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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)
- * JAMA

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Highlights

- In adolescents and young adults with bipolar disorder, alterations in fronto-limbic gray matter volume, white matter integrity, and functional connectivity are evident among those who have attempted suicide. (AJP)
- RCT shows efficacy of liraglutide (glucagon-like peptide-1 receptor agonist) for the treatment of prediabetes and obesity in schizophrenia subjects treated with clozapine and olanzapine. (JAMA-P)
- Meta-analysis shows that suicide risk is markedly elevated after psychiatric hospitalization with persistently elevated risk up to 10 years post-discharge. (JAMA-P)
- Depression in mid-life does not appear to have an increased risk of dementia, however, depression in late-life does. (JAMA-P)
- Meta-analysis shows that methylphenidate derivatives decrease the risk of irritability in children with ADHD while amphetamine derivatives increase the risk. (JCP)
- Acute use of alcohol and CNS depression – but not cannabis and CNS stimulants – appears to be associated with an increased risk of attempting suicide within a 24-hour period. (JCP)
- Finish cohort study shows that out of all psychotropics, lithium – especially without antidepressants – has the lowest risk of readmission for subjects with unipolar depression. (LP)
- In an analysis from UK, smoke-free policies were associated with a 39% reduction in number of physical assaults per month in psychiatric inpatient settings. (LP)
- Danish cohort study shows that subjects with ADHD are less likely to become parents in general, but are more likely to become parents while being teenagers. (JAACP)
- Aripiprazole augmentation has a small efficacy advantage over switching to bupropion (higher remission and response rates) and bupropion augmentation (higher response rates only) in the treatment of depression. (JAMA)

The American Journal of Psychiatry

Volume 174, Issue 7

Gaze-Contingent Music Reward Therapy for Social Anxiety Disorder: A Randomized Controlled Trial

Lazarov, et al.

This parallel group randomized control trial (N=40) examined the efficacy of a novel attention bias modification treatment (gaze-contingent music reward therapy) for social anxiety disorder aimed at reducing attention dwelling on threats. Participants were randomly assigned to eight sessions of gaze contingent music reward therapy, designed to divert patients' gaze to neutral rather than threat stimuli, or to a control condition. Symptoms of Social Anxiety Disorder were assessed via clinician administered Leibowitz Social Anxiety Scale (LSAS) and self-rated Social Phobia Inventory (SPIN) pre-treatment, 1 week post-treatment, and at 3-month follow-up. Following the 1-month intervention, subjects in the music contingent condition were significantly more likely to have reductions in time spent on threatening stimuli but also on both clinician-rated and self-reported measures of social anxiety. The effects of gaze contingent music reward therapy were maintained at 3 month follow-up, with 75% of the gaze-continent subjects meeting clinically significant change compared with 30% of the placebo group.

Multimodal Neuroimaging of Frontolimbic Structure and Function Associated with Suicide Attempts in Adolescents and Young Adults with Bipolar Disorder

Johnston, et al.

Gray matter volume, white matter integrity, and functional connectivity were studied in 26 adolescents and young adults with bipolar disorder who have attempted suicide, 42 nonattempters, and in a healthy control group (n=45). Participants completed scales assessing mood, suicidal ideation, intent, attempt, and lethality, hopelessness, and impulsivity, and underwent structural MRI (sMRI), diffusion tensor imaging (DTI), and functional MR (fMRI) scans. Compared with the nonattempter group, attempters demonstrated significantly lower gray matter volume in the right orbitofrontal cortex, hippocampus, and bilateral cerebellum. Attempters had lower fractional anisotropy in the left uncinate fasciculus region, and they demonstrated lower functional connectivity from the amygdala to the left ventral prefrontal region versus nonattempters. As compared with healthy controls, attempters (but not nonattempters) demonstrated significantly lower right hippocampal volume and functional connectivity in the left ventral prefrontal cortex, and lower (but not significantly) fractional anisotropy in bilateral uncinate fasciculi.

Identification of Common Neural Circuit Disruptions in Cognitive Control Across Psychiatric Disorders

McTeague, et al.

This meta-analysis was conducted to study transdiagnostic functional impairment in whole brain activation during cognitive control task performance. PubMed search was conducted and 283 relevant experiments were selected that compared patients with axis I conditions and matched healthy controls.

