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Research Watch is an initiative by the residents of Case Western Reserve University/University Hospitals Case Medical Center, and it aims to inform psychiatry residents and faculty of notable articles published in prominent research journals.

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)
* International Journal of Psychoanalysis & The American Journal of Psychoanalysis

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Highlights

- Researchers identified three neurobiologically distinct psychosis biotypes that cut across, and show higher heritability than, DSM categories of schizophrenia, schizoaffective disorder, and bipolar disorder with psychosis. (AJP)
- A high risk for psychosis is associated with increased resting hyperperfusion in the hippocampus, midbrain, and basal ganglia. (AJP)
- Lurasidone is shown to be a safe and effective treatment for major depressive disorder with mixed features in a randomized, double-blind, placebo controlled trial. (AJP)
- Twice-weekly high-dose unilateral ECT is non-inferior to bitemporal ECT for depression, and appears to have a better cognitive side-effect profile. (AJP)
- Presence of executive impairment (Trail Making Test <7) is predictive of poor rate of remission with aripiprazole augmentation for treatment-resistant late-life depression. (JAMA-P)
- Cortical inhibition measures may be indicators of remission of suicidal ideation following a course of magnetic seizure therapy in treatment-resistant depression. (JAMA-P)
- There is a genetic overlap between schizophrenia pathogenesis and antipsychotic mechanism of action, and treatment efficacy appears to be polygenic. (LP)
- Childhood maltreatment is predictive of unfavorable clinical features and course of illness in individuals with bipolar disorder. (LP)
- Dialectical Behavioral Therapy adapted for adolescents is superior to enhanced usual care in reducing the frequency of self-harm in adolescents. (JAACAP)
- Children at high risk for depression show blunted ventral striatal activation to gain feedback. (JAACAP)

The American Journal of Psychiatry

Volume 173, Issue 4

Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program

Kane, et al.

This study evaluated the quality of life of patients experiencing first-episode psychosis who received community care versus NAVIGATE, a comprehensive, multidisciplinary, team-based treatment approach. The study measured the participants' sense of purpose, motivation, emotional and social interactions, role functioning and engagement in regular activities using the Heinrichs-Carpenter Quality of Life Scale. Results showed participants in NAVIGATE remained in treatment longer and experienced greater improvement in quality of life and psychopathology compared to their community care counterparts. It was also found that those who had a shorter duration of untreated psychosis showed greater improvement.

Identification of Distinct Psychosis Biotypes Using Brain-Based Biomarkers

Clementz, et al.

Researchers applied a broad range of neurobiological measures (neuropsychological, stop signal, saccadic control, and auditory stimulation paradigms) to individuals with psychotic disorders (schizophrenia, schizoaffective disorder and bipolar disorder with psychosis), their first-degree relatives and healthy volunteers and identified three "biotypes" that showed higher heritability compared to the DSM diagnoses. The biotypes differed primarily across the neurocognitive domains of sensorimotor reactivity and cognitive control, with biotype 1 showing severe deficits in both domains, biotype 2 showing deficits only in cognitive control and biotype 3 showing the least cognitive impairment and symptoms. These biotypes map better on available neurochemical models. They also explain the heterogeneity of biomarker observations when studies are conducted using DSM diagnoses as the gold standard.

Resting Hyperperfusion of the Hippocampus, Midbrain, and Basal Ganglia in People at High Risk for Psychosis

Allen, et al.

Animal models suggest hyperactivity in the hippocampus, and increased activity in the midbrain and basal ganglia result in the development of psychosis. This functional imaging study used pseudo-continuous arterial spin labeling imaging to measure resting regional cerebral blood flow (rCBF) in healthy volunteers and individuals at ultra-high risk for psychosis to correlate this hypothesis in human subjects. Results showed ultra-high risk subjects demonstrate elevated rCBF in the hippocampus, basal ganglia and midbrain compared to healthy volunteers. Severity of psychotic symptoms was assessed using the Comprehensive Assessment of At-Risk Mental States and ultra-high risk subjects were reassessed after a mean of 17 months. Subjects who showed resolution of symptoms and no longer met criteria for ultra-

high risk at follow up demonstrated normalization of activity within the hippocampus, midbrain and basal ganglia as well as longitudinal reduction in left hippocampal rBCF that was not evident in subjects who remained high-risk or became psychotic.

Lurasidone for the Treatment of Major Depressive Disorder With Mixed Features: A Randomized, Double Blind, Placebo-Controlled Study

Suppes, et al.

