Department of Psychiatry
RESEARCH WATCH

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Chief Curator: Awais Aftab

Assistant Curator: Erin Fulchiero

Curators:
Erum Ahmad
Samantha Latorre
Cheryl Chen
Christine LaGrotta
John DeMott
Rob Siedler
Prakash Mishra

Research Watch is an initiative by the residents of University Hospitals Cleveland Medical Center/ 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)

Contact:
muhammad.aftab@uhhospitals.org

Highlights

- The preference to receive psychotherapy or medication in treatment-naive MDD patients does not appear to moderate symptomatic outcomes. (AJP)
- Study showing selective loss of smaller spines in primary auditory cortex runs counter to excessive-synaptic-pruning hypothesis of schizophrenia, which would have shown a selective loss of larger spines. (AJP)
- National cohort study suggests that stimulant medication use lowers the risk of motor vehicle crashes in patients with ADHD. (JAMA-P)
- In a large multicenter study, an ED-initiated intervention led to a 30% decrease in the total number of suicide attempts in a sample of high-risk patients. (JAMA-P)
- Lower cingulo-opercular network global efficiency appears to be a shared neurobiological mechanism underlying cognitive impairment across schizophrenia, schizoaffective disorder, and psychotic bipolar disorder. (JAMA-P)
- Depression and psychiatric medication use are potential risk factors for osteoporotic fracture risk that are not captured by the commonly utilized FRAX model. (JAMA-P)
- Bipolar I subjects show a decrease in degree centrality (index of focal connectivity) in the cortical regions and increase in degree centrality in subcortical regions, suggesting a pattern of cortical-subcortical dissociation. (JCP)
- Anticonvulsant use in veterans with PTSD is increasing but appears to be driven by increased prevalence of comorbid conditions such as pain and headache disorders. (JCP)
- Analysis reveals different types and severity of perinatal depression with varying time of onset throughout pregnancy and postpartum. (LP)
- Cohort study supports the use of reductions in WHO drinking risk levels as an efficacy outcome in alcohol dependence clinical trials. (LP)
- Association between autism and violent crime was explained by ADHD and conduct disorder comorbidity in Swedish population study. (JAACAP)

The American Journal of Psychiatry
Volume 174, Issue 6

Effects of Patient Preferences on Outcomes in the Predictors of Remission in Depression to Individual and Combined Treatments (PReDICT) Study

Dunlop, et al.

The PReDICT Study evaluated whether treatment preferences impacted outcomes in treatment-naïve patients (N=344) with major depression. Participants were asked to indicate whether they preferred therapy based treatment (16 50-minute sessions of CBT) or medication based treatment (escitalopram 10-20mg/day or duloxetine 30-60mg/day) and then were randomly assigned to a treatment arm. The primary outcome measure was changes in the HAM-D administered by a blinded rater. Results demonstrated similar overall decreases in HAM-D scores in all three treatment arms. However, patients matched to their preferred treatment did not significantly moderate symptomatic outcomes, but were more likely to complete the trial.

Functional Neuroimaging Predictors of Self-Reported Psychotic Symptoms in Adolescents

Bourque, et al.

Functional imaging responses were collected in youths as part of the IMAGEN study. Participants with psychotic-like experiences were matched to control subjects (subsample N=246, full sample N=1196.) Results demonstrated increased hippocampus/amygdala activity during processing of neutral faces and reduced dorsolateral prefrontal activity during failed inhibition in youths experiencing psychotic-like symptoms compared to controls.

Selective Loss of Smaller Spines in Schizophrenia

MacDonald, et al.

This study compared the deep layer 3 spine density and volume of the auditory cortex in 20 pairs of schizophrenia subjects and matched comparison subjects using immunohistochemistry-confocal microscopy and targeted mass spectrometry. The findings revealed that only the smallest spines were lost in the deep layer 3 of the primary auditory cortex while larger spines were preserved in subjects with schizophrenia. It was also found that overexpression of the schizophrenia risk gene CACNB4 resulted in a lower density of smaller spines in primary neuronal cultures. This finding runs counter to the hypothesis that schizophrenia results from increased pruning of excess synapses during adolescence, as increased pruning would likely result in a deficit of large spines in adulthood.