These were included in the meta-analysis, consisting of 5728 controls and 5493 patients with various psychiatric disorders. Results demonstrated disruptions of neural circuitry in the left prefrontal cortex and anterior insula, the right ventrolateral prefrontal cortex, the right intraparietal cortex, the anterior midcingulate/presupplementary motor cortex, and the anterior dorsal cingulate cortex. Areas of disruption demonstrated in this study parallel the “multiple demand network” seen in intact cognition.

JAMA Psychiatry

Volume 74, Issue 7

Trajectories of Depressive Symptoms Before Diagnosis of Dementia: A 28-Year Follow-up Study

Singh-Manoux, et al.

This 28-year follow-up cohort study aimed to characterize the trajectory of depressive symptoms over 28 years prior to dementia diagnosis to determine the relationship between depressive symptoms and dementia risk. A total of 10,308 subjects, aged 35 to 55 years, were recruited to the Whitehall II cohort study. Those reporting depressive symptoms in study phase corresponding to midlife, even when chronic/recurrent, did not have significantly increased risk for dementia; however, those with depressive symptoms in late-life had an increased risk (HR, 1.72; 95% CI, 1.21-2.44). Analysis of trajectory of depressive symptoms showed them to emerge approximately a decade prior to dementia diagnosis. These results suggest that depressive symptoms may be a prodromal feature of dementia or that both late-life depression and dementia may share common causes. Authors found no support for the construct that depressive symptoms are a risk factor for dementia.

Effect of Liraglutide Treatment on Prediabetes and Overweight or Obesity in Clozapine- or Olanzapine-treated Patients With Schizophrenia Spectrum Disorder: A Randomized Clinical Trial

Larsen, et al.

This randomized controlled trial evaluated the effects of adjunctive treatment with the glucagon-like peptide-1 receptor agonist liraglutide in patients on antipsychotic therapy for schizophrenia spectrum disorders. Among 103 participants who were randomized to receive liraglutide or placebo, all were receiving stable treatment for a schizophrenia spectrum disorder (excluding schizoaffective disorder) with clozapine or olanzapine, were overweight or obese, and had prediabetes. After 16 weeks of treatment, glucose tolerance improved significantly ($P < .001$) in the experimental group with a 23% larger reduction in a 2-hour glucose tolerance test. There was a mean weight loss difference between liraglutide and placebo of -5.3 kg. Waist circumference, BMI, total cholesterol levels, and low-density lipoprotein levels were decreased significantly with liraglutide versus placebo after adjustment. Overall, 63.8% of the liraglutide group developed normal glucose tolerance, compared with 16.0% in the placebo group, which corresponds to a number needed to treat of 2.

Suicide Rates After Discharge From Psychiatric Facilities: A Systematic Review and Meta-analysis

Chung, et al.

A meta-analysis of 100 studies of suicide rates among persons discharged after psychiatric hospitalization estimated a pooled post-discharge suicide rate of 484 suicides per 100,000 person-years, which is 44 times the national suicide rate of 11.4 per 100,000 person-years. During the first 3 months after discharge, the overall suicide rate across studies was 1132 per 100,000 person-years. Although the rate decreased to 654 per 100,000 person-years during the subsequent 9 months, it remained markedly elevated (277 per 100,000 person-years) at least 10 years after hospital discharge. Additionally, the suicide rate among patients with prior suicidal behavior was nearly 4 times higher than that of inpatients without such behavior. An overall trend of increased suicide risk after hospital discharge was noted with the suicide rate per 100,000 person-years of follow-up increased by more than one-third between earlier (1975-1984 and 1985-1994) and later (1995-2004 and 2004-2016) periods.

Real-World Effectiveness of Antipsychotic Treatments in a Nationwide Cohort of 29,823 Patients with Schizophrenia

Tiihonen, et al.

