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Research Watch is a resident-led monthly initiative, which aims to inform psychiatry residents of notable articles published in prominent research and educational journals, with the hope of promoting a culture of incorporating latest research in our psychiatric worldview.

Journals Covered:

- * American Journal of Psychiatry (AJP)
- * AJP – Resident’s Journal (RJ)
- * JAMA Psychiatry (JAMA-P)
- * Lancet Psychiatry (LP)
- * Journal of the American Academy of Child & Adolescent Psychiatry (JAACAP)
- * Current Psychiatry (CP)

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Highlights

- Oxytocin plays a role in the pathophysiology of borderline personality disorder by altering reward and empathy networks. (AJP)
- Cognitive behavioral therapy and light therapy are equally effective for seasonal affective disorder. (AJP)
- Brexpiprazole, at doses of 2mg and 4mg, is an effective and well-tolerated treatment for acute schizophrenia with akathisia and moderate weight gain as the most common adverse side effects. (AJP)
- Individuals who experienced severe childhood abuse demonstrated increased brain activation in error processing areas of the dorsomedial frontal cortex on fMRI studies. (AJP)
- Screening for anti-NMDA receptor autoantibodies should be considered in postpartum psychosis, especially with acute onset of atypical symptoms, particularly in the setting of other neurological symptoms or extrapyramidal side effects after initiation of antipsychotic treatment. (AJP)
- During the years from 2006-2010, antipsychotic use increased for adolescents and young adults but not for those under the age of 12, with use primarily directed towards impulsive and aggressive behaviors as opposed to psychosis. (JAMA-P)
- fMRI scans suggest a higher rate of thalamic dysconnectivity in individuals with high risk for psychosis. (JAMA-P)
- Self-identification with goth subculture is associated with an increased risk of depression and self-harm. (LP)

- Mortality in people with mental illness is far higher in individuals with substance use disorders than in those without. (LP)
- A recent meta-analysis of 22 double-blinded, randomized, placebo-controlled trials does not point towards an association between new onset tic or worsening of tics and psychostimulant use in children. (JAACAP)
- Dopamine transporter in the striatum is the most likely useful target to stratify patients with ADHD into stimulant-responsive and stimulant-unresponsive subtypes. (CP)
- **Research Watch Bonus Material: An Overview of Rexulti (Brexpiprazole)**

The American Journal of Psychiatry

Volume 172, Issue 9

A New Perspective on the Pathophysiology of Borderline Personality Disorder: A Model of the Role of Oxytocin

Herpetz and Bertsch

This review summarizes the accumulating evidence of the oxytocinergic system's role in the pathophysiology of borderline personality disorder and other psychiatric disorders where mal-adaptive parent-infant attachment is an etiological factor. Oxytocin is thought to alter reward and empathy networks, normalize top-down processes in affect regulation, improve social reward experiences in the mesolimbic circuit, engage the brain salience network to favor adaptive social approach behaviors and modulate brain regions involved in cognitive and emotional empathy. There is also preliminary data suggesting involvement of oxytocin within the cannabinoid system, with implications in pain processing.

Cognitive Enhancement Treatment for People with Mental Illness Who Do Not Respond to Supported Employment: A Randomized Controlled Trial

McGurk, et al.

This study randomized 107 participants with severe mental illness who had difficulty maintaining employment to receive enhanced supported employment with either specialized cognitive training or the Thinking Skills for Work Program (TSWP.) TSWP is a standardized cognitive enhancement program that includes computer cognitive exercises, strategy coaching and teaching of coping skills. After assessment by blinded evaluators, participants who received enhanced supported employment with TSWP performed better than their counterparts, suggesting cognitive enhancement interventions can reduce cognitive impairments and increase the number of individuals who can benefit from employment.

Randomized Trial of Cognitive-Behavioral Therapy Versus Light Therapy for Seasonal Affective Disorder: Acute Outcomes

Rohan, et al.

This randomized trial compared the efficacy of CBT versus light therapy for seasonal affective disorder. Participants were randomized to undergo either 12 sessions of CBT over six weeks or a treatment algorithm of light therapy. The results showed significant and comparable improvement in both treatment modalities, without difference in remission rates, proposing that both CBT and light therapy are viable treatment options for seasonal affective disorder.

Efficacy and Safety of Brexpiprazole for the Treatment of Acute Schizophrenia: A 6-week Randomized, Double-Blind, Placebo-Controlled Trial

Correll, et al.

