



Department of Psychiatry
RESEARCH WATCH



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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)
- * British Journal of Psychiatry (BJP)
- * Acta Psychiatrica Scandinavica (APS)

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Highlights

- Pre-reactivation propranolol (trauma memory reactivation performed under the influence of propranolol) appears to be an efficacious treatment for PTSD. (AJP)
- Fetal exposure to elevated placental CRH levels is shown to be associated with thinning of selective cortical regions and with cognitive and emotional deficits in school-aged children. (AJP)
- A significant decline of insular and dorsolateral prefrontal cortex volume is associated with relapse in major depression. (JAMA-P)
- Early intervention in first-episode psychosis is associated with reduction in the suicide rate over subsequent 12 years. (JAMA-P)
- Literature review suggests youth with autism spectrum disorder are up to 30 times more likely to present to the ED, and more likely to do so for behavioral problems, than youth without autism. (JCP)
- RCT shows that adding preventive cognitive therapy to antidepressant treatment is superior to antidepressants alone in prevention of depressive relapse or recurrence. (LP)
- A 10-year follow-up study shows that in patients with first-episode psychosis with a full initial response to treatment, medication continuation for at least the first 3 years decreases the risk of relapse and poor long-term clinical outcome compared to earlier discontinuation. (LP)
- Maternal antenatal depression is associated with lower epigenetic gestational age – a novel biomarker of aging at birth – in offspring, which in turn is associated with internalizing problems in boys. (JAACAP)
- In a retrospective study of 124 clinically diagnosed psychotic patients without neurological symptoms, all were negative for antineuronal antibodies tested in cerebrospinal fluid. (BJP)
- A large historical cohort study reports that conversion from unipolar depression to bipolar disorder is predicted by severe depression requiring inpatient treatment, psychotic symptomatology, and parental history of bipolar. (APS)

The American Journal of Psychiatry

Volume 175, Issue 5

Reduction of PTSD Symptoms with Pre-Reactivation Propranolol Therapy: A Randomized Controlled Trial

Brunet, et al.

This double-blinded, placebo-controlled RCT evaluated the impact of pre-reactivation propranolol on PTSD symptoms in a series of weekly treatment sessions over 6 weeks. Adults (N=61) with PTSD were randomly assigned to treatment or placebo. 90 minutes after administration of study medication, a blinded therapist asked participants to write a narrative of their trauma with associated bodily sensations in the present tense and then read back the narrative. Primary outcome measures included the patient-rated PTSD Checklist-Specific (PCL-S) and the Clinician-Administered PTSD Scale (CAPS). Results demonstrated a significant post-treatment CAPS score group difference of 11.5 ($p=0.034$). Within-group pre- to post-treatment effect sizes (Cohen's d) were 1.76 for propranolol and 1.25 for placebo. Time-by-group interaction scores on the PCL-S decreased an average of 2.43 points per week in the propranolol group, 14.58 points above that of placebo. Pre- to post-treatment effect sizes of PCL-S were 2.74 for propranolol and 0.55 for placebo.

Cortical Abnormalities Associated with Pediatric and Adult Obsessive-Compulsive Disorder: Findings from the ENIGMA Obsessive-Compulsive Disorder Working Group

Boedhoe, et al.

The authors of this paper ran meta- and mega-analyses on data from the ENIGMA OCD working group in order to compare cortical measures in adult and pediatric patients with OCD to healthy controls. Structural T1-weighted brain MRIs were acquired for adults and children with (N=1,905) and without (N=1,760) OCD and evaluated for cortical thickness (age and sex adjusted) and corrected surface area measurements. Adults with OCD had a significantly thinner inferior parietal cortex (Cohen's $d=-0.14$) and a lower surface area for the left transverse temporal cortex (Cohen's $d=-0.16$) vs. controls; medicated OCD adults had thinner cortices throughout the brain overall (Cohen's d ranged between -0.1 and -0.26). Pediatric OCD patients had significantly thinner cortices in the inferior and superior parietal regions and left lateral occipital cortex compared to controls (Cohen's d ranged between -0.24 and -0.31). While unmedicated pediatric OCD patients showed no significant differences in surface area, medicated patients demonstrated decreased surface area in frontal regions (Cohen's d was between -0.27 and -0.33).

Cortical Thinning and Neuropsychiatric Outcomes in Children Exposed to Prenatal Adversity: A Role for Placental CRH?

Sandman et al.

