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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
- \* Miscellaneous: J Neuropsychiatry Clin Neurosci, MMWR Recomm Rep.

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**Highlights**

- In nursing home residents with dementia, antipsychotic review reduces antipsychotic use by 50%, however, when accompanied without social interventions, there are significantly worse outcomes in neuropsychiatric symptoms. (AJP)
- Current data from the MGH National Pregnancy Registry shows no significant difference in the risk of major malformations between infants exposed to atypical antipsychotics versus controls. (AJP)
- DSM conception of mental disorders is problematic from the point of view of naturalism, and none of the leading naturalist accounts of mental disorders (by Szasz, Boorse, and Wakefield) are satisfactory. (RJ)
- In a study from Sweden, maternal and paternal depression anywhere from before the child’s birth up until 16 years of age was associated with worse school performance. (JAMA-P)
- A cohort study reports that negative symptoms and anxiety disorders, but not psychotic experiences, are more common in adolescents with a higher genetic risk for schizophrenia. (JAMA-P)
- Data from Denmark registry reveals that subjects with obsessive-compulsive disorder have a higher risk of mortality from both natural and unnatural causes. (JAMA-P)
- Continued cannabis use after onset of psychosis is associated with higher relapse rates, longer admissions, and more severe positive symptoms compared to individuals who discontinue cannabis use. (LP)
- Data from UK psychiatric services shows that suicide in the perinatal period is more likely to occur in those with a depression diagnosis and no active treatment at the time of death. (LP)
- Human endogenous retroviruses have been presented as possible candidates explaining the connections between the genetic, infectious, neurodevelopmental, and neuroinflammatory aspects of schizophrenia. (J Neuropsychiatry Clin Neurosci)
- CDC has released guidelines for prescribing opioids for chronic pain which include 12 recommendations. (MMWR Recomm Rep)

## **The American Journal of Psychiatry**

### **Volume 173, Issue 3**

#### **Post-Stroke Depression: A Review**

Robinson and Jorge

This literature review summarized recent findings and advances on post-stroke depression (PSD) including meta-analyses of randomized controlled trials showing treatment efficacy of antidepressants in PSD. Studies also found significant decreases in incidence of PSD when antidepressants were used prophylactically compared to placebo. Early antidepressant treatment of PSD may increase survival by up to 10 years after a stroke and may also improve physical and cognitive recovery. Current hypotheses suggest inflammatory processes are associated with depressive symptoms, but overall further studies are needed to better understand the etiology of PSD, including genetic and epigenetic variations, white matter disease, cerebrovascular deregulation, altered neuroplasticity and changes in glutamate neurotransmission.

#### **Impact of Antipsychotic Review and Nonpharmacological Intervention on Antipsychotic Use, Neuropsychiatric symptoms and Mortality in People with Dementia Living in Nursing Homes: A Factorial Cluster-Randomized Controlled Trial by the Well-Being and Health for People with Dementia (WHELD) Program**

Ballard, et al.

This randomized controlled study utilized antipsychotic review, social interaction interventions and exercise interventions in nursing homes over the course of 9 months and assessed the effects on antipsychotic use, agitation, depression, neuropsychiatric symptoms and mortality. Results showed antipsychotic review significantly reduced antipsychotic use by 50% and antipsychotic review plus social interaction intervention significantly reduced mortality compared to the group receiving neither. However, the group receiving antipsychotic review without social intervention showed significantly worse outcomes in neuropsychiatric symptoms compared to the group receiving neither. None of the interventions had significant impact on agitation. Thus, although there are interventions that can be implemented to reduce antipsychotic use in patients with dementia, it may not be of benefit to this population unless other nonpharmacological interventions are provided concurrently.

#### **Reproductive Safety of Second-Generation Antipsychotics: Current Data from the Massachusetts General Hospital National Pregnancy Registry for Atypical Antipsychotics**

Cohen, et al.

This prospective study assessed the risk of major malformations in infants exposed to second generation anti-psychotics during pregnancy relative to a comparison group of unexposed infants of mothers with histories of psychiatric morbidity. The absolute risk of major malformations was 1.4% for exposed infants

and 1.1% for unexposed infants. The risk of a major malformation was not significantly different between the two groups.

### **An 8-Week Randomized, Double-Blind, Placebo-Controlled Evaluation of the Safety and Efficacy of Cariprazine in Patients with Bipolar I Depression**

Durgam, et al.

