized, double-blind, placebo-controlled study sought to evaluate the efficacy of low-dose lurasidone in adults with schizophrenia and to assess the effect of dose increase in patients who showed inadequate response to standard-dose lurasidone. A total of 412 patients were randomly assigned in a 1:2:1 ratio to receive lurasidone 20 mg/d, lurasidone 80 mg/d, or placebo. Those assigned to lurasidone 20 mg/d or placebo received the same medication throughout the study while those assigned to 80 mg/day receive this dose for the first two weeks, at which time they were classified

as early responders ($\geq 20\%$ improvement from baseline PANSS total score) or early nonresponders ($< 20\%$ improvement). Early responders continued to take lurasidone 80 mg/d, while early nonresponders were re-randomized in a 1:1 ratio to continue lurasidone 80 mg/d or to receive 160 mg/d for the remainder of the study. At the 6 week endpoint, dose increase to 160 mg/d at week 2 significantly reduced PANSS total score versus static 80 mg/d dose. Although a comparable magnitude of change was observed in Clinical Global Impression-Severity (CGI-S), this was not statistically significant. Patients receiving lurasidone 20 mg/d did not demonstrate improvement relative to placebo in PANSS total or CGI-S scores.

The Lancet Psychiatry

Volume 4, Issue 1

Prevalence and clinical characteristics of serum neuronal cell surface antibodies in first-episode psychosis: a case-control study

Lennox, et al.

This case-control study aimed to investigate whether people with circumscribed schizophrenia-like illness have antibodies against the N-methyl-D-aspartate receptor (NMDAR). 20 (9%) of 228 patients with first-episode schizophrenia had serum antibodies against one or more of the neuronal cell surface antibodies compared with four (4%) of 105 controls (unadjusted odds ratio 2.4, 95% CI 0.8–7.3). Seven (3%) patients had NMDAR antibodies compared with no controls ($p=0.0204$). The other antibodies did not differ between groups. However, antibody-positive patients did not appear to differ from antibody negative patients in over-all clinical characteristics and 6 month outcomes.

Efficacy of early administration of escitalopram on depressive and emotional symptoms and neurological dysfunction after stroke: a multicenter, double-blind, randomized, placebo-controlled study

Kim, et al.

This placebo controlled, double-blind trial aimed to evaluate the efficacy of early administration of escitalopram to reduce moderate or severe depressive symptoms and improve emotional and neurological dysfunction in patients with stroke. As per the researchers 237 patients were assigned to placebo and 237 patients were assigned to escitalopram. 195 in placebo group and 210 in escitalopram group were included in full analysis set. The primary outcome did not differ by study group in the full analysis set (25 [13%] patients in the placebo group vs 27 [13%] in the escitalopram group; odds ratio [OR] 1.00, 95% CI 0.56-1.80; $p>0.99$) or in the intention-to-treat analysis (34[14%] vs 35[15%]; OR 1.01, 95% CI 0.61-1.69, $p=0.96$). The study medication was generally well tolerated. The study interpreted that Escitalopram did not significantly reduce moderate to severe depressive symptoms in patients with acute stroke.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 56, Issue 1

Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents with Obsessive Compulsive Disorder: A Randomized Controlled Trial

Lenhard, et al.

This study's objective was to evaluate the efficacy of therapist-guided internet-based cognitive behavioral therapy (ICBT) for adolescents with obsessive-compulsive disorder (OCD). Sixty-seven adolescents ranging from the ages of 12-17 were randomly assigned to a 12-week clinician-and parent-supported ICBT program or a control waitlist condition. The primary outcome was rating measured on the Children Yale-Brown Obsessive Compulsive Scale (CY-BOCS) administered before and after the intervention. Individuals were followed for up to 3 months after the intervention. In intention-to-treat analyses, parent-supported ICBT was superior to waitlist on the CY-BOCS. This group also showed further improvement from post-treatment to 3-month follow-up.

Maternal Depressive Symptoms During and After Pregnancy and Psychiatric Problems in Children

Lahti, et al.

Authors of this study examined whether maternal depressive symptoms during pregnancy predict child psychiatric problems, whether these associations are gestational-week –or trimester specific, and whether maternal depressive symptoms after pregnancy mediate or add to the prenatal effects. The study sample comprised 2, 296 women and their children born in Finland between 2006-2010, participating in the prospective pregnancy cohort study Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) and followed up from 1.9 to 5.9 years of age. The women completed the Center for Epidemiologic Studies Depression Scale biweekly between 12 and 38 weeks of gestation. In the follow-up, they completed the Beck Depression Inventory-II and Child Behavior Checklist. Psychiatric problems were greatest in children whose mothers reported clinically significant depressive symptoms across pregnancy trimesters and during and after pregnancy. Maternal depressive symptoms during pregnancy predicted significantly higher internalizing, externalizing, and total problems in children. Results support the implementation and utilization of preventive interventions from early pregnancy.

Trends in Antipsychotic Prescribing in Medicaid-Eligible Youth

Edelsohn, et al.

The purpose of this study was to assess trends in the use of antipsychotic medication in Medicaid-eligible youth from 2008 to 2013 and the factors associated with this use. Youth aged 0 to 17 years with at least one claim indicating use of antipsychotic medication were identified from the network of a behavioral health managed care organization. Demographic and clinical variables were derived from state eligibility data and service claims data from the behavioral health managed care organization. The overall trend in prevalence for antipsychotics for youth decreased from 49.52 per 1,000 members in 2008 to 30.54 in

2013. Controlling for demographic and clinical variables, children age 0 to 5 years old were 79% less likely to be prescribed antipsychotic medications compared to the oldest youth, 13 to 17 years of age. Rates were higher for males versus females regardless of age. Children with a diagnosis of attention-deficit/hyperactivity disorder were less likely to be prescribed antipsychotics compared to those with diagnoses of autism spectrum disorder, bipolar disorder, psychoses, and depression.

Cortical Morphology Characteristics of Young Offspring of Patients with Schizophrenia or Bipolar Disorder

Sugranyes, et al.

This study's purpose was to examine cortical morphologic measurements in children and adolescents at genetic risk for schizophrenia and bipolar disorder. One hundred thirty-seven participants, including 36 offspring of patients with schizophrenia, 54 offspring of patients with bipolar disorder, and 47 offspring of community controls, 6 to 17-year olds, were assessed with clinical and neuroimaging methods. Sixty-nine percent of the sample was reassessed at 27.6 month follow-up. The schizophrenia group demonstrated a cross-sectional decrease in global, parietal, and occipital lobe surface area compared with the community control group and in the occipital lobe compared with the bipolar disorder group. In the schizophrenia group, global and parietal surface area values were inversely associated with attenuated positive and negative prodromal symptom scores.

Journal of the American Psychoanalytic Association

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The Analyst's Offer

Morris H

Morris focuses on the particular aspects of how analyses begin and their ethical implications for the analytic relationship as a whole.

The Fundamental Ethical Ambiguity of the Analyst as a Person

Kite JV

Kite considers analytic work from the perspective of "radical self-exposure" in contrast to other ideas about analysts as being more opaque. She explores ways that analysts reveal themselves in their attempts to protect their character. Kite goes on to hope that analysts learn by example from their analysts' "ethical nudity" the ability to be curious about the unknown parts of the self.