This prospective cohort study examined the effect of elevated placental CRH (pCRH) level exposure in utero on brain development and neuropsychiatric outcomes in school-aged children. Blood-samples were

obtained from mothers at 5 separate intervals during gestation. Children (48 boys, 49 girls) with stable neonatal courses and no known congenital or neurologic abnormalities underwent high resolution T1 anatomical structural brain MRI at mean age of 7.3 years. Cognitive and emotional function were assessed through the Child Behavioral Checklist, structured interviews with mothers, and the flanker task. Results showed that elevated fetal exposure to pCRH was associated with significant cortical thinning in the frontal poles with early exposure (19 weeks gestation) and lateral temporal and paracentral regions with late exposure (31 weeks gestation); there were stronger associations in girls vs. boys for both exposure periods. Cortical thinning was associated with externalizing behaviors (indirect effect= 0.93; 95% bias-corrected confidence interval [BCCI]=0.17, 2.05; $p < 0.05$) and poorer performance on visual processing and sustained attention tasks (indirect effect=42.11; 95% BCCI=4.27, 128.31; $p, 0.01$).

JAMA Psychiatry

Volume 75, Issue 5

Association of Brain Cortical Changes With Relapse in Patients With Major Depressive Disorder

Zaremba, et al.

This longitudinal case-control study included 64 patients with acute MDD at baseline and 59 healthy controls to evaluate the association between relapse in major depressive disorder and morphologic brain changes. All participants underwent structural magnetic resonance imaging at baseline and approximately 2 years later. Patients with at least one additional episode (relapse) between baseline and follow-up showed a significant decline of insular volume ($P = .04$) and dorsolateral prefrontal volume ($P < .001$) from baseline to follow-up. In patients without relapse, gray matter volume in these regions did not change significantly. Volume changes were not correlated with psychiatric medication or with severity of depression at follow-up.

Consanguineous Marriage and the Psychopathology of Progeny: A Population-wide Data Linkage Study

Maguire, et al

A retrospective population-wide cohort study in Northern Ireland evaluated the risk of common mood disorders or psychoses in children of consanguineous parents. Potential mental ill health was estimated by receipt of psychotropic medication. Of the 363,960 individuals included in the final sample, 609 (0.2%) were born to consanguineous parents. Multilevel logistic regression models found that children of first-cousin consanguineous parents were more than 3 times as likely to be in receipt of antidepressant or anxiolytic medications (OR 3.01) and more than twice as likely to be in receipt of antipsychotic medication (OR 2.13) compared with children of nonrelated parents.

Association of an Early Intervention Service for Psychosis With Suicide Rate Among Patients With First-Episode Schizophrenia-Spectrum Disorders

Kit Wa Chan, et al

This historical control study of 1,234 patients with first-episode schizophrenia-spectrum disorders examined the association of a 2-year early intervention service with suicide reduction during 12 years. The analysis included 1234 patients, with 617 each in the early intervention and standard care groups. The suicide rates were 7.5% in the standard care group and 4.4% in the early intervention group (McNemar $\chi^2 = 5.55$, $P = .02$). Patients in the EI group had significantly better survival (propensity score-adjusted HR 0.57; $P = .02$), with the maximum association observed in the first 3 years. The number needed to treat was 62 at year 1 and 29 at year 12.

Neural Markers of Resilience in Adolescent Females at Familial Risk for Major Depressive Disorder

Fischer, et al.

A longitudinal study was carried out to examine neural functional connectivity correlates of resilience in adolescent females. Sixty-five participants were followed over the course of adolescence from age 9 through age 18 years, for a mean of 7.6 years: 20 at high familial risk in whom depression did not develop (resilient), 20 at high familial risk in whom depression developed (converted), and 25 at low familial risk with no history of psychopathology (control). Participants in the resilient group had greater connectivity between the amygdala and orbitofrontal cortex ($P < .001$) and between the dorsolateral prefrontal cortex and frontotemporal regions ($P < .001$) than did converted adolescent females. Participants in the resilient group only, strength of amygdala-orbitofrontal cortex connectivity was correlated with positive life events ($r = 0.48$; $P = .03$). Resilient adolescent females had greater connectivity within frontal ($P < .001$) and limbic ($P < .001$) networks than did control individuals.

The Journal of Clinical Psychiatry

Volume 79, Issue 3

Youth With Autism Spectrum Disorder in the Emergency Department

Lytle, et al.