This study comprised 571 patients diagnosed with Bipolar I Disorder experiencing a current major depressive episode who were randomly assigned to receive placebo or cariprazine 0.75mg, 1.5mg or 3.0mg/day. Cariprazine at 1.5mg/day demonstrated consistent efficacy compared with placebo across outcomes and was generally well tolerated. The most common adverse side effects of cariprazine were akathisia and insomnia. Weight gain was slightly higher with cariprazine than with placebo.

### **Neural Correlates of the Propensity for Retaliatory Behavior in Youths with Disruptive Behavior Disorders**

White, et al.

This study included 30 youths with disruptive behaviors disorders (DBD) and 26 healthy controls who participated in an ultimatum game task during functional MRI. Results demonstrated youths with DBD had greater increases in activation of basic threat circuitry when punishing others, dysfunctional down-regulation of the ventromedial prefrontal cortex during retaliation and reduced amygdala-ventromedial prefrontal cortex connectivity during high provocation. This suggests that ventromedial prefrontal cortex-amygdala connectivity is critical for regulating retaliation/reactive aggression and contributes to reactive aggression when dysfunctional.

## **The American Journal of Psychiatry - Resident's Journal** **Volume 11, Issue 3**

### **Mental Disorders and Naturalism**

Aftab A.

Naturalistic accounts of mental disorder define disorder as biological dysfunction, which can be determined as a matter of objective natural fact, without recourse to social or moral value judgments. This narrative review discusses the compatibility of DSM conception of mental disorder with naturalism. DSM conflates pathology with disability and diagnosis with need for treatment. It does not define dysfunction and makes little to no reference to underlying dysfunction in diagnostic criteria. The boundaries of disorders are based on clinical significance. All of these are problematic from the point of view of naturalism. The primary challenge for naturalism is the problem of establishing a satisfactory objective, scientific distinction between normal and abnormal human functioning, and it is argued that none of the leading naturalist accounts of mental disorders (by Szasz, Boorse, and Wakefield) are satisfactory.

## **Diagnosis and the Structure of Scientific Revolutions**

McBride, J.

The commentary reflects on the theories and assumptions that underlie psychiatry, its paradigm. Drawing heavily on Thomas Kuhn's work, from which we get the idea of a paradigm, the author argues that psychiatry may be ripe for scientific revolution.

## **JAMA Psychiatry**

### **Volume 73, Issue 3**

#### **Prognosis of Brief Psychotic Episodes - A Meta Analysis**

Fusar-Poli, et al.

This meta-analysis showed that there is a statistically significant increased risk of psychotic recurrence in remitted first-episode schizophrenia versus brief psychotic episodes (0.78). However, the various varieties of brief psychotic episodes did not have a significant difference in psychotic recurrence when compared with each other. Brief psychotic episodes included acute and transient psychotic disorder, brief psychotic disorder, brief intermittent psychotic symptoms and brief limited intermittent psychotic symptoms.

#### **Associations of Parental Depression with Child School Performance at Age 16 Years in Sweden**

Shen, et al.

Maternal and paternal depression at any time before the final compulsory school year was associated with worse school performance in this study cohort that comprised 1,124,162 children. This included maternal and paternal depression anywhere from before the child's birth up until 16 years of age. The study also showed that maternal depression had a greater impact on girls' school performance versus boys' school performance.

#### **Phenotypic Manifestation of Genetic Risk for Schizophrenia During Adolescence in the General Population**

Jones, et al.

This cohort study examined how an increased genetic risk for schizophrenia is manifest phenotypically during adolescence in the general population. The study found that the negative symptoms and anxiety disorders were more common in adolescents with a higher genetic risk for schizophrenia. There was no evidence of an association of high genetic risk with the occurrence of psychotic experiences or depressive disorder in adolescence. Results are suggestive that the genetic risk for schizophrenia appears to be manifest as anxiety and negative symptoms during adolescence rather than psychotic experiences.

## **Type 2 Diabetes Mellitus in Youth Exposed to Antipsychotics: A Systematic Review and Meta-analysis**

Galling, et al.

