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Research Watch is an initiative by the residents of University Hospitals Cleveland Medical Center/ 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)

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Highlights

- Computerized cognitive training shows moderate effects on global cognition and psychosocial functioning in those with mild cognitive impairment. (AJP)
- Swedish registry study reports methylphenidate does not increase risk of treatment-emergent mania in bipolar disorder, if it is used in conjunction with mood-stabilizer. (AJP)
- Population-based Swedish cohort study suggests that inadequate maternal gestational weight gain is associated with an increased risk for nonaffective psychosis. (JAMA-P)
- Rates of paternal depression symptoms are higher during the postpartum period compared to antenatal, and are associated with adverse social and relationship factors. (JAMA-P)
- Biologic females with a more male-typic brain anatomy are 3 times more likely to have ASD than females with a characteristically female brain phenotype. (JAMA-P)
- Differences in corticothalamic circuitry may be linked to smoking relapse vulnerability. (JAMA-P)
- Use of long-acting injectable antipsychotic aripiprazole once-monthly significantly delayed and reduced recurrence of mood symptoms in patients with bipolar I disorder in RCT. (JCP)
- Mega-analysis reveals that individuals with ADHD have differences in subcortical brain volumes and intracranial brain volumes with the most pronounced effects noted in childhood. (LP)
- Starting opioid substitution therapy appears to be associated with a reduction in frequent use of heroin, cocaine, and, to a less extent, benzodiazepines and alcohol. (LP)
- Euthymic youth with bipolar disorder are found to have significant impairments across a range of cognitive measures. (JAACAP)
- Child abuse is associated with reduced prefrontal and temporal cortical thickness, and structural differences in select areas are associated with antisocial behavior and generalized anxiety. (JAACAP)
- Data analysis from the MTA study shows no evidence that ADHD increases the risk for psychotic symptoms. (JAACAP)

The American Journal of Psychiatry

Volume 174, Issue 4

Computerized Cognitive Training in Older Adults With Mild Cognitive Impairment or Dementia: A Systematic Review and Meta-Analysis

Hill, et al.

This systematic review and meta-analysis of 17 randomized controlled trials of computerized cognitive training (CCT) found moderate effects on cognition in individuals with mild cognitive impairment. CCT was found to be efficacious on global cognition, select cognitive domains and psychosocial functioning in those with mild cognitive impairment. More investigation is necessary to examine the effects on conversion to dementia and efficacy for individuals who have already progressed to dementia.

The Risk of Treatment-Emergent Mania With Methylphenidate in Bipolar Disorder

Viktorin, et al.

This retrospective cohort study utilized Swedish national registries to identify 2,307 adults with bipolar disorder who initiated methylphenidate therapy between 2006 and 2014. The cohort was divided into two subgroups: one subgroup was treated with concomitant mood-stabilizing treatment and the other, methylphenidate monotherapy. The relative risk of mania among patients on methylphenidate monotherapy was increased in the first 3 months after medication initiation (hazard ratio=6.7), with similar results for the following 3 months. In contrast, among patients treated with a concurrent mood stabilizer, risk of mania was reduced in the initial 3 months (hazard ratio=0.6) and slightly reduced in the subsequent 3 months.

Prediction of Relapse After Discontinuation of Antipsychotic Treatment in Alzheimer's Disease: The Role of Hallucinations

Patel, et al.

Post hoc analyses of the multicenter Antipsychotic Discontinuation in Alzheimer's Disease (ADAD) trial examined the associations between neuropsychiatric symptoms before and after open risperidone treatment and computed the likelihood of relapse after randomization to continued treatment versus discontinuation to placebo. Among 180 patients with Alzheimer's disease and symptoms of agitation or psychosis, 112 responded to treatment with risperidone for 16 weeks. Of these, 110 patients were assigned randomly to continue risperidone for 32 weeks, to continue risperidone for 16 weeks then switch to placebo for 16 weeks, or to receive placebo for 32 weeks. Results showed that patients with severe baseline hallucinations were more likely to relapse after randomization, although visual hallucinations were not predictive of relapse. The effect was increased significantly in patients with baseline hallucinations if risperidone treatment was discontinued.