JAMA Psychiatry
Volume 74, Issue 6

Suicide Prevention in an Emergency Department Population, The ED-SAFE Study
Miller, et al.

This multicenter study examined whether emergency department (ED)–initiated intervention can reduce subsequent suicidal behavior in a sample of high-risk ED patients. The ED-SAFE study observed 1376 adult patients with a recent suicide attempt or suicidal ideation for up to 52 weeks following discharge from 1 of 8 EDs across 7 US states. The study tested whether universal suicide risk screening alone and in combination with a brief ED-initiated intervention would significantly reduce suicide attempts relative to treatment as usual (TAU). Intervention included a secondary risk screen by the ED physician, discharge resources, and post-ED telephone calls focused on reducing suicide risk. This intervention resulted in a 5% absolute decrease in the proportion of patients subsequently attempting suicide and a 30% decrease in the total number of suicide attempts over a 52-week follow-up period.

US Adult Illicit Cannabis Use, Cannabis Use Disorder, and Medical Marijuana Laws
Hasin, et al.

Over the last 25 years, 28 states have passed medical marijuana laws (MMLs) and this study was conducted to show the change in prevalence of cannabis use disorders using three different cross-sectional US adult surveys. Overall, from 1991/92 to 2012/13, the increase in illicit cannabis use in MML states was 1.4 percentage points greater than non-MML, and increase in cannabis use disorders was greater by 0.7 percentage point. Authors conclude that MMLs appear to have contributed to increased prevalence of illicit cannabis use and cannabis use disorders.

Association Between Medication Use for Attention-Deficit Hyperactivity Disorder and Risk of Motor Vehicle Crashes
Chang, et al.

A US national cohort of patients with ADHD (mean age 32.5 years, 51.7% female) were identified using commercial health insurance claims in those who followed up for emergency department visits for motor vehicle crashes (MVCs). The study compared risk of MVCs during the months in which participants received ADHD medication (any stimulant or atomoxetine) and those months without ADHD medication. Male patients had a 38% lower risk of MVCs when receiving medication and female patients had a 42% lower risk compared to months without ADHD medications. Estimated population-attributable fraction suggested that up to 22.1% of MVCs in patients with ADHD could have been avoided if they had received medication.

Transdiagnostic Associations Between Functional Brain Network Integrity and Cognition
Sheffield, et al.

In this case-control study, cingulo-opercular network but not frontoparietal network efficiency was significantly reduced in patients with schizophrenia ($P < .001$), schizoaffective disorder, and psychotic bipolar disorder ($P = .002$) compared with healthy control individuals. Lower cingulo-opercular network

global efficiency was associated with worse general cognitive ability and mediates the association between psychotic disorder status and cognitive function. This provides support for the hypothesis that a shared neurobiological mechanism underlies cognitive impairment in psychotic disorders.

Association Between Deliberate Self-harm and Violent Criminality
Sahlin, et al.

This population-based longitudinal cohort study of 1,850,525 individuals aged 15-32 investigated the association between non-fatal self-harm and risk of aggression towards others as determined by being convicted of a violent crime according to the Swedish penal code. The crude hazard ratio was 4.9 (95% CI, 4.8-5.0) for violent crime conviction in exposed individuals compared with the unexposed group and after adjustment for relevant psychiatric comorbidities and socioeconomic status, an almost doubled hazard of violent offense remained (hazard ratio, 1.8; 95% CI, 1.8-1.9).

Skin Conductance Responses and Neural Activations During Fear Conditioning and Extinction Recall Across Anxiety Disorders
Marin, et al.

This cross-sectional, case-control study attempted to determine studies if individuals with anxiety disorders exhibit dysregulated psychophysiological and neuroimaging profiles during fear conditioning and extinction recall. The results indicated that individuals with anxiety disorders (generalized anxiety disorder, social anxiety disorder, specific phobia, and panic disorder) activated the ventromedial prefrontal cortex less during fear conditioning and extinction recall compared with healthy controls. This hypoactivation was more pronounced in those diagnosed as having multiple anxiety disorders than in those having only one anxiety disorder.

Association of Mental Disorders and Related Medication Use With Risk for Major Osteoporotic Fractures
Bolton, et al.