This double blind, placebo-controlled study enrolled 209 patients who met criteria for Major Depressive Disorder and subthreshold hypomanic symptoms (two or three protocol-defined manic symptoms) and randomly assigned them to 6 weeks of treatment with either lurasidone at 20 to 60mg/day or placebo. Results showed significant improvement in depressive symptoms and overall illness severity as measured by the Montgomery-Asberg Depression Rating Scale score, Clinical Global Impressions severity subscale score and Young Mania Rating Scale. Additionally, lurasidone was generally well tolerated and rate of discontinuation due to adverse events was low. The most common adverse side effects were nausea (6.4% lurasidone treated vs. 2.0% placebo) and somnolence (5.5% lurasidone treated and 1.0% placebo.)

Bitemporal Versus High-Dose Unilateral Twice-Weekly Electroconvulsive Therapy for Depression (EFFECT-Dep): A Pragmatic, Randomized, Non-Inferiority Trial

Semkowska, et al.

This patient- and rater-blinded, noninferiority trial randomized 138 patients with major depressive disorder to receive either bi-weekly moderate-dose (1.5x seizure threshold) bitemporal ECT or bi-weekly high-dose (6x seizure threshold) unilateral ECT for up to 12 sessions. The primary outcome was change in the 24-item Hamilton Depression Rating Scale score, which was measured at baseline and after the ECT course. The prespecified noninferiority margin was 4.0 points. Results show that high-dose unilateral ECT was noninferior to moderate dose bilateral ECT and may be preferable due to its better cognitive side-effect profile. There were no significant differences in response, remission or 6-month relapse status and high-dose unilateral ECT subjects recovered orientation quicker following their treatment compared to their bilateral ECT counterparts (median= 19.1 minutes versus 26.4 minutes.)

The American Journal of Psychiatry - Resident's Journal

Volume 11, Issue 4

The Burden of Mental Illness Beyond Clinical Symptoms: Impact of Stigma on the Onset and Course of Schizophrenia Spectrum Disorders

Hoftman G

This article defines stigma and describes how it affects the onset and course of schizophrenia spectrum disorders. Stigma can be separated into 3 categories: internalized, interpersonal, and institutional. The stigma associated with schizophrenia can precipitate initial episodes of psychosis, trigger relapses, and

promote a more severe course. People with severe mental illnesses like schizophrenia spectrum disorders are often targets of negative attitudes and social labels that lead to stigma. Mental health professionals can perpetuate stigma in people with mental illness, unless care is taken to provide a collaborative and empathic relationship focused on patient empowerment.

Management of Depression in Parkinson's Disease

Frenklach A

Symptoms of Parkinson's disease can include depression, anxiety, apathy, psychosis, cognitive impairment, impulse control disorders, and sleep disturbances. Depression is one of the most common neuropsychiatric complications. The author states there is not a clear consensus for which antidepressants are best for depression in Parkinson's disease and states that SSRI and SNRIs are first line with monoamine oxidase type B inhibitors and tricyclic antidepressant among the less used second line agents. ECT and TMS may be used for severe, refractory cases. Psychotherapy, particularly cognitive-behavioral therapy, is increasingly being studied with promising results.

JAMA Psychiatry

Volume 73, Issue 4

Euthanasia and Assisted Suicide of Patients with Psychiatric Disorders in the Netherlands 2011 to 2014

Scott, et al.

Objective was to describe the characteristics of patients receiving euthanasia and assisted suicide (EAS) for psychiatric conditions and how the practice is regulated in the Netherlands as EAS is increasing in Belgium and the Netherlands. Case summaries were reviewed for the clinical and social characteristics of patients, the physician review process and the euthanasia review committees' assessments. Results showed that persons receiving EAS for psychiatric disorders were mostly women (77%) of diverse ages. Most had chronic conditions, previous suicide attempts, and personality disorders. Depressive disorders (55%) were the primary psychiatric condition. The granting of patient EAS involved considerable physician judgement, involving multiple physicians, but the euthanasia review committees generally defer to the judgements of the physicians performing the EAS.

Analyzing the Role of MicroRNAs in Schizophrenia in the Context of Common Genetic Risk Variants.

Hauberg, et al.

Study used summary statistics from the largest schizophrenia genome-wide association study meta-analysis to examine the role of miRNAs in schizophrenia in the context of disease associated genetic variation. The authors explored the role of miRNA in the regulation of the 108 schizophrenia risk genes. The authors found an association between MIR9-2 (miRNA) and a genomic region associated with schizophrenia. Authors noted that MIR9-2 has an established tie with a regulatory loop for fragile X and regulates dopamine D2 receptor density.