This nationwide cohort study utilized prospective data from gathered between 2006 and 2013 among 29,823 patients in Sweden, ages 16 to 64, with a diagnosis of schizophrenia to assess the clinically meaningful differences between specific antipsychotic medications or routes of administration on rehospitalization and treatment failure. Risk of rehospitalization was lowest with once-monthly long-acting injectable paliperidone (HR, 0.51; 95% CI, 0.41-0.64), long-acting injectable zuclopenthixol (HR, 0.53; 95% CI, 0.48-0.58), clozapine (HR, 0.53; 95% CI, 0.44-0.77), long-acting injectable perphenazine (HR, 0.58; 95% CI, 0.52-0.65), and long-acting injectable olanzapine (HR, 0.58; 95% CI, 0.44-0.77) compared with no antipsychotic medication. Oral flupentixol (HR, 0.92; 95% CI, 0.74-1.14), quetiapine (HR, 0.91; 95% CI, 0.83-1.00), and oral perphenazine (HR, 0.86; 95% CI, 0.77-0.97) were associated with the highest risk of rehospitalization. Clozapine and long-acting injectable antipsychotics were associated highest rates of prevention of relapse in schizophrenia, as compared with the most widely used oral medication, olanzapine. Long-acting injectable medications were associated with a 20% to 30% lower risk of rehospitalization relative to equivalent oral formulations.

The Journal of Clinical Psychiatry

Volume 78, Issue 6

Risk of Irritability with Psychostimulant Treatment in Children With ADHD: A Meta-Analysis

Stuckelman, et al.

This meta-analysis sought to quantify the risk of irritability as a side effect of psychostimulant treatment for ADHD after reviewing 32 prior double-blind, randomized, placebo-controlled studies. The relative risk of irritability significantly differed between psychostimulant classes. Methylphenidate derivatives were associated with a significantly decreased risk of irritability compared to placebo (RR=0.89), whereas amphetamine derivatives were associated with a significantly increased risk of irritability (RR=2.90).

Future head-to-head trials between methylphenidate and amphetamine derivatives examining effects on irritability are recommended.

Acute Substance Use as a Warning Sign for Suicide Attempts: A Case-Crossover Examination of the 48 Hours Prior to a Recent Suicide Attempt

Bagge, et al

This study aimed to quantify the near-term effects of sole use and co-use of substances on medically attended suicide attempts of 363 patients presenting at Level 1 trauma hospital between October 2008 and April 2014. The authors used a case-crossover design, comparing substance use within the 24 hours prior to a suicide attempt. Results indicated that patients were at increased odds of attempting suicide after drinking alcohol within a 24-hour period (OR = 4.40; 95% CI, 2.31–8.40) and using CNS depressants such as sedatives/anxiolytics and opioids (OR = 2.82; 95% CI, 1.13–7.01). The acute use of cannabis and CNS stimulants (stimulants/amphetamines and cocaine) was not uniquely associated with suicide attempt. Findings suggest the importance of considering acute alcohol use and use of CNS depressants, and the concurrent use of both substances, when evaluating short-term risk for suicide attempts in clinical settings.

Intermittent Explosive Disorder and Substance Use Disorder: Analysis of the National Comorbidity Survey Replication Sample

Coccaro, et al

This article assessed the relationship between intermittent explosive disorder (IED) and substance use disorder (SUD) as the authors indicated a lack of studies between impulsive aggression and substance use. Examination of the severity of IED and of SUD revealed that the presence of IED increases SUD severity but that the presence of SUD does not increase IED severity. It was found that the onset of IED preceded that of SUD in 92.5% of comorbid IED + SUD cases. IED was determined to be a risk factor to developing SUD. The authors recommend treating the IED before the onset of substance abuse, which could potentially prevent or delay the development of SUD.

The Lancet Psychiatry

Volume 4, Issue 7

Pharmacological treatment and risk of readmission to hospital for unipolar depression in Finland: a nationwide cohort study

Tiihonen, et al.

This nationwide cohort study aimed to study the effectiveness of pharmacological treatments in relapse prevention in a nationwide cohort of patients who had been admitted to hospital at least once as a result of unipolar depression. Data from 123,712 patients were included in the total cohort, with a mean follow-up time of 7.9 years. Lithium use was associated with a lower risk of re-admission to hospital than no

lithium use (hazard ratio [HR] 0.47), whereas antidepressants and antipsychotics were not associated with a reduced risk of readmission to hospital. Risk of hospital readmission was lower during lithium therapy alone than during use of lithium with antidepressants. After lithium, clozapine (HR 0.65) and amitriptyline (HR 0.75) were agents associated with the next lowest risk of readmission.

Effect of implementation of a smoke-free policy on physical violence in a psychiatric inpatient setting: an interrupted time series analysis

Robson, et al.

This interrupted time series analysis aimed to assess the effect of implementing a comprehensive smoke-free policy on rates of physical assaults in a large UK mental health organization. The researchers analyzed the incident reports of physical assault 30 months before and 12 months after the implementation of the policy in the inpatient wards of South London and Maudsley National Health Service Foundation Trust, London, UK. After adjusting for confounders, there was a 39% reduction in the number of physical assaults per month after the policy introduction compared with beforehand (incidence rate ratio 0.61), suggesting that smoke-free policies could be a violence reduction strategy in psychiatric settings.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 56, Issue 7

Childhood Psychiatric Disorders as Risk Factor for Subsequent Substance Abuse: A Meta-Analysis
Groenman, et al.

This meta-analysis of thirty-seven studies assessed the prospective risk of developing substance-related disorders in individuals diagnosed with attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder (CD), anxiety disorder, or depression during childhood. Outcome measures included undefined substance-use disorders (SUD), alcohol-related disorder, drug-related disorder, nicotine-related disorder, and overall addiction. Overall, childhood ADHD, ODD, CD, and depression increased risk for all previously defined outcome measures. Depression increased risk of SUDs, alcohol-related and nicotine-related disorders, and addiction. Younger age at diagnosis was associated with higher risk of addiction in all disorders.

Social Skills Training for Children and Adolescents with Autism Spectrum Disorder: A Randomized Controlled Trial

Olsson, et al.

This 12-week RCT of 296 children and adolescents from 13 different outpatient sites in Sweden sought to evaluate the effectiveness of a standardized social skills group training (SSGT) intervention, "KONTAKT", for children with autism spectrum disorder (ASD) where SSGT was broadly defined as any intervention that employs socially instructive techniques and behavioral modification principles in a group setting. Children with comorbid diagnoses of intellectual disability (IQ <70), conduct disorder, personality disorders, or severe psychotic disorders were not included in the study. The primary outcome measure

included parent- and teacher-reported Social Responsiveness Scale Results (SRS). Significant improvement was seen in parent-reported scores for adolescents (ages 13-17) both post-treatment and at follow-up. There was significant improvement in group scores for females at post-treatment, but not at follow-up. No significant group difference was found in children (ages 7-12).

Teenage Parenthood and Birth Rates for Individuals With and Without Attention-Deficit/Hyperactivity Disorder: A Nationwide Cohort Study

Soren, et al.

The study investigated the association between attention deficit/hyperactivity disorder (ADHD) and parenthood, including rates of teenage pregnancy, rates of lifetime parenthood overall, and total number of children. Using the Danish Civil Registration System and the Danish Psychiatric Central Research Register, a cohort was defined of 2,698,052 individuals born between 1980-1994, including 27,479 individuals diagnosed with ADHD between the ages of 12-19. Compared to individuals without ADHD, those with ADHD i) are more likely to become parents while being teenagers, ii) are less likely to become parents in general, iii) are more likely to have many children (three or more for males and four or more for females) if they do become parents, and iv) have fewer children on average (only males). Authors discuss that this pattern is likely to be a consequence of ADHD and not of confounding.

Miscellaneous

JAMA

Volume 318, Issue 2

Effect of Antidepressant Switching vs Augmentation on Remission Among Patients With Major Depressive Disorder Unresponsive to Antidepressant Treatment: The VAST-D Randomized Clinical Trial
Mohamed, et al.

This 12-week RCT of 1522 patients with major depressive disorder unresponsive to previous antidepressant treatment sought to compare the efficacy and safety of 3 intervention strategies: switch to bupropion, augment with bupropion, and augment with aripiprazole. Primary outcome was QIDS-C16 defined remission. Remission rates at 12 weeks were 22% for the switch group, 27% for the augment-bupropion group, and 29% for the augment-aripiprazole group. Aripiprazole augmentation was significantly superior to switching to bupropion, but was not significantly superior to bupropion augmentation. Response rates were 62% for the switch group, 66% for the augment-bupropion group, and 74% for the augment-aripiprazole group, with aripiprazole augmentation significantly superior to both other strategies for response. Nearly half of the subjects had PTSD, and it is possible that the modest advantage of aripiprazole augmentation in this study may be partly due to the enrichment in patients with MDD and comorbid PTSD. Anxiety was most frequent in the 2 bupropion groups, whereas somnolence, akathisia, and weight gain were most common among patients treated with aripiprazole.