This comprehensive literature review found that youth (ages 0-17) with Autism Spectrum Disorder (ASD) were 30 times more likely to present to the ED than youth without ASD. These individuals with ASD who visited the ED tended to be older, more likely to have repeat visits to the ED, more likely to be admitted to psychiatric unit or medical floor, more likely to have public insurance, and more likely to have nonurgent ED visits than youth without ASD. Up to 13% of their visits to the ED were related to behavioral or psychiatric problems (externalizing problems or psychotic symptoms) compared to less than 2% for youth without ASD. The authors concluded that significant gaps are present in the literature related to ED services use by youth with ASD, recommending further research to avoid unnecessary ED utilization and hospitalization, reduce medical costs, and improve outcome for youth with ASD.

The Lancet Psychiatry

Volume 5, Issue 5

Effectiveness of preventive cognitive therapy while tapering antidepressants versus maintenance antidepressant treatment versus their combination in prevention of depressive relapse or recurrence (DRD study): a three-group, multicenter, randomized controlled trial

Bockting, et al.

This single-blind, multicenter, parallel, three-group, randomized controlled trial aimed to compare the effectiveness of antidepressant alone, with Preventive Cognitive Therapy (PCT), or PCT added to antidepressants in the prevention of depressive relapse and recurrence. 289 patients with history of at least two unipolar depressive episodes currently on antidepressants were randomly assigned to PCT and antidepressant (n=104), antidepressant alone (n=100), or PCT with tapering of antidepressant (n=85). Antidepressants alone were not superior to PCT while tapering off antidepressants in terms of the risk of relapse or recurrence. PCT plus antidepressants was superior to antidepressants alone: adding PCT to antidepressant treatment resulted in a 41% relative risk reduction compared with antidepressants alone (HR 0.59; p=0.026). Investigators conclude that maintenance antidepressant treatment is not superior to PCT after recovery from depression, whereas adding PCT to antidepressant treatment after recovery is superior to antidepressants alone.

Long-term effects of discontinuation from antipsychotic maintenance following first-episode schizophrenia and related disorders: a 10-year follow-up of a randomised, double-blind trial

Hui, et al.

This 10-year follow-up study of a randomized, double-blind trial assesses the relation between early maintenance therapy decisions in first-episode psychosis and the subsequent clinical outcome at 10 years. 178 patients with first-episode psychosis with full positive symptom resolution after at least 1 year of antipsychotic treatment were given maintenance treatment (n=89; oral quetiapine 400 mg daily) or early treatment discontinuation (n=89; placebo) for 12 months. After the trial, patients received naturalistic treatment. Poor outcome was defined as a composite of persistent psychotic symptoms, a requirement for clozapine treatment, or death by suicide. Poor 10-year clinical outcome occurred in 35 (39%) of 89 patients in the discontinuation group and 19 (21%) of 89 patients in the maintenance treatment group (risk ratio 1.84, p=0.012). Mediation analysis suggested that the consequences of early discontinuation for long-term poor clinical outcome were mediated in part through early relapse during the 12-month period of the randomized trial. Overall this cohort of patients had received about 3 years of treatment before entering the follow-up phase of the study (about 2 years of maintenance treatment before study entry and 1 year of treatment in the trial). Based on this, the authors conclude that in patients with first-episode psychosis with a full initial response to treatment, medication continuation for at least the first 3 years after starting treatment decreases the risk of relapse and poor long-term clinical outcome.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 57, Issue 5

The Epigenetic Clock at Birth: Associations With Maternal Antenatal Depression and Child Psychiatric Problems

Suarez, et al.

This study examined the association between maternal antenatal depression, epigenetic gestational age (GA; a novel biomarker of aging at birth), and psychiatric problems in young children (age 2-6; mean age: 3.7). 694 women from the PREDO Study were identified who provided information regarding pre-pregnancy depression and antenatal depressive symptoms; of these, 407 completed the Child Behavior Checklist on psychiatric problems. Two models were utilized for analysis, model 1 correcting for child-specific factors and model 2 for maternal-specific factors. Maternal history of depression before pregnancy and greater antenatal depressive symptoms were associated with lower epigenetic GA; effects were not additive. Child's lower epigenetic GA prospectively predicted total and internalizing problems in boys but not girls (Bonferroni-corrected 95% CI = 0.02-0.48 and 0.01-0.46 in models 1 and 2, respectively). Epigenetic GA partially mediated the association between antenatal depression and internalizing problems.

Autistic Traits and Suicidal Thoughts, Plans, and Self-Harm in Late Adolescence: Population-Based Cohort Study

Culpin, et al.