JAMA Psychiatry
Volume 74, Issue 4

Paternal Depression Symptoms During Pregnancy and After Childbirth Among Participants in the Growing Up in New Zealand Study

Underwood, et al.

This longitudinal cohort study looked at data from men who completed interviews during their partner's pregnancy and 9 months after birth of the child. Depression symptoms were measured using the Edinburgh Postnatal Depression Scale and PHQ-9. Elevated antenatal depression was found in 2.3% of the fathers and was associated with perceived stress (OR 1.38) and fair to poor health during their partner's pregnancy (OR 2.06). Elevated postnatal depression was found in 4.3% of fathers and was associated with perceived stress in pregnancy (OR 1.12), no longer being in a relationship with the mother (OR 6.36), having fair to poor health at 9 months (OR 3.29), being unemployed at 9 months (OR 1.86), and a history of depression (OR 2.84).

Efficacy of Psychotherapies for Borderline Personality Disorder: A Systematic Review and Meta-Analysis

Cristea, et al.

The authors report a meta-analysis of 33 randomized clinical trials of psychotherapies for borderline personality disorder populations. A total of 2,256 patients were included and combined outcomes of symptoms, self-harm, and suicide assessed. Results showed that investigated psychotherapies were moderately more effective than control interventions in stand-alone design (mean difference, g , of 0.32) and add-on designs (g 0.40). Results were similar in other outcomes, which favored psychotherapy, including: self-harm (g 0.32), suicide (g 0.44), health service use (g 0.40), and general psychopathology (g 0.32). There was no significant difference in treatment retention. DBT (g 0.34) and psychodynamic approaches (g 0.41) were the only types of therapies more effective than control. Publication bias was persistent, particularly for follow-up. Authors concluded that the effects in the studies are small, inflated by the risk of bias, and unstable at follow-up.

Association Between the Probability of Autism Spectrum Disorder and Normative Sex-Related Phenotypic Diversity in Brain Structure

Ecker, et al.

Etiological models suggest that neuroanatomical male phenotypes carry a higher intrinsic risk for Autism Spectrum Disorder (ASD) when compared to female phenotypes. This case-control study used a cross sectional sample of high-functioning adults with ASD to directly test this hypothesis. Cortical thickness was measured and assessed via MRI. A predictive model of biological sex based on cortical thickness measures assessed via MRI in neurotypical controls was developed. Results showed a significant increase in predictive probability for the male neuroanatomical brain phenotype and ASD. For example,

biologic females with a more male-typic brain anatomy were 3 times more likely to have ASD than biological female individuals with a characteristically female brain phenotype. This suggests that neuroanatomical sex-related brain phenotypes should be considered in determination of an individual's risk for ASD.

Association of Gestational Weight Gain and Maternal Body Mass Index in Early Pregnancy With Risk for Nonaffective Psychosis in Offspring

Mackay, et al.

There is a known association between exposure to famine and an increased risk for nonaffective psychosis. The Swedish population-based cohort study used population registry data to look at gestational weight gain and maternal BMI during the first antenatal visit. Among persons with nonaffective psychosis, 6.32% (HR 1.32) had mothers with extremely inadequate weight gain (<8 kg). Maternal mild thinness (BMI between 17 and 18.5) in early pregnancy was weakly associated with an increased risk of nonaffective psychosis with a HR of 1.21, and paternal severe thinness (BMI <16) was associated with a HR of 2.53. There was no association with maternal overweight or obesity.

Efficacy of Self-guided Internet-Based Cognitive Behavioral Therapy in the Treatment of Depressive Symptoms: A Meta-analysis of Individual Participant Data

Karyotaki, et al.