Indicators for Remission of Suicidal Ideation Following Magnetic Seizure Therapy in Patients with Treatment-Resistant Depression

Sun, et al.

Goal of study was to identify a biomarker that may serve as an indicator of remission of suicidal ideation following a course of magnetic seizure therapy (MST) using cortical inhibition measures (N100 and LICl) from TMS-EEG. Data of 27 patients from an open-label clinical trial of MST treatment was used for the study; baseline TMS-EEG measures (in the left dorsolateral prefrontal cortex and the left motor cortex) were completed within 1 week before the initiation of MST treatment. Suicidal ideation was evaluated before and after MST using the Scale for Suicidal Ideation (SSI). At baseline, patients had a mean SSI score of 9.0, but after MST, they had a mean SSI score of 4.2 (with 18 individuals having a post-treatment score of 0). Results from TMS-EEG showed that cortical inhibition measures in the frontal cortex, but not the motor cortex, were indicators of remission of suicidal ideation with 89% accuracy. Therefore, these results suggest that cortical inhibition measures may be used to identify patients with treatment resistant depression who are most likely to experience remission of suicidal ideation following a course of MST.

Cannabis Use and Risk of Psychiatric Disorders: Prospective Evidence From a US National Longitudinal Study.

Blanco, et al.

Study examined the prospective associations between cannabis use and risk of mental health and substance use disorders in the general population; a national sample of US adults aged 18 years or older was interviewed three years apart. The authors measured the association between cannabis use and incident and prevalent psychiatric disorders three years later. Results showed that within the general population, cannabis use was associated with an increased risk for several substance use disorders: alcohol use disorder (OR 2.7), cannabis use disorder (OR 9.5), and nicotine dependence (OR 1.7). Cannabis use was not associated with any mood disorder (OR 1.1), or anxiety disorder, (OR 0.9). Of note, psychotic disorders were not included in the study.

Heterogeneity in 10-Year Course Trajectories of Moderate to Severe Major Depressive Disorder - A Danish National Register-Based Study

Musliner, et al.

This Danish national register-based study characterized patterns and correlates of 10-year course trajectories of Major Depressive Disorder. Four trajectory classes were identified: brief contact (77.0%) (characterized by low probability of contact after 2 years); prolonged initial contact (12.8%) (characterized by high decreasing probability of contact during the first 5 years); later reentry (7.1%) (characterized by moderate probability of contact during the second 5 years); and persistent contact (3.1%) (characterized by high or moderate probability of contact throughout). Among various correlates described in the paper, parental schizophrenia was associated with the persistent contact class.

Predictors and Moderators of Remission with Aripiprazole Augmentation in Treatment-Resistant Late-Life Depression - An Analysis of the IRL-Grey Randomized Clinical Trial

Kaneriya, et al.

Subjects 60 years of age or older whose major depression had failed to remit with venlafaxine monotherapy were treated with aripiprazole or placebo augmentation. Remission occurred in 43% of subjects with aripiprazole and 29% with placebo. Baseline set shifting moderated the efficacy of aripiprazole augmentation: Among participants with a Trail Making Test scaled score of 7 or higher, the odds of remission were significantly higher with aripiprazole than with placebo (OR 4.11). Among participants with a Trail Making Test scaled score of less than 7, aripiprazole and placebo were equally efficacious. Executive impairment appears to be predictive of poor rate of remission with aripiprazole augmentation.

The Lancet Psychiatry

Volume 3, Issue 4

Childhood maltreatment and unfavourable clinical outcomes in bipolar disorder: a systematic review and meta-analysis

Agnew-Blais & Danese

This systematic review and meta-analysis examined the association of childhood maltreatment (physical, sexual, or emotional abuse, neglect, or family conflict) before age 18 years with clinical features and course of illness in bipolar disorder. Childhood maltreatment was predictive of unfavorable clinical features and course of illness. These unfavorable features include greater severity of mania, depression and psychosis, higher rates of comorbidity, earlier age of onset, higher risk of rapid cycling, and higher risk of suicide attempt.

Polygenic overlap between schizophrenia risk and antipsychotic response: a genomic medicine approach

Ruderfer, et al.