Fracture Risk Assessment Tool (FRAX) is commonly utilized assessment tool for the prediction of fractures in men and women with use of clinical risk factors. In this longitudinal cohort study, FRAX scores were calculated for 68,730 individuals to determine the association between mental disorders and psychotropic medication use with osteoporotic fracture risk in routine clinical practice. FRAX significantly underestimated 10-year hip fracture risk in those with depression by 51% and in those using selective serotonin reuptake inhibitors by 57%, those using mood stabilizers by 98%, those using antipsychotics by 171%, and those using benzodiazepines by 31%. Depression and psychiatric medication use are potential risk indicators that are independent of FRAX estimates, this not fully captured by FRAX estimates.

Trait-Related Cortical-Subcortical Dissociation in Bipolar Disorder: Analysis of Network Degree Centrality

Zhou, et al.

This article investigated "network degree centrality," defined as a robust index of focal connectivity in which the number of direct connections from one node to all nodes is counted, in patients with bipolar I disorder (DSM-IV criteria). Resting state fMRIs were performed on 52 patients with bipolar I disorder compared to 70 healthy controls. Degree centrality was calculated within cerebral gray matter for each participant. Those with bipolar I disorder had significant decrease in degree centrality in the cortical regions including the middle temporal pole, inferior temporal gyrus, and ventral prefrontal cortex, but showed significant increase in degree centrality mainly in subcortical regions, including caudate, thalamus, parahippocampal gyrus, hippocampi, anterior cingulate, insula, and amygdala, and a small portion of cortical regions, such as superior and middle frontal gyrus (P < .05, corrected). These findings further contribute to the mounting evidence of cortical-subcortical dissociation in bipolar disorder pathophysiology.

Anticonvulsant Medication Use in Veterans With Posttraumatic Stress Disorder

Shiner, et al.

This article looked at trends and factors associated with anticonvulsant prescriptions among veterans with PTSD, as a large and increasing proportion of veterans with PTSD receive anticonvulsant medication. This analysis examined whether this significant and increasing use is for the treatment of PTSD itself or for other comorbid conditions. Data was examined from the VA from 2004 through 2013. A total of 24.9% of patients in the cohort received an anticonvulsant during their initial year of PTSD treatment, with 94.6% having an indication unrelated to PTSD. 51.2% initiated anticonvulsant use before their PTSD diagnosis. While this study shows that an increasing proportion of veterans with PTSD receives anticonvulsant prescriptions, the use appears to be driven by increased prevalence of comorbid conditions such as pain and headache disorders, for which anticonvulsant use may be clinically appropriate.

A Systematized Review of Atypical Antipsychotics in Pregnant Women: Balancing Between Risks of Untreated Illness and Risks of Drug-Related Adverse Effects

Tosato, et al.

This review article summarized risks associated with atypical antipsychotics in pregnant women with bipolar disorder and schizophrenia and their offspring. PubMed, Ovid, Scopus, PsycINFO, and Cochrane Library were searched from the date of the first available article through October 2015. Abrupt discontinuation of treatment-exposed mothers with bipolar disorder or schizophrenia led to a high risk

of relapses during pregnancy. Results suggest bipolar disorder and schizophrenia are linked to a slightly increased risk of obstetric complications for mothers (schizophrenia) and the newborn (bipolar disorder and schizophrenia). Evidence regarding the potential effects of SGAs on child neurodevelopment remains reassuring. The authors conclude that the most reasonable and less harmful choice for treating future mothers with bipolar disorder or schizophrenia appears to be maintaining them at the safest minimum dosage.

The Lancet Psychiatry
Volume 4, Issue 6

Change in non-abstinent WHO drinking risk levels and alcohol dependence: a 3 year follow-up study in the US general population
Hasin, et al.

This population-based cohort study aimed to examine the relationship between reduction in WHO drinking levels and subsequent reduction in the risk of alcohol dependence. The researchers included data from 22,005 drinkers who were interviewed during 2001-02 (wave 1) and re-interviewed 3 years later (wave 2) in the US National Epidemiologic Survey on Alcohol and Related Conditions. The researchers found that at wave 1, 2.5% of the respondents were very-high-risk drinkers, 2.5% were high-risk drinkers, 4.8% were moderate-risk drinkers and most (90.2%) were low-risk drinkers. Reduction in WHO drinking risk level predicted significantly lower odds of alcohol dependence at Wave 2, particularly among very-high-risk drinkers, and among those with alcohol dependence at Wave 1. This supports the use of reductions in WHO drinking risk levels as an efficacy outcome in alcohol dependence clinical trials.