This multicenter study randomized patients experiencing an acute episode of schizophrenia to receive either 0.25mg, 2mg, 4mg or placebo for 6 weeks. Brexpiprazole was found to be well-tolerated and effective in improving symptoms at 2mg and 4mg dosages compared to placebo. Most common adverse side effects were akathisia and moderate weight gain. Akathisia was found in 4.4% and 7.2% of participants taking 2mg and 4mg, respectively. Weight gain averaged 1.45kg and 1.28kg for 2mg and 4mg, respectively. There were no statistically significant changes in lipid and glucose levels or extrapyramidal symptom ratings.

Neural Correlates of Error Processing in Young People With a History of Severe Childhood Abuse: An fMRI Study

Lim, et al.

This fMRI study found increased brain activation in the typical error processing regions of the dorsomedial frontal cortex, including the left and right presupplementary and supplementary motor areas of the anterior cingulate cortex in young individuals who had experienced severe childhood abuse compared to their healthy counterparts during failed inhibition of a stop signal task. These findings provide anatomical evidence to support the pathological development of inhibitory deficits and hypersensitivity to negative feedback in individuals with history of childhood abuse.

Autoimmune encephalitis in postpartum psychosis

Bergink, et al.

This large cohort study used immunohistochemistry-based screening to test for CNS autoantibodies in postpartum psychosis (PPP) to evaluate for possible autoimmune encephalitis. Ninety-six consecutive patients with postpartum psychosis and 64 controls were included. Two women with PPP tested positive for anti-NMDA receptor antibody in a three-step immunohistochemistry-based screening. Both women had EPS secondary to low dose haloperidol. Authors recommend that screening for anti-NMDA receptor autoantibodies should be considered in PPP with acute onset of atypical symptoms, particularly in the setting of other neurological symptoms or extrapyramidal side effects after initiation of antipsychotic treatment.

The American Journal of Psychiatry - Resident's Journal **Volume 10, Issue 9**

This month's issue focuses on Pediatric Neuropsychiatry.

Advances in Differentiating Pediatric Bipolar Disorder From Attention Deficit Hyperactivity Disorder

Goodwin RE

A multidimensional combination of several clinical risk factors like family history and early mood dysregulation symptoms, combined with imaging differences or other biomarkers, can suggest high index

of suspicion for pediatric bipolar disorder. High scores on the Family Index of Risk for Mood issues are most specific to children with a mood disorder, rather than ADHD or disruptive behavior disorder. Children with ADHD demonstrate left amygdala hyperactivity compared with children who have bipolar disorder. By measuring ratios of certain cerebral metabolites, proton magnetic resonance spectroscopy is another promising imaging modality.

Pediatric Anti-NMDA Receptor Encephalitis

Sahasranaman V

The typical patient is a previously healthy young female presenting with viral-like symptoms rapidly progressing to altered behavior/consciousness and autonomic instability. Diagnosis is confirmed by the presence of NMDA-receptor antibodies in serum or CSF. Intrathecal synthesis of immunoglobulin G antibodies occurs in virtually all patients. All patients should be examined for an underlying tumor, mainly an ovarian teratoma or a testicular germ cell tumor. First-line immunotherapies include corticosteroids, intravenous immunoglobulin, or plasma exchange. 80% of patients experience near-complete or full recovery with adequate treatment.

Case Report: A Patient With Guillain-Barré Syndrome Masquerading as Conversion Disorder

Jolly TS

Some common conditions misdiagnosed as conversion disorder include: frontal lobe epilepsy, amyotrophic lateral sclerosis, myasthenia gravis, multiple sclerosis, CNS tumor, peripheral nerve palsy and systemic lupus erythematosus.

Case Report: Delineating PANDAS/PANS Diagnosis

Severe J

It discusses delineating pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections and pediatric acute-onset neuropsychiatric syndrome in the case of an 8-year-old patient.

JAMA Psychiatry

Volume 72, Issue 9

Treatment of Young People with Antipsychotic Medications in the United States

Olfson, et al.

A retrospective analysis of antipsychotic prescription patterns among patients from 1 to 24 years of age with data collected from a large USA pharmacy database indicated that antipsychotic use increased from 2006 to 2010 for adolescents and young adults but not for children under the age of 12. The percentage of antipsychotic use in 2006 and 2010, respectively, was 1.10% and 1.19% for adolescents, and 0.69% and 0.84% for young adults. The most common diagnoses were attention-deficit/hyperactivity disorders in

children and adolescents and depression in young adults (ages 19-24) and use appeared primarily directed towards impulsive and aggressive behaviors as opposed to psychosis.

