



Department of Psychiatry
RESEARCH WATCH



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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)

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Highlights

- Of the individuals who died by suicide in a large cohort study following patients with suicide attempts, almost 60% died on the index suicide attempt. (AJP)
- Right unilateral ultrabrief pulse ECT, combined with venlafaxine, appears to be a rapid, effective and well-tolerated treatment for geriatric depression. (AJP)
- PRIDE study shows that after a successful course of acute ECT, continuation ECT plus medication leads to lower depression scores compared to medication only. (AJP)
- Meta-analysis suggests 40-Hz auditory steady-state response could be a potential biomarker in patients with schizophrenia. (JAMA-P)
- Prospective birth cohort study suggests that SSRI use during pregnancy may be associated with an increased risk of speech/language disorders in the offspring. (JAMA-P)
- Meta-analysis suggests a potential link between prediabetic markers (insulin resistance and impaired glucose tolerance) and first-episode psychosis. (LP)
- Contrary to popular belief, the average placebo response rates in antidepressant trials have been stable (between 35-40%) for more than 25 years. (LP)
- In a retrospective longitudinal study, paliperidone palmitate treatment was associated with significantly lower total health care costs (attributable to reduced inpatient admissions) among veterans with schizophrenia, compared to treatment with oral atypical antipsychotics. (JCP)
- A post-hoc analysis of 2 RCTs found that lurasidone monotherapy is significantly effective in adults with bipolar depression aged 55 years and older, while adjunctive therapy was not associated with significant improvement. (JCP)
- Severity of childhood ADHD, present of comorbid diagnoses, and parental mental health problems serve as predictors for persistence of ADHD symptoms into adulthood. (JAACAP)

The American Journal of Psychiatry

Volume 173, Issue 11

Suicide Attempt as a Risk Factor for Completed Suicide: Even More Lethal Than We Knew

Bostwick, et al.

This observational retrospective-prospective cohort study identified 1490 individuals making first lifetime suicide attempts reaching medical attention from 1986-2007. During the study period, 81 individuals (5.4%) died by suicide. Of these 81, 48 (59.3%) died on index attempt. 27 of 33 index attempt survivors (81.8%) died by completed suicide within a year. Survivors given follow-up psychiatric appointments had significantly lower likelihood of subsequent suicide (odds ratio=0.212, 95% CI=0.089–0.507). The completed suicide prevalence of 5.4% is almost 59% higher than what has been previously reported, which can be attributed to the unique study design which included index suicide attempt deaths.

Right Unilateral Ultrabrief Pulse ECT in Geriatric Depression: Phase 1 of the PRIDE Study

Kellner, et al.

The authors present the phase 1 results of the Prolonging Remission in Depressed Elderly (PRIDE) study, a two-phase multisite study that evaluated the efficacy of right unilateral ultrabrief pulse electroconvulsive therapy (ECT) combined with venlafaxine for the treatment of geriatric patients with unipolar depression. Overall, 70% met response criteria, 61.7% met remission criteria, 28.3% dropped out and 10.0% did not remit. The mean number of ECT treatments to remission was 7.3. This supports right unilateral ultrabrief pulse ECT, combined with venlafaxine as a rapidly acting, highly effective and well-tolerated treatment for the depressed geriatric population.

A Novel Strategy for Continuation ECT in Geriatric Depression: Phase 2 of the PRIDE Study

Kellner, et al.

Phase 2 of the PRIDE study evaluated the efficacy and tolerability of continuing ECT versus medication alone after a successful course of ECT in Phase 1 of the study. Phase 2 compared medication only (venlafaxine plus lithium over 24 weeks) and ECT plus medication (four continuation ECT treatments over 1 month, plus additional ECT as needed in addition to venlafaxine and lithium) arms and found that the ECT plus medication group had significantly lower HAM-D scores and were rated “not ill at all” on CGI-S compared to their medication-only counterparts. As in the phase 1 portion of the trial, global cognitive functioning did not differ between the two treatment groups, and few adverse effects were reported.

Meta-Analysis of fMRI Studies of Disruptive Behavior Disorders

Alegria, et al.

A meta-analysis of 24 imaging studies evaluating 338 youths with disruptive behavior disorders or conduct problems found dysfunction in the rostro-dorsomedial, fronto-cingulate and ventral-striatal regions.

These areas mediate reward-based decision making. Studies also consistently found youths with psychopathic traits had dysfunction of the ventromedial prefrontal cortex and limbic system as well as hyperfunctioning of the dorsal and fronto-striatal areas. This likely reflects poor affect reactivity and empathy in the presence of hyperactive executive control.

JAMA Psychiatry

Volume 73, Issue 11

Short-term Suicide Risk After Psychiatric Hospital Discharge

Olfson, et al.

A longitudinal cohort study evaluated Medicaid data to evaluate the risk of suicide during the first 90 days after hospitalization for individuals with first-listed diagnoses of psychiatric disorders. In this national retrospective longitudinal cohort of almost 1.9 million adult inpatients, suicide rates were highest for patients with depressive disorder, closely followed by those with bipolar disorder, schizophrenia, and substance use disorders. Rates were substantially lower for patients with non-psychiatric diagnoses or the US general population. Among the cohort with mental disorders, adjusted hazard ratios of suicide were associated with inpatient diagnosis of depressive disorder, outpatient diagnosis of schizophrenia, outpatient diagnosis of bipolar disorder, and an absence of any outpatient healthcare in the 6 months preceding hospital admission.

Association of Perinatal Risk Factors With Obsessive-Compulsive Disorder: A Population-Based Birth Cohort, Sibling Control Study

Brander, et al.

In this longitudinal, population-based cohort study, the authors aimed to explore the potential causal link between OCD and a range of perinatal factors. From the study cohort of 2.4 million children in Sweden, a subsample of differentially exposed siblings were evaluated. Maternal smoking during pregnancy, breech presentation, delivery by cesarean section, preterm birth, low birth weight, being large for gestational age, and Apgar distress scores were associated with a higher risk of developing OCD. This was independent of shared familial confounders including sex, year of birth, maternal and paternal age at birth, and parity. A dose-response association was identified for a number of perinatal events, with a higher risk for OCD noted in individuals with a greater number of events.

The 40-Hz Auditory Steady-State Response in Patients With Schizophrenia: A Meta-analysis

Thuné, et al.

This systematic meta-analysis attempted to determine if 40-Hz auditory steady-state response (ASSR) could be a biomarker in patients with schizophrenia. The 40-Hz ASSR reflect the propensity of neurons to oscillate at a particular gamma-band “resonant” frequency induced by external periodic stimulation and are important because gamma-band (30-200 Hz) oscillations may play a role in the cognitive deficits in

schizophrenia. Of the 20 studies analyzed, 17 reported significant reductions in 40-Hz ASSR spectral power and/or phase locking in patients with schizophrenia compared with healthy controls.

Association of Hormonal Contraception with Depression

Skovlund, et al.

In a prospective cohort study of Denmark, women and adolescents (aged 15 to 34 years) without prior diagnosis of depression or other major psychiatric disorders, treatment with antidepressants, or contraindications to hormonal contraceptive use were followed. When compared with non-users of contraceptives, users of combined oral contraceptives had an incidence rate ratio (RR) of first use of an antidepressant of 1.23. Users of progesterone-only pills had an RR for first use of an antidepressant of 1.34; users of a patch, 2.0; vaginal ring, 1.6, and of a levonorgestrel IUD, 1.4. Estimates were similar for diagnosis of depression. There was increased risk when combined oral contraceptive was used as an adolescent. The RR peaked on average 6 months after starting hormonal contraceptives.

Association of Selective Serotonin Reuptake Inhibitor Exposure During Pregnancy With Speech, Scholastic, and Motor Disorders in Offspring

Brown, et al.

This Finland prospective birth cohort study examined pregnant women and their singleton offspring based on maternal use of antidepressant and depression related psychiatric disorders during pregnancy. There were three groups: mothers with a diagnosis and history of SSRI purchase, mothers with a diagnosis but without history of SSRI purchase, and mother with no history of diagnosis or purchase. The cumulative incidence of speech/language, scholastic, and motor disorders were evaluated from birth to 14 years. Mothers who purchased SSRIs at least twice during pregnancy had a 37% increased risk of speech/language disorders in their offspring with a hazard ratio of 1.37. There was no difference in scholastic and motor disorders between the SSRI-exposed and unmedicated groups.

Association Between Continued Cannabis Use and Risk of Relapse in First-Episode Psychosis: A Quasi-Experimental Investigation Within an Observational Study

Schoeler, et al.

This prospective cohort study of new onset psychosis patients in England sought to clarify the association between changes in cannabis use and risk of relapse of psychosis, defined as subsequent hospitalization. Longitudinal modeling was used to examine whether changes in cannabis use and risk of relapse over time is due to shared vulnerability between psychosis and cannabis use, psychosis increasing risk of cannabis use (reverse causation), or the causal effect of cannabis use on psychosis relapse. The authors found that among 220 patients studied two years after first-episode psychosis, there was an increase in the odds of experiencing a relapse of psychosis during periods of cannabis use. Change in pattern of continuation significantly increased the risk, suggesting a dose-dependent association. Cross-lagged analysis confirmed that this association reflected an effect of cannabis use on relapse risk rather than an effect of relapse on cannabis use.

Activity-Dependent Changes in Gene Expression in Schizophrenia Human-Induced Pluripotent Stem Cell Neurons

Roussos, et al.

The authors sought to examine whether neuronal activity-dependence changes in gene expression are dysregulated in schizophrenia. Differential expression analysis and gene coexpression analysis were used to identify activity dependent or disease-specific changes in RNA of individuals with schizophrenia compared to controls. Ultimately, 1,669 genes were found to be significantly different in schizophrenia-associated stem-cell derived neurons with 1,119 of these altered in cells in response to depolarization. This resulted in a blunted effect of activity-dependent changes of gene expression in schizophrenia-associated neurons.

The Journal of Clinical Psychiatry

Volume 3, Issue 10

Increasing Versus Maintaining the Dose of Olanzapine or Risperidone in Schizophrenia Patients Who Did Not Respond to a Modest Dosage: A Double-Blind Randomized Controlled Trial

Sakurai, et al.

This double-blind randomized controlled trial of 103 patients with schizophrenia studied patients who did not respond to olanzapine 10mg/d or risperidone 3mg/d. The patients were then randomly assigned to a dose-increment or continuation group. Those in the dose-increment group had their antipsychotic doses doubled whereas those in the continuation group were kept at the same dose over a 4 week period. Generally no significant superiority was observed in any of the outcome measures in the increment group compared to the continuation group, however those with lower plasma concentrations of olanzapine on their initial treatment showed a greater improvement on the Positive and Negative Syndrome Scale (PANSS) positive subscale when their dose was increased ($P=.042$). Over-all it appears that patients with schizophrenia failing to respond to moderate antipsychotic doses may not benefit from an increase in dose.

Impact of Paliperidone Palmitate versus Oral Atypical Antipsychotics on Health Care Resource Use and Costs in Veterans with Schizophrenia

Young-Xu, et al.

A retrospective longitudinal study determined that paliperidone palmitate (PP) treatment was associated with significantly lower total health care costs (attributable to reduced inpatient admissions) among veterans with schizophrenia compared to treatment with oral atypical antipsychotics. An analysis of 10,290 veterans utilizing electronic health record data from the VA showed that PP was associated with less frequent all-cause inpatient hospitalizations and more frequent mental health intensive case management visits compared to OAs. PP treatment was associated with higher likelihood of increased income and lower likelihood of homelessness. While mean annual pharmacy and outpatient costs were

higher among PP users, mean annual inpatient costs were lower, resulting in average annual total health care (medical and pharmacy) cost savings associated with PP relative to OAAs. The authors indicate that higher mental health intensive case management participation among PP users may have contributed to the differences observed.

Efficacy of Lurasidone in Adults Aged 55 Years and Older With Bipolar Depression: Post Hoc Analysis of 2 Double-Blind, Placebo-Controlled Studies

Sajatovic, et al.

This post hoc analysis found that monotherapy with lurasidone was significantly effective while adjunctive therapy was not associated with significant improvement in adults aged 55 years and older with bipolar depression using the Montgomery-Åsberg Depression Rating Scale (MADRS). Both monotherapy and adjunctive therapy with lurasidone were safe and well-tolerated in this population. These results were obtained from an older adult population subgroup of 142 meeting DSM-IV criteria for bipolar I depression in 2 placebo-controlled, 6-week, randomized, double-blind studies.

The Lancet Psychiatry

Volume 3, Issue 11

The association between first-episode psychosis and abnormal glycemic control: systematic review and meta-analysis

Perry, et al.