This meta-analysis identified randomized clinical trials (total participant number of 3,876) in which self-guided internet-based cognitive behavioral therapy (iCBT) was compared with a control (usual care, waiting list, or attention control) in individuals with symptoms of depression. Results showed that self-guided iCBT was significantly more effective than controls on depressive symptom severity and treatment response. Adherence to treatment was associated with lower depressive symptoms ($P = .001$) and greater response to treatment ($P < .001$).

Reevaluating the Efficacy and Predictability of Antidepressant Treatments: A Symptom Clustering Approach

Chekroud, et al.

Data from 9 clinical trials of major depression in 7,221 patients were analyzed using machine-learning approaches to determine whether antidepressants are equally effective at treating different kinds of symptoms in depression. Antidepressants in general (8 of 9 treatments) were more effective for core emotional symptoms (energy, concentration, anhedonia, mood, worthlessness) than for sleep or atypical symptoms. Differences in efficacy between drugs were often greater than the difference in efficacy between certain treatments and placebo (for instance, high-dose duloxetine was superior to escitalopram in treating core emotional symptoms, while escitalopram did not differ from placebo). Selecting antidepressant based on efficacy for a particular cluster may be a beneficial strategy.

Association Between Baseline Corticothalamic-Mediated Inhibitory Control and Smoking Relapse Vulnerability

Froeliger, et al.

In two functional magnetic resonance imaging studies, a smoking cessation study (n = 81) and a laboratory-based smoking assessment (n = 26), baseline differences in corticothalamic circuitry function were associated with mediated inhibitory control and smoking relapse vulnerability. This information could help play a part in future interventions for augmenting corticothalamic neurotransmission and enhancing inhibitory control during the course of tobacco use disorder treatment.

Disruption of Reward Processing in Addiction: An Image-Based Meta-analysis of Functional Magnetic Resonance Imaging Studies

Luijten, et al.

This meta-analysis looked at 25 studies and included 643 individuals with addictive behaviors and 609 healthy control individuals. During reward anticipation, individuals with substance and gambling addictions showed decreased striatal activation compared with healthy control individuals. During reward outcome, individuals with substance addiction showed increased activation in the ventral striatum, whereas individuals with gambling addiction showed decreased activation in the dorsal striatum compared with healthy control individuals.

The Journal of Clinical Psychiatry

Volume 78, Issue 3

Efficacy and Safety of Aripiprazole Once-Monthly in the Maintenance Treatment of Bipolar I Disorder: A Double-Blind, Placebo-Controlled, 52-Week Randomized Withdrawal Study

Calabrese, et al.

This multicenter, double-blind, placebo-controlled, randomized 52-week withdrawal study evaluated the efficacy of the long-acting injectable antipsychotic aripiprazole once-monthly 400 mg (AOM 400) as maintenance treatment for bipolar I disorder, as well as safety and tolerability. Patients meeting diagnostic criteria for bipolar I disorder (DSM-IV) and experiencing a manic episode at study enrollment were stabilized sequentially on oral aripiprazole and AOM 400, and then randomized to AOM 400 or placebo thereafter. Of 1,175 patients screened, 266 entered the double-blind withdrawal phase and were randomly assigned to AOM 400 (n = 133) or placebo (n = 133). A total of 64 (48.1%) and 38 (28.6%) in the AOM 400 and placebo groups, respectively, completed the study. Recurrence of mood symptoms was significantly delayed and reduced in those receiving AOM 400 vs placebo (HR: 0.45; $P < .0001$). Effectiveness of AOM 400 was further supported by improvement in mania severity as assessed by YMRS. AOM 400 was generally safe and well tolerated, with weight increase, akathisia, and anxiety as the most noted adverse events.

The Relationship Between Stressful Life Events and Axis I Diagnoses Among Adolescent Offspring of Proband With Bipolar and Non-Bipolar Psychiatric Disorders and Healthy Controls: The Pittsburgh Bipolar Offspring Study (BIOS)

Pan, et al.