Course of Posttraumatic Stress Disorder 40 years After the Vietnam War: Findings from the National Vietnam Veterans Longitudinal Study

Marmar, et al.

The National Vietnam Veterans Longitudinal Study was used to evaluate the prevalence, course, and comorbidities of war-zone post-traumatic stress disorder (PTSD) across a 25-year interval in an attempt to characterize readjustment of military personnel. In male veterans, prevalence of current war-zone related PTSD was estimated to be 4.5% and lifetime prevalence was estimated to be 17%. In female veterans, the lifetime prevalence of war-zone PTSD was estimated to be 15.2% and the prevalence of current-war zone related PTSD was 6.1%. One-third of the veterans with current full-PTSD plus subthreshold war-zone PTSD were noted to have a current major depressive disorder.

Association of Thalamic Disconnectivity and Conversion to Psychosis in Youth and Young Adults at Elevated Clinical Risk

Anticevic, et al.

This multicenter, 2 –year follow up case control study consisted of 397 participants between the ages of 12-35 and utilized functional magnetic resonance imaging scans to determine whether baseline thalamocortical connectivity differed between individuals at high clinical risk for psychosis and healthy controls. Results indicated that thalamic disconnectivity was evident in individuals at high risk for psychosis and was more prominent in those who eventually converted to psychosis. Dysconnectivity correlated with symptom severity.

Adult Functional Outcomes of Common Childhood Psychiatric Problems: A Prospective, Longitudinal Study

Copeland, et al.

This study explored the effects of childhood psychiatric disorders on outcomes in adulthood. Participants of the Great Smoky Mountain Study ranging from ages 19-26 were evaluated for adverse outcomes and subthreshold problems. Participants with a childhood disorder had 6 times higher odds of at least 1 adverse adult outcome compared with those with no history of psychiatric illness. Those with subthreshold symptoms had 3 times higher odds of an adverse outcome.

Delayed Development of Brain Connectivity in Adolescents with Schizophrenia and Their Unaffected Siblings

Zalesky, et al.

This study used prospective structural brain magnetic resonance imaging to evaluate altered corticocortical connections in adolescents with childhood-onset schizophrenia compared to unaffected

siblings. In patients with childhood onset schizophrenia, delayed maturation of occipitotemporal connectivity was observed along with a milder endophenotypes in unaffected siblings that normalized by mid-adolescence whereas affected siblings demonstrated longer maturational delays.

Suicide Attempts in the US Army During the Wars in Afghanistan and Iraq, 2004 to 2009

Ursano, et al.

This longitudinal retrospective cohort study was part of the Army Study to Assess Risk and Resilience in Servicemembers (STARRS) and was designed to identify risk factors for suicide attempts among active-duty members of the Army during a five year period. Authors of this study identified female sex, young age, non-Hispanic white race/ethnicity, and lower educational achievement as factors that predicted an increased likelihood for suicide attempt. Soldiers with a recent mental health diagnosis were at greatest risk.

Association Between Obstetric Mode of Delivery and Autism Spectrum Disorder: A Population-Based Sibling Design Study

Curran, et al.

Although results of this study are consistent with previous reports that children born by cesarean section (CS) are 20% more likely to be diagnosed with autistic spectrum disorder, in analysis of sibling controls there was no association found between mode of delivery and autism spectrum disorder which suggests at contributing environmental or genetic factors.

The Lancet Psychiatry

Volume 2, Issue 9

Risk of depression and self-harm in teenagers identifying with goth subculture: a longitudinal cohort study

Bowes, et al.

A prospective study of children followed from age 15 to 18 revealed that self-identification with goth subculture was associated with an increased risk of depression and self-harm with a dose-response association. Compared to controls, those who somewhat identified and those who very much identified as being a goth were 1.6 times and 3.6 times more likely to have depression and self-harm.

Association between alcohol and substance use disorders and all-cause and cause-specific mortality in schizophrenia, bipolar disorder, and unipolar depression: a nationwide, prospective, register-based study

Hjorthøj, et al.