This study sought to examine the relationship between ASD in childhood and suicidal thoughts, plans, and self-harm. Of 14,684 adolescents enrolled in the ALSPAC study, 5,031 were identified with data on suicidal behavior and ideation up to age 16 years. Four measures predictive of autism diagnosis via parental questionnaires were analyzed including reduced social communication, repetitive behavior, reduced sociability, and reduced coherence. Regression analysis revealed effect of impaired social communication on risk of self-harm with suicidal intent (ARR = 2.14, 95% CI = 1.28-3.58, $p = 0.004$), but not self-harm without suicide intent. There was also evidence for effect of impaired social communication on risk of suicidal thoughts (ARR .42, 95% CI = 1.06-1.91, $p = 0.179$) and suicidal plans (ARR = 1.95, 95% CI = 1.09-3.47, $p = 0.24$). An indirect pathway from impaired social cognition to self-harm via depressive symptoms accounted for 32% of the total estimated association between impaired social cognition and self-harm.

The British Journal of Psychiatry

Volume 212, Issues 5

Absences of cerebrospinal fluid antineuronal antibodies in schizophrenia spectrum disorders

Oviedo-Salcedo, et al.

The authors of this retrospective study investigated the prevalence of neuronal antibodies in the serum and CSF of patients with a first or recurrent episode of psychosis presenting without major neurological symptoms. Subject exclusion criteria were organic and/or drug-induced psychotic disorders or clinical signs of possible underlying autoimmune encephalitis (e.g. seizures). CSF (n=124) and serum (n=81)

samples from subjects with schizophrenia spectrum disorders were analyzed. None showed positive CSF results; 3 subjects (3.7%) had low-titer neuronal antibodies in the serum. However, 14.6% of subjects showed intrathecal oligoclonal bands and 4.6% showed a mild pleocytosis, pointing possibly to a not yet fully understood central nervous system inflammatory or immune process in schizophrenia spectrum disorders. This study had significant limitations, namely retrospective and open design, single-screening method, lack of a control group, and lack of longitudinal data.

Acta Psychiatrica Scandinavica

Volume 137, Issue 5

Patterns and predictors of conversion to bipolar disorder in 91 587 individuals diagnosed with unipolar depression

Musliner, et al.

A historical prospective cohort study based on 91,587 individuals diagnosed with Unipolar Depression (UD) in a psychiatric hospital in Denmark was followed up to examine the association between a series of potential predictors and the conversion from UD to bipolar disorder (BD). The cohort was followed for a total of 702,710 person-years (ranged from 1 day to 22 years), during which 3,910 individuals with UD developed BD. The overall cumulative incidence of conversion from UD to BD diagnosis was 8.7% in females and 7.7% in males. The strongest predictor of conversion from UD to BD was parental history of BD (adjusted hazard ratio (aHR) = 2.60, 95% CI: 2.20–3.07). Other predictors included psychotic depression at the index UD episode (aHR = 1.73, 95% CI: 1.48–2.02), a prior/concomitant non-affective psychosis (aHR = 1.73, 95% CI: 1.51–1.99), and inpatient treatment at the index episode (aHR = 1.76, 95% CI: 1.63–1.91).

N-acetylcysteine for major mental disorders: a systematic review and meta-analysis of randomized controlled trials

Zheng W, et al.

This systematic review and meta-analysis of randomized controlled trials (RCTs) examined the efficacy and safety of adjunctive N-acetylcysteine (NAC) in treating major depressive disorder (MDD), bipolar disorder (BD) and schizophrenia. Three RCTs for schizophrenia (n = 307), two RCTs for BD (n = 125) and one RCT for MDD (n = 269) compared the NAC groups (1.2–6 g/day) with control groups. The 3 RCTs for schizophrenia assessed efficacy with the Positive and Negative Syndrome Scale (PANSS). NAC showed statistical significance in improving total psychopathology over placebo (SMD = -0.74, P = 0.03), but not in positive, negative, or general psychopathology scales of the PANSS. In the 2 RCTs for BD it showed no significant effect on depressive and manic symptoms as assessed by the Young Mania Rating Scale in bipolar disorder, and there was no significant difference in the single MDD RCT on major depressive symptoms as assessed by the Montgomery–Asberg Depression Rating Scale (MADRS). The NAC group had more frequent gastrointestinal (33.9% vs. 18.4%; P = 0.005) and musculoskeletal complaints (3.9% vs. 0%; P = 0.025).