Authors aimed to examine the overlap between schizophrenia risk loci and gene targets of medications. Schizophrenia risk loci were defined as genomic regions reaching genome-wide significance in the latest Psychiatric Genomics Consortium schizophrenia genome-wide association study. Authors collated drug targets into 167 gene sets targeted by pharmacologically similar drugs and examined enrichment of schizophrenia risk loci in these sets. They also linked the data with Swedish drug registry to assess the contribution of rare variants to treatment response. Significant enrichment of schizophrenia risk loci was found in both known targets of antipsychotics (70 genes) as well as novel predicted targets (277 genes). Patients with treatment-resistant schizophrenia had an excess of rare disruptive variants in gene targets of antipsychotics and in genes with evidence for a role in antipsychotic efficacy. The results are suggestive that there is a genetic overlap between schizophrenia pathogenesis and antipsychotic mechanism of

action. Results are also consistent with the notion that treatment efficacy is polygenic and single-target therapeutics might be insufficient.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 55, Issue 4

Association of Lifetime Mental Disorders and Subsequent Alcohol and Illicit Drug Use: Results from the National Comorbidity Survey-Adolescent Supplement

Conway, et al.

This study's purpose was to measure the association of prior lifetime mental disorders with transitions across stages of substance use in a cross-sectional sample of US adolescents. Direct interviews with 10,123 adolescents aged 13-18 years who participated in the National Comorbidity Survey-Adolescent Supplement (NCS-A) were utilized. Results indicated that adolescents with prior lifetime mental disorders had high rates of alcohol (10.3%) and illicit drug (14.9%) abuse, with or without features of dependence. Alcohol and drug abuse were highest among adolescents with prior anxiety and behavior disorders. Furthermore, any prior disorder significantly increased the risk of transition from nonuse to first use, and from transition from use to problematic use. Results support treatment of primary mental disorders as an intervention to target the prevention of secondary substance use disorders in adolescents.

Dialectical Behavior Therapy Compared With Enhanced Usual Care For Adolescents With Repeated Suicidal and Self-Harming Behavior: Outcomes Over a One-Year Follow-Up

Mehlum, et al.

This was a 1-year prospective follow-up study of posttreatment clinical outcomes in adolescents with recent and repetitive self-harm who were randomly allocated to receive 19 weeks of either DBT adapted for adolescents or enhanced usual care at community child and adolescent psychiatric outpatient clinics. At the end of the 19-week treatment period and at follow-up 1 year later, patients were assessed for self-harm, suicidal ideation, depression, hopelessness, borderline symptoms and global level of functioning. The study was able to capture 98% of the adolescents at both time points. Over the total 52-week time period, DBT-A remained superior to the enhanced usual care in reducing the frequency of self-harm. For other outcomes including SI, hopelessness, and depressive or borderline symptoms and for global level of functioning, inter-group differences that were apparent at 19-weeks were no longer observed.

Depression Risk Predicts Blunted Neural Responses to Gains and Enhanced Responses to Losses in Healthy Children

Luking, et al.

This study's objective was to assess the relationship between neural response to gain/loss feedback, major depressive disorder risk, and child depressive symptoms in order to clarify whether alterations in neural response to reward can be detected in school-aged children at high risk before the typical increase in

reward response observed in adolescence. Forty-seven psychiatrically healthy 7-to-10 –year old children (16 of which were at high risk given maternal MDD) completed questionnaires and a functional magnetic resonance imaging (fMRI) card-guessing game in which candy was gained and lost. High risk-children showed blunted ventral striatal activation to gain feedback. Ventral striatal deactivation to loss was a stronger predictor of MDD risk. Anhedonia was related to reduced sensitivity to loss feedback whereas negative mood was related to enhanced sensitivity to loss in the ventral striatum.

International Journal of Psychoanalysis

Volume 97, Issue 1

Psychosomatic breast and alexithymic breast: A Bionian Psychosomatic Perspective

Magenat L.

Drawing from clinical and theoretical material, Magenat explores Bion’s concept of the psychosomatic breast (i.e. the breast in charge of primary symbolization and integration of the infant’s raw experiences as well as perceptions). The psychosomatic breast is a prototype for a mother. However, Magenat explains, potential failure can lead to the development of an “alexithymic breast.” – the one that is obstructive and impervious to communication via projective identification. He goes on to describe clinical material interested in healing the development that led to an alexithymic breast.

The American Journal of Psychoanalysis

Volume 97, Issue 1

On Being Tricked

Fuery K

Fuery integrates perspectives from Winnicott, Bollas, and Lacan to evaluate the function and effect of trickery.

Helplessness and the Analyst’s War Against Feeling It

Hoffer A & Buie DH

Hoffer and Buie investigate helplessness in the analytic situation. They pay particular attention to ways that the analyst may resolve and/or hold such feelings in a way that allows the analyst to better-empathize with the patient.