This prospective, register-based cohort study from Denmark reveals that mortality in people with mental illness is far higher in individuals with substance use disorders than in those without. In schizophrenia the standardized mortality ratio (SMR) in those with lifetime substance use disorder was 8.46 compared with 3.63 in those without. Respective SMRs for bipolar disorder were 6.46 and 2.93, and for depression 6.08 and 1.93.

Hospital management of suicidal behaviour and subsequent mortality: a prospective cohort study

Kapur, et al.

This is a prospective cohort study in which adults with self-harm presentation to emergency dept were assessed for suicide & all cause mortality within 12 months of presentation. 0.7% died from suicide and 2.2% from all causes. Psychiatric admission had the highest unadjusted hazard ratio for both suicide and all-cause mortality, however the adjusted hazard ratio was no longer significant. Authors speculate that rather than suggesting a detrimental effect of psychiatric admission, these findings probably suggest a selection effect, with clinical services preferentially providing treatment to those most at risk of suicide.

Psychiatric disorders and suicide attempts in Swedish survivors of the 2004 southeast Asia tsunami: a 5 year matched cohort study

Amberg, et al.

Using data obtained from the Swedish patient register, it was reported that Swedish survivors of tsunamis from the 2004 Sumatra–Andaman earthquake were 2 times more likely to be diagnosed with a stress-related disorder and 1.5 times more likely to have suicide attempts, with no increased risk of mood or anxiety disorders 5 years after repatriation.

Detection and treatment of at-risk mental state for developing a first psychosis: making up the balance

Hieman and McGorry

A blend of clinical staging and profiling, which naturally incorporates at-risk mental state (ARMS), might be a better guide for treatment of patients in different stages of psychiatric illness than the categorical DSM and ICD systems. Treatment of ARMS leads to a significant reduction in transition rate to a first psychosis. Stigma associated with ARMS arises largely from negative societal views on psychiatric disorders and not from engagement in treatment for ARMS per se.

Journal of the American Academy of Child and Adolescent Psychiatry

Volume 54, Issue 9

Web Interventions for Adolescents Affected by Disaster: Population-Based Randomized Controlled Trial

Ruggiero, et al.

This population-based randomized trial assessed the efficacy of a modular, Web based intervention for disaster-affected adolescents and their parents (called Bounce Back Now). The study population consisted of 2,000 adolescents and parents from communities affected by tornadoes in Joplin, Missouri and several areas in Alabama. Primary outcomes measured were adolescent symptoms of posttraumatic stress disorder (PTSD) and depression. Fewer PTSD and depressive symptoms were identified in adolescents utilizing the program compared to controls at 12 –month follow up.

Neuromotor Adverse Effects in 342 Youth During 12 Weeks of Naturalistic Treatment with 5 Second - Generation Antipsychotics

Carbon, et al.

This study assessed the effect of second-generation antipsychotics in youth to quantify extrapyramidal side effects (EPS) and identify risk factors for treatment-emergent EPS. EPS was assessed at baseline, 4, 8 , and 12 weeks after initiation of a second generation antipsychotic for schizophrenia, mood, disruptive behavior, and autism spectrum disorder. Rates did not exceed those reported in adults. Controlling for all confounding factors, low rates of drug induced Parkinsonism were noted in individuals taking quetiapine and olanzapine. Higher rates of treatment-emergent dyskinesias were noted with olanzapine and ziprasidone.

Meta-Analysis: Risk of Tics Associated with Psychostimulant Use in Randomized, Placebo-Controlled Trials

Cohen, et al.

This meta-analysis examined the risk of new onset or exacerbation of underlying tics as an adverse side effect of psychostimulants in 22 randomized, placebo-controlled trials. The risk of new onset or worsening of tics associated with psychostimulant treatment was similar to that observed with placebo, irrespective of the type of psychostimulant, dose, duration, or age of participant.

Child Maltreatment and Neural Systems Underlying Emotion Regulation

McLaughlin, et al

In this investigation, a total of 42 adolescents from the ages of 13 to 19, of which half were exposed to physical and/or sexual abuse were observed for neural responses during passive viewing of negative and positive emotional stimuli. Maltreated adolescents showed heightened response in areas such as the amygdala, putamen, and anterior insula. In addition, maltreatment was associated with more effort required to modulate heightened responses.

Intrinsic Amygdala Functional Connectivity in Youth With Bipolar Disorder

Singh, et al.

This study compared resting state connectivity patterns in amygdala subregions in youth with Bipolar I Disorder with patterns in healthy controls. Abnormal patterns in areas important for emotional processing and self-awareness were noticed in youth with bipolar disorder compared to healthy controls.

Current Psychiatry

Volume 14, Issue 9

Evidence-Based Reviews: What does molecular imaging reveal about the causes of ADHD and the potential for better management?

Binkovitz and Thacker.

ADHD is one of the most common pediatric psychiatric disorders, occurring in approximately 5% of children and persists into adulthood in 50%. Molecular changes in the dopaminergic-frontostriatal pathway are associated with the behavior constellation of symptoms. Findings suggest that the dopamine transporter (DaT) in the striatum is the most likely useful target to stratify patients with ADHD. Stratification might allow for refinement in the diagnostic categorization of ADHD, with introduction of stimulant-responsive and stimulant-unresponsive subtypes that are based on DaT imaging findings.

Med/Psych Update: Head pain and psychiatric illness: Applying the biopsychosocial model of care.

Ramezani, et al.

Many unusual responses to pain treatment, questionable validity of pain behavior, and disproportionate pain perception and functional decline can be best explained by a biopsychosocial approach. Psychiatric conditions are highly comorbid with chronic headache and can have a direct effect on it. A psychodiagnostic assessment can help the astute clinician identify comorbid psychiatric conditions, psychological factors, and somatic symptoms to develop a comprehensive biopsychosocial treatment plan for patients with chronic head pain.

Out of the Pipeline: 3-Month paliperidone palmitate for preventing relapse in schizophrenia

Kubik P.

The 3 month Invega Trinza was approved by the FDA in May 2015. It can be administered to patients with schizophrenia who have been the taking the monthly Invega Sustenna for at least 4 months. It reaches a maximum plasma concentration between day 30 and day 33. The dose of Invega Trinza is based on the last 1 month dosing and is 3.5 times the dose of Sustenna. For example, for 156 mg Invega Sustenna dose, the equivalent Invega Trinza dose is 546 mg.

Pearls: “It’s my money, and I want it now!” Clinical variables related to payeeship under Social Security

Amdur MA.

Based on his personal experience, author shares his approach to help physicians determine capability and payeeship for disability beneficiaries. Some situations that strongly suggest the need for a payee include: bankruptcy or excessive credit card debt, dementia, manic spending, gambling, homelessness, intellectual limitation, profound depression, psychotic disorganization, substance abuse and vulnerability to exploitation.

Research Watch Bonus Material: An Overview of Rexulti (Brexiprazole)

Indications:

- 1) Adjunctive treatment for MDD
- 2) Schizophrenia

Mechanism of Action: Brexpiprazole is considered to be a successor of aripiprazole. It is a partial agonist at 5-HT_{1A} and dopamine D₂ receptors with similar potency, and it is an antagonist at 5-HT_{2A}.

Dosage: It is administered once daily.

MDD: Starting dose is 0.5-1mg/day, recommended dose is 2 mg/day, and maximum is 3 mg/day. Titrate dose at weekly intervals.

Schizophrenia: Starting dose is 1 mg/day, recommended is 2-4 mg/day, and maximum is 4 mg/day. Start at 1 mg/day on days 1 through 4. Use 2 mg/day on days 5 through 7, and go up to 4 mg/day on day 8.

In moderate to severe hepatic impairment & moderate, severe or end-stage renal impairment, maximum dose is 2 mg/day for MDD and 3 mg/day for schizophrenia.

Efficacy:

Efficacy in MDD was assessed using change from baseline to week 6 in Montgomery-Asberg Depression Rating Scale (MADRS) total score. Interestingly 2 mg was found to be statistically significantly superior to placebo, but 1 mg and 3 mg dose was not. Placebo-subtracted difference in MADRS for 2 mg dose was 3.2 points.

Efficacy in schizophrenia was assessed using change from baseline to Week 6 in the Positive and Negative Syndrome Scale (PANSS) total score. 2 mg and 4 mg doses were found to be statistically significantly superior to placebo, with placebo-subtracted difference ranging in different studies from 6.5 to 8.7.

(As a comparison, placebo-subtracted difference for ARIPIPRAZOLE for MADRS ranged from 2.84 to 3.01 [5-20 mg] and for PANSS ranged from 9.4 to 12.6 [15 mg dose] in FDA approval studies.)

Adverse Reactions: Most common adverse reactions are weight gain and akathisia. In initial studies, brexpiprazole does not prolong the QTc interval to any clinical relevant extent.