This study assessed the impact that stressful life events have on the development of mood disorders. The Stressful Life Events Schedule (SLES) was used to examine the frequency and nature of the stressful life events compared among 3 groups of adolescent offspring of probands with bipolar disorder (BD), with non-BD psychiatric disorders, and healthy controls. Offspring of probands with BD have greater exposure to independent and neutral life events than offspring of healthy controls. Greater frequency and severity of stressful life events were associated with Axis I disorder in offspring of both BD and non-BD affected probands.

Adverse Childhood Experiences and Risk for First-Episode Major Depression During the Menopause Transition

Epperson, et al.

Authors examined the impact of early life stress as assessed by the Adverse Childhood Experiences Questionnaire (ACE-Q) on the first episode of major depressive disorder during the menopause transition among participants in the 16-year, longitudinal Penn Ovarian Aging Study (POAS). Adverse childhood experiences (ACEs) and their onset with respect to puberty were evaluated in 243 members of the cohort. The cumulative incidence of lifetime MDD was 43.1%. Women reporting ≥ 2 total ACEs were at significantly greater risk for lifetime MDD and incident menopause MDD relative to those reporting no ACEs. Women with ≥ 2 postpubertal ACEs were 2.3 times more likely to experience incidence menopause MDD after controlling for race, smoking, body mass index, and employment.

The Lancet Psychiatry

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Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis

Hjortshøj, et al.

This systematic review and meta-analysis attempted to estimate years of potential life lost and life expectancy in individuals with schizophrenia, which the authors believe to be more direct, absolute measures of increased mortality than used in prior studies. The researchers identified 11 studies, which included 247, 603 patients across all continents but South America. Although there was some variation between samples, patients with schizophrenia lose between 13 and 15 years of potential life, with higher loss for men than women. Regional differences were noted with the least years of loss in the Asian study and a strikingly high estimate of 27 years lost in the African study. The overall weighted average life expectancy was 64.7 years and was lower for men than women (59.9 years vs. 67.6 years). Life expectancy was lowest in Africa and Asia. The effects of schizophrenia on years of potential life lost

and life expectancy seem to be substantial and not to have lessened over time.

Subcortical brain volume differences in participants with attention deficit hyperactivity disorder in children and adults: a cross-sectional mega-analysis

Hoogman, et al.

Neuroimaging studies have shown structural alterations in several brain regions in children and adults with attention deficit hyperactivity disorder (ADHD). Through the formation of the international ENIGMA ADHD working group, this study aimed to address weaknesses of previous imaging studies and meta-analyses, namely inadequate sample size and methodological heterogeneity. This cross-sectional, multisite mega-analysis included 23 cohorts comprising 1,713 participants with ADHD and 1,529 controls. The study revealed that participants with ADHD had significantly smaller volumes for the volumes of accumbens, amygdala, caudate, hippocampus, putamen, and intracranial volume with the largest effect in the amygdala. There was no difference in volume size in the pallidum ($p=0.95$) or thalamus ($p=0.39$). Exploratory lifespan modelling suggested a delay of maturation and a delay of degeneration, as effect sizes were highest in most subgroups of children (<15 years) versus adults. However, there was no difference between children and adults for the pallidum or thalamus. Case-control differences in adults were non-significant (all $p>0.03$). Psychostimulant medication use and comorbid psychiatric disorders did not impact results (For this analysis, p values were considered significant at a corrected threshold of $p=0.0156$).

Changes in substance use in patients receiving opioid substitution therapy and resulting clinical challenges: a 17-year treatment case register analysis.

Herdener, et al.

The authors sought to evaluate short-term and long-term changes in substance use in opioid-dependent patients on opioid substitution therapy, including methadone or buprenorphine. The researchers investigated a treatment case register of a large sample of patients on opioid substitution ($n = 8,962$) over 17 years and evaluated frequency of use of heroin, cocaine, benzodiazepines, and alcohol under naturalistic conditions. The study revealed that most frequent use of heroin (OR 5.30), cocaine (2.30) and, to a lesser extent, benzodiazepines (1.34) and alcohol (1.21) was found in previously untreated individuals compared with patients already receiving treatment 6 months after starting opioid substitution therapy, corroborating a strong effect of starting substitution therapy. An overall decline of frequent heroin and cocaine use among patients on opioid substitution therapy was significant between 1998 and 2014, while frequent use of alcohol increased.

Journal of the American Academy of Child and Adolescent Psychiatry

Volume 56, Issue 4

Cognitive Impairment in Euthymic Pediatric Bipolar Disorder: A Systematic Review and Meta-Analysis

Elias, et al.

Authors conducted a systematic review and meta-analysis of studies investigating neurocognition in euthymic youths with bipolar disorder compared to healthy controls. A systematic literature search yielded a total of 24 original peer-reviewed studies meeting inclusion criteria. Overall, euthymic youth with bipolar disorder were found to have significant impairments in verbal learning, verbal memory, working memory, visual learning, and visual memory with moderate to large effect sizes. There was substantial heterogeneity in the effect size across studies.

Parental Psychopathology and Tourette Syndrome/Chronic Tic Disorder in Offspring: A Nationwide Case-Control Study

Leivonen, et al.

Data from three national registries in Finland were analyzed in this nested case-control study to determine associations between parental psychopathology and diagnosis of Tourette syndrome/chronic tic disorder in offspring. In total, up to one-fifth of patients with Tourette syndrome/chronic tic disorder had a mother with a psychiatric diagnosis, compared to a little more than one-tenth of controls. Paternal psychopathology also correlated with a diagnosis of Tourette syndrome/chronic tic disorder in offspring. A stronger association was found between maternal psychiatric diagnosis and Tourette syndrome/tic disorder in offspring.

Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study

Groth, et al.

The aim of this prospective follow-up study was to describe the clinical course of tics and comorbidities during adolescence and understand the prevalence of coexisting psychopathologies. Subjects were recruited at the Danish National Tourette Clinic and data was recorded at baseline and at follow-up six years later. Individuals were between 5-19 years of age. The Development and Well-Being Assessment was used to diagnose coexisting psychopathologies. Severity of tics and obsessive-compulsive symptoms declined during adolescence. At follow-up, 63% of participants were found to have comorbidities or coexistent psychopathology.

Child Abuse, Neural Structure, and Adolescent Psychopathology: A Longitudinal Study

Busso, et al.

This longitudinal design study aimed to prospectively identify neural mediators of the association between child abuse and psychiatric disorders in a community sample of adolescents. Among 51 adolescents, 19 of whom were exposed to physical or sexual abuse, assessment was conducted for abuse exposure and observations were made on MRI imaging and mental health assessments over a mean period of 23 months. Abuse was associated with reduced cortical thickness in medial and lateral prefrontal and temporal lobe regions. Thickness of the left and right parahippocampal gyrus predicted antisocial behavior symptoms, and thickness of the middle temporal gyrus predicted symptoms of

generalized anxiety disorder. Thickness of the left parahippocampal gyrus mediated the longitudinal association of abuse with antisocial behavior.

Psychotic Symptoms in Attention-Deficit/Hyperactivity Disorder: An Analysis of the MTA Database

Vitiello, et al.

The purpose of this study was to assess the prevalence of psychotic symptoms among youths (ages 14-25) with a childhood diagnosis of attention-deficit/hyperactivity disorder (ADHD) combined type. Participants in the Multimodal Treatment Study of Children with ADHD and a local normative comparison group were systematically assessed at various time points after enrollment. There was no evidence that ADHD increased the risk for psychotic symptoms. The prevalence of clinician-confirmed psychotic symptoms was 1.1% in the MTA study group and 0.7% in the comparison ($p=0.72$). Greater cannabis use was reported by those with confirmed psychotic symptoms.