Department of Psychiatry

RESEARCH WATCH

February 2017 - Volume 3, Issue 2

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

- Patient expectancy appears to be a significant mediator of placebo effects in antidepressant trials. (AJP)
- Meta-analysis finds few differences in clinical efficacy and acceptability between the different rTMS modalities, except novel rTMS interventions (accelerated, synchronized, and deep rTMS) which were found to be no more effective than sham. (JAMA-P)
- First trimester exposure to SSRIs was associated with a slightly increased risk of autism in meta-analysis, however the association remains unclear. (JCP)
- Vortioxetine's beneficial effects on cognitive function appear to be most pronounced in working patients with major depressive disorder. (JCP)
- At 9-months postpartum, majority of patients with postpartum psychosis appear to have good functioning with resumption of employment/household responsibilities. (JCP)
- Cumulative exposure to Herpesviridae and Toxoplasma gondii infections is associated with worse working memory in both psychiatric patients and healthy controls. (JCP)
- Low HDL and high triglyceride levels may be linked with delayed recovery from depression. (JCP)
- CBT, short-term psychoanalytical therapy and brief psychosocial intervention were found equally effective in maintenance of reduced depression symptoms 12 months after treatment. (LP)
- Self-reported depression and self-worth in socially transitioned transgender children appears to be comparable to their peers. (JAACAP)
- 12 year trajectories of substance use disorder in youth after detention appear to follow 3 patterns: bell-shaped, steady decline, or persistent use. (JAACAP)

Altered Expression of ARP2/3 Complex Signaling Pathway Genes in Prefrontal Layer 3 Pyramidal Cells in Schizophrenia
Datta, et al.

Findings in this study suggest down-regulation of the ARP2/3 complex signaling pathway compromises the structure and causes loss of dendritic spines in layer 3 and 5 pyramidal cells of the dorsolateral prefrontal cortex (DLPFC.) This likely contributes to the cognitive dysfunction in schizophrenia. Additionally, these spine deficits in the DLPFC may also lead to the excess dopamine release in the striatum via excitatory projections between the two structures, causing the psychosis seen in schizophrenia.

Neural Predictors of Initiating Alcohol Use During Adolescence
Squeglia, et al.

This prospective study identified 34 predictors that contributed to alcohol use by age 18. Demographic and behavioral factors for at-risk youth included male gender, higher socioeconomic status, early dating, more externalizing behaviors and positive alcohol expectancies. Other predictors included worse executive functioning, thinner cortices and less brain activation in diffusely distributed regions of the brain.

Patient Expectancy as a Mediator of Placebo Effects in Antidepressant Clinical Trials
Rutherford, et al.

A prospective, randomized controlled trial evaluated whether patient expectancy mediates placebo effects in antidepressant studies. Adult patients with MDD were assigned to open or placebo-controlled citalopram treatment. Following measurements of pre- and post-randomization expectancy, participants were treated with citalopram or placebo for 8 weeks. Patients assigned to open citalopram had greater expectancy of improvement and experienced greater reductions in depressive symptoms compared with those randomly assigned to placebo-controlled citalopram. Additionally, increased expectancy appeared to produce greater reductions in depression symptoms by an average of 6 HAM-D points.

Predicting Suicidal Behavior From Longitudinal Electronic Health Records
Barak-Corren, et al.

Electronic health record (EHR) data derived from a large electronic health database of inpatient and outpatient visits spanning 15 years was used to develop and validate a risk prediction model for suicidal behavior (suicide attempt or death). The model achieved sensitive (33-45% sensitivity), specific (90-95% specificity) and early (3-4 years in advance) prediction of patients' future suicidal behavior. Strongest

predictors identified included both well-known (e.g., substance abuse and psychiatric disorders) and less conventional (e.g., certain injuries and chronic conditions) risk factors.

JAMA Psychiatry
Volume 74, Issue 2

Antecedents of New-Onset Major Depressive Disorder in Children and Adolescents at High Familial Risk
Rice, et al.

This 4-year longitudinal study looked at 337 children of depressed parents to elucidate developmental pathways leading to incident cases of adolescent-onset major depressive disorder. The authors utilized a theoretical model of depression in adolescents, which simultaneously examined familial/genetic risk factors, social risk factors, and clinical antecedents and accounted for their co-occurrence. On average, children and adolescents had a mean of 1.85 DSM-IV symptoms of MDD at follow-up, and twenty had new-onset MDD. Irritability and fear/anxiety were significant independent clinical antecedents of new-onset MDD, but disruptive behavior and low mood were not.

Women's Mental Health and Well-being 5 years After Receiving or Being Denied an Abortion: A Prospective, Longitudinal Cohort Study
Biggs, et al.

Data from the Turnaway Study, a prospective longitudinal study with a quasi-experimental design, was used to examine psychological trajectories of women just under the facility's gestational limit (near-limit group) who received desired abortions compared to women who were denied an abortion (turnaway group) because they were beyond the facility gestational age limit. At 1 week after seeking an abortion, women who were denied abortion reported more anxiety symptoms, lower self-esteem, lower life satisfaction, but similar levels of depression than the near-limit group. Psychological well-being improved over time such that both groups of women converged by 6 months to 1 year.

Association of Fluid Intelligence and Psychiatric Disorders in a Population-Representative Sample of US Adolescents
Keyes, et al.

A population-based study evaluated the association of fluid intelligence and past-year and lifetime psychiatric disorders, disorder at the age of onset and disorder severity in a national sample of adolescents from the National Comorbidity Survey Replication-Adolescent Supplement. After adjusting for confounders, lower mean IQ was observed in adolescents with past year Bipolar Disorder (94.2), ADHD (96.3), ODD (97.3), Conduct Disorder (97.1), Substance Use Disorders (alcohol 96.5 and drugs 97.6), and specific phobia (97.1). Intelligence was positively associated with past year major depression (100). Across disorders, higher disorder severity was associated with lower fluid intelligence. The authors

conclude that stronger associations of current rather than past disorders with intelligence suggest that active symptoms of psychiatric disorders interfere with cognitive functioning.

Effects of Contemplative Dyads on Engagement and Perceived Social Connectedness Over 9 Months of Mental Training: A Randomized Clinical Trial
Kok, et al.

A new daily practice format, the contemplative dyad, was introduced in the context of the ReSource Project, a 9-month open-label efficacy trial of three secularized mental training models. A randomized clinical trial of 242 healthy adults sought to evaluate the impact of two newly developed dyadic contemplative exercises on perceived social connectedness. Intention-to-treat analyses showed that social closeness increased during a 10-minute dyadic practice session for both a socioaffective affect dyad and the sociocognitive perspective dyad. In addition, predyad social closeness and self-disclosure increased significantly for both dyads over the 3 months of a given training module.

Acute and Chronic Posttraumatic Stress Symptoms in the Emergence of Posttraumatic Stress Disorder: A Network Analysis
Bryant, et al.

This prospective cohort study of 1138 patients with traumatic injury used a network analysis approach to estimate the nature of the association between PTSD symptoms in the acute phase after trauma and the chronic phase. Reexperiencing symptoms were central to other symptoms in the acute phase, with intrusions and physiological reactivity among the most central symptoms in the networks. Among 852 patients who completed the 12-month assessment, overall network connectivity was significantly stronger than in the acute phase, and fear circuitry and dysphoric symptoms of posttraumatic stress disorder emerged as connected networks. This study thus showed that trauma memories are centrally linked to other symptoms in the acute trauma phase, highlighting possible early intervention strategies.

Repetitive Transcranial Magnetic Stimulation for the Acute Treatment of Major Depressive Episodes: A Systematic Review With Network Meta-analysis
Brunoni, et al.

This systematic review and network meta-analysis aimed to determine the compare the efficacy and tolerability of repetitive transcranial magnetic stimulation (rTMS) modalities in the treatment of acute depressive disorder. The researchers collected data from 81 randomized clinical trials (4233 patients) and found that priming low-frequency, bilateral, high-frequency, low-frequency, and θ-burst rTMS—but not novel (accelerated, synchronized, and deep rTMS) strategies—were more effective than sham regarding response rates. All interventions were at least as acceptable as sham. The authors concluded that only few differences were found in clinical efficacy and acceptability between the different rTMS and this current evidence cannot support novel rTMS interventions for treating acute depression.

The Journal of Clinical Psychiatry
Volume 4, Issue 1

The Association Between Antenatal Exposure to Selective Serotonin Reuptake Inhibitors and Autism: A Systematic Review and Meta-Analysis
Brown, et al.

This meta-analysis examines the relationship between antenatal SSRI exposure and child autism, accounting for the potential confounding factor of maternal mental illness (MMI). MEDLINE, Embase, PsycINFO, and CINAHL were searched from inception through January 28, 2016 including 4 case-control studies and 2 cohort studies. The authors looked at same design studies of SSRI exposure any time during pregnancy in addition to SSRI exposure in the first trimester with sub-analyses created for MMI and restricted to MMI. In MMI-adjusted analyses, only first trimester exposure remained statistically significant (aPOR = 1.8; 95% CI, 1.1–3.1). No other groups were found to be statistically significant. It remains unclear whether there is an association between first trimester SSRI exposure and child autism. Future studies require more robust measurement of MMI prior to and during pregnancy.

Efficacy of Vortioxetine on Cognitive Functioning in Working Patients with Major Depressive Disorder
McIntyre, et al.

This post hoc analysis from population data from FOCUS, a double-blind, randomized-controlled study investigated the efficacy of vortioxetine on cognitive functioning and depressive symptoms in the working adult population with major depressive disorder. The Digit Symbol Substitution Test (DSST), Trail Making Test A/B (TMT-A/B), Stroop, and Perceived Deficits Questionnaire (PDQ) were used to analyze mean change from baseline scores. In addition, change in depression severity was analyzed using the Montgomery-Asberg Depression Rating Scale (MADRS) according to patients' working status at baseline and workplace position. The effect on the DSST was significant versus placebo: 5.6 for 10 mg and 5.0 for 20 mg in working patients; the effect was 4.0 in total study population. Similar patterns were observed for other tests. The greatest beneficial effects on objective and subjective measures on cognitive functioning were therefore seen in working patients with MDD, and this was independent on any improvements in depressive symptoms.

Functional Recovery After Postpartum Psychosis: A Prospective Longitudinal Study
Burgerhout, et al.

This prospective longitudinal study followed 78 patients with postpartum psychosis over a 9-month period. Functional recovery was studied, which included psychosocial functioning and presence of psychological distress. Patients with postpartum onset with DSM-IV-TR diagnoses of psychotic disorder not otherwise specified, brief psychotic disorder, or mood disorder with psychotic features were included. At nine months postpartum 74% of the patients reported good functioning over 4 domains (work, interpersonal relations, recreation, and global satisfaction) and 88% of patients resumed premorbid

employment and household responsibilities. Overall, patients reported