This systematic review and meta-analysis aimed to assess whether the first-episode psychosis is associated with pre-diabetic markers, or developing diabetes, to determine whether intrinsic disease links could cause these disorders to develop in unison. The researchers used PRISMA criteria and searched for clinical studies published between database inception and January 6, 2016. Pooled analyses found first-episode psychosis to be related to insulin resistance (mean difference 0.30 [95% CI 0.18 to 0.42]), impaired glucose tolerance (mean difference 1.31 [0.37 to 2.25]), and the number of patients with impaired glucose tolerance (odds ratio 5.44), but not fasting plasma glucose. Their findings suggested a potential link between prediabetic markers and first-episode psychosis.

Placebo response rates in antidepressant trials: a systematic review of published and unpublished double-blind randomized controlled studies

Furukawa, et al.

This systematic review of placebo-controlled randomized controlled trials aims to examine associations between placebo-response rates and study and patient characteristics. The researchers searched for published and unpublished double-blind randomized placebo-controlled trials of first-generation and second-generation antidepressants for acute treatment of major depression in adults. The team identified 252 placebo-controlled trials done between 1978 and 2015. They found that average placebo response

rates in antidepressant trials have remained constant in range between 35% and 40%. The length of the study and the number of study centers were significant factors (RR 1.03, 95% CI 1.01-1.05 for 1 more week in trial length; 1.32, 1.11-1.57 for multicenter vs single-center trials). Thus, contrary to widely held belief, the average placebo response rates in antidepressant trials have been stable for more than 25 years.

Journal of the American Academy of Child and Adolescent Psychiatry

Volume 55, Issue 11

Childhood Attention-Deficit/Hyperactivity Disorder and Homelessness: A 33-Year Follow-Up Study

Lourdes, et al.

This 33-year prospective, controlled, follow-up study was performed to assess whether the persistence of childhood ADHD influences the likelihood of homelessness in adulthood. In clinic-referred patients, a follow-up was performed of 6-12 year old boys of white ethnicity with ADHD, at a mean age of 41 years. Comparisons of children without ADHD were matched for age and socioeconomic status. Probands had significantly higher rates of homelessness than comparisons. Those with persistent ADHD through adolescence had significantly more homelessness than those in whom ADHD had remitted, although this relationship was no longer significant when conduct disorder at the age of 18 was controlled for.

Children of Parents with Serious Mental Illness: With Whom Do They Grow Up? A Prospective, Population-Based Study

Ranning, et al.

This was a prospective, register-based cohort study that covered all children in the Danish population born after 1982 and their parents with a diagnosis of schizophrenia, depression, bipolar disorder, or none of the above. The objective was to calculate the proportion living in different household living arrangements. When parents had serious mental illness (SMI), children's living arrangements were characterized by more single-parent-headed households. Up to one-fifth of children lived with a single mother with a serious mental illness. Risks for dissolution of family varied with parents' socioeconomic position across all diagnostic groups.

Functional Adult Outcomes 16 Years After Childhood Diagnosis of Attention-Deficit/Hyperactivity Disorder: MTA Results

Hechtman, et al.

This study's objective was to compare educational, occupational, legal, emotional, substance use disorder, and sexual behavior outcomes in young adults with persistent and desistent attention-deficit hyperactivity disorder symptoms and a normal comparison group in the Multimodal Treatment Study of Children with ADHD. Data from 476 participants with ADHD (diagnosed at age 7-9) was collected at 12, 14, and 16 years postbaseline and from 241 age- and sex-matched classmates. The normative comparison group fared better in terms of outcomes related to education, employment, risky sexual behaviors. Persistent ADHD

demonstrated worse outcomes in terms of emotional outcomes, whereas the normal comparison group and symptom-desistent ADHD group did not differ. Overall, adult functioning after childhood ADHD was found to be generally worse when ADHD symptoms persisted.

Childhood Factors Affecting Persistence and Desistance of Attention-Deficit/Hyperactivity Disorder Symptoms in Adulthood: Results from the MTA

Roy, et al.

This study aimed to determine childhood factors that predicted persistence and desistance of ADHD symptoms in adulthood. Participants were 453 individuals from the Multimodal Treatment Study of Children and ADHD. Persistence of ADHD was defined using DSM-5 symptom counts either with or without impairment, as well as mean ADHD symptom scores on the Conners' Adult ADHD Rating Scale. The most important childhood predictors of adult ADHD symptom persistence were initial ADHD symptom severity, comorbidities, and parental mental health problems.