Objective of the review was to assess type 2 diabetes mellitus (T2DM) risk in youth exposed to antipsychotic treatment. Thirteen longitudinal studies were included which reported T2DM incidence in youth 2 to 24 years old, with exposure to antipsychotics for at least 3 months. The exposed youth had a cumulative T2DM risk of 5.72 per 1000 patients which was associated with longer follow-up, Olanzapine prescription, and male sex. The incidence rate was 3.09 cases per 1000 patient-years which was associated with second-generation antipsychotics and less autism spectrum disorder diagnosis. The cumulative T2DM risk (OR 2.09) and incidence rate ratio (IRR 1.79) were significantly higher in antipsychotic-exposed youth compared to both healthy and psychiatric controls.

## **Biological Motion Perception, Brain Responses, and Schizotypal Personality Disorder**

Hur, et al.

Study investigated the specificity of brain regions responsive to biological motion perception in individuals with Schizotypal Personality Disorder (SPD) compared to healthy control individuals. Functional MRI scans showed that individuals with SPD have heightened activation in reward and decision making pathways when viewing biological motion stimuli. The authors suggest that this heightened activation of these particular pathways are related to the peculiar ways in which individuals with SPD behave in social contexts.

## **Mortality Among Persons With Obsessive-Compulsive Disorder in Denmark**

Meier, et al.

Study determined whether persons with OCD are at an increased risk of death using data from Danish registers to conduct a prospective cohort study (participants were born between 1955 and 2006). It found that the risk of death by natural or unnatural causes was significantly higher among persons with OCD, mortality rate ratio (MRR) of 1.68 for natural causes and 2.61 for unnatural causes. After exclusion of persons with co-morbid anxiety, depression, or substance use disorder, OCD was still associated with an MRR of 1.88.

## **Familial Liability for Eating Disorders and Suicide Attempts: Evidence From a Population Registry in Sweden**

Yao, et al.

Study examined the association between eating disorders and suicide attempts in regards to contributions from familial risk factors. The birth cohort included individuals born between 1979 and 2001, followed starting at age 6 years. Overall, the study was underpowered to explore the familial liability for this association. There was an increased risk of suicide attempts, OR 1.82, and death by suicide, OR 2.04, for any eating disorder, even after adjusting for co-morbid depression, anxiety, and substance use disorders.

Individuals who had a full sibling with any eating disorder had an increased risk of suicide attempts, OR 1.41, but was attenuated for any eating disorder in more distant relatives.

## **The Lancet Psychiatry**

### **Volume 3, Issue 3**

#### **Continued versus discontinued cannabis use in patients with psychosis: a systematic review and meta-analysis**

Schoeler, et al.

In this systematic review and meta-analysis continued cannabis use after onset of psychosis was associated with adverse outcomes such as higher relapse rates, longer hospital admissions, and more severe positive symptoms compared to individuals who discontinue cannabis use and those who are non-users.

#### **Suicide in perinatal and non-perinatal women in contact with psychiatric services: 15 year findings from a UK national inquiry**

Khalifeh, et al.

A comparison of suicides among perinatal and non-perinatal women who had been in contact with UK psychiatric services reveals that suicides in the perinatal period were more likely to occur in those with a depression diagnosis (adjusted OR 2.19) and no active treatment at the time of death (adjusted OR 0.46). These women were also more likely to be younger, married, and with shorter illness duration.

#### **Cross-trial prediction of treatment outcome in depression: a machine learning approach**

Chekroud, et al.

Authors used data from level 1 of the STAR\*D trial to identify variables that were most predictive of treatment outcome, and used these variables to train a machine-learning model to predict clinical remission. The model predicted outcomes in STAR\*D with 64.6% accuracy. The model was externally validated in the escitalopram treatment group of an independent clinical trial COMED, and showed an accuracy of 59.6%. The model also performed above chance for combined escitalopram-bupropion treatment group in COMED, but not for combined venlafaxine-mirtazapine group, suggesting that the model may be specific to the underlying mechanisms of the medication in question.

## **Journal of the American Academy of Child and Adolescent Psychiatry**

### **Volume 55, Issue 3**

#### **Prevention of Depression in At-Risk Adolescents: Predictors and Moderators of Acute Effects**

Weersing, et al.

This study assessed predictors and moderators of a cognitive –behavioral prevention program (CBP) for adolescent offspring of parents with depression. It was a 4-site randomized trial that evaluated CBP compared to usual community care (UC) in 310 adolescents with familial (parental depression) and individual (youth history of depression or current subsyndromal symptoms) risk for depression. Results indicated that depression onset was predicted by lower functioning and higher sense of hopelessness in adolescents. The effect of CBP was lessened when parents were currently depressed at baseline or had a history of hypomania, or when adolescents reported higher depressive symptoms, higher anxiety, higher hopelessness, or lower functioning. Results indicate that such programs as CBP may produce better effects when timed at moments of relative wellness in high-risk families.