Clinical phenotypes of perinatal depression and time of symptom onset: analysis of data from an international consortium
Putnam, et al.

This analytical study sought to empirically identify and describe clinically relevant phenotypic subtypes of perinatal depression, and further characterize subtypes by time of symptom onset within pregnancy and three post-partum periods. The data were assembled from a subset of 19 international sites in the postpartum depression: Action Towards Causes and Treatment (PACT) Consortium and the analysis was restricted to women aged 19-40 years with information about onset of depressive symptoms in the perinatal period and complete prospective data for the ten-item Edinburgh postnatal depression scale (EPDS). These analyses included data for 663 women and the researchers found evidences of three underlying dimensions measured by the EPDS: depressed mood, anxiety and anhedonia. On the basis of these dimensions, the researchers identified five distinct subtypes of perinatal depression: severe anxious depression, moderate anxious depression, anxious anhedonia, pure anhedonia and resolved depression. These subtypes were found to have clear differences in symptom quality and time of onset. Anxiety and anhedonia emerged as prominent symptom dimensions with post-partum onset and were notably severe.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 56, Issue 6

What is the Male-to-Female Ratio in Autism Spectrum Disorder? A Systematic Review and Meta-Analysis
Loomes, et al.

This was a systematic analysis of fifty-four studies with 13, 784, 284 participants of whom 54, 712 had ASD. The aim was to calculate the proportion of boys and girls with autism spectrum disorder. In the analysis of the results, of the children meeting criteria for ASD, the true male-to male female ratio was not 4:1 and is closer to 3:1. One possibility for this gender bias was that girls who met criteria for ASD were at disproportionate risk of not receiving a clinical diagnosis of ASD.

Specific Components of Pediatricians' Medication-Related Care Predict Attention-Deficit/Hyperactivity Disorder Symptom Improvement
Epstein, et al.

The purpose of this study was to identify which components of ADHD care best predict patient outcomes. Parents of 372 medication-naïve children in grades 1 to 5 presenting to their community-based pediatrician for an ADHD-related concern and who were subsequently prescribed ADHD medication were identified. Parents completed the Vanderbilt ADHD Parent Rating Scale at the time ADHD was raised as a concern and then approximately 12 months after starting medication. Twelve different components of ADHD care were reviewed. Shorter times to first contact and more teacher ratings collected in the first year of treatment significantly predicted a better outcome. ADHD symptom decrease was greater with timeliness of contacts, defined office visits, phone calls, or email communication.

Autism and Convictions for Violent Crimes: Population-Based Cohort Study in Sweden
Heermaun, et al.

This study was designed to investigate whether autism is associated with convictions for violent crimes and to study the associated risk and protective factors. Data was taken from the Stockholm Youth Cohort that consisted of 295, 734 individuals followed up between 15 and 27 years of age. The main outcome was a conviction for violent crimes identified using the Swedish National Crime Register. Unadjusted analysis indicated an association between autism and violent offenses, but the association was markedly attenuated when co-occurring ADHD or conduct disorder was taken into account. Male sex and psychiatric conditions were the strongest predictors of violent criminality, along with parental criminal and psychiatric history and socioeconomic characteristics. Better school performance and intellectual disability appeared to be protective.

Cognitive-Behavioral Family Treatment for Suicide Attempt Prevention: A Randomized Controlled Trial
Asarnow, et al.

The aim of this randomized controlled trial was to evaluate a cognitive-behavioral, dialectical-behavior therapy-informed family treatment program to promote safety. The study involved youth ages 12-18 years with suicide attempts or other self-harming behavior within the past 3 months. Youth were randomized either to the manualized program or to treatment as usual. Primary outcome was youth-reported incident suicide attempts on 3 months follow-up. Survival analysis showed a significantly higher probability of survival without a suicide attempt in the intervention group compared to treatment as usual.