### **Gender Differences in Associations Between Attention Deficit/Hyperactivity Disorder and Substance Use Disorder**

Ottosen, et al.

This cohort study's aim was to examine gender differences in the comorbidity of attention-deficit/hyperactivity disorder (ADHD) and substance use disorder (SUD). All children born in Denmark from 1990-2003 from nationwide registers were studied regarding birth characteristics, socioeconomic status, familial psychiatric history, and diagnoses of ADHD along with comorbidities and SUD. Results indicate that ADHD increased the risk of alcohol abuse, cannabis abuse, and other illicit substance use. Among individuals with ADHD without comorbidities, females had higher SUD risk than males. Comorbid conditions such as depression, bipolar disorder, and schizophrenia further increased the risk of SUD. Autism spectrum disorder in males with ADHD lowered the SUD risk.

### **Marital Hostility, Hostile Parenting, and Child Aggression: Associations From Toddlerhood to School Age**

Stover, et al.

This study was designed to examine the hypothesis that childhood aggression results from spillover of interparental conflict to poor parenting. It examined this hypothesis in non-genetically related parent-child dyads from the toddler period through age 6 years. A sample of 361 sets of children, adoptive parents, and birth parents from the Early Growth and Development Study was assessed from child age 9 months to 6 years on measures of adoptive parent financial strain, antisocial traits, marital hostility, hostile parenting, and child aggression. Marital conflict from child age 18 to 27 months was associated with more parental hostility in mothers and fathers at 27 months. Adoptive fathers' parental hostility, but not mothers' was associated with aggression in children at age 4.5 years. There was no significant spillover from hostile parenting at 4.5 years to child aggression at 6 years. Results support the benefit of early identification of marital hostility.

## **International Journal of Psychoanalysis**

### **Volume 97, Issue 1**

### **Infantile defences in parent-infant psychotherapy: The example of gaze avoidance**

Salomonsson B

Salomonsson places intersubjective and classical psychoanalytic conceptions of the infant in contrast with one another. While an intersubjective analytic conceptualization is interested in the infant as an interactive partner with the parent, the classical approach is more concerned with speculation about the infant's unconscious experiences and representations. As an example, he is interested in modern observations about infant gaze avoidance and considering that it may fit more closely with a classical definition of a defence.

### **Bi-ocularity, the functioning mind of the psychoanalyst**

Birksted-Breen D

Drawing from clinical material, Birksted-Breen highlights the importance of a “bi-ocular” mode of attentiveness in the analytic situation – on the one hand attending to the material in a reverie while on the other analyzing it. Birksted-Breen proposes that this is a necessary skill to develop a psychic space wherein unconscious experiences can come into focus.

## **Miscellaneous**

### **Pathophysiological Role of HERV-W in Schizophrenia**

Aftab, et al.

*The Journal of Neuropsychiatry and Clinical Neurosciences* 2016. 28:17–25.

Schizophrenia is a neuropsychiatric disorder of complex etiology. Human endogenous retroviruses (HERVs) have been presented as possible candidates explaining the connections between the genetic, infectious, neurodevelopmental, and neuroinflammatory aspects of schizophrenia, with the human endogenous retrovirus type W family (HERV-W) showing the greatest evidence of association. Studies have identified retroviral nucleotide sequences, envelope and capsid proteins, and elevated transcription of HERV-W elements in CSF, blood, and brain samples from individuals with schizophrenia. The HERV-W elements can trigger the immune system in a variety of ways. HERV genetic elements may be activated by various prenatal maternal infections, leading to neuroinflammation and genetic abnormalities, altering the development of the brain, and eventually culminating in the development of schizophrenia. This review presents a concise synthesis of available evidence and theoretical speculation regarding the role of HERV-W in schizophrenia.

### **CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016.**

Dowell, et al.

*MMWR Recomm Rep.* ePub: 15 March 2016.



CDC has released guidelines for prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline includes 12 recommendations. The complete guidelines are available on the CDC website: <http://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1er.htm>

These include:

- \* Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate
- \* Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety
- \* When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed
- \* Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms.
- \* Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program
- \* Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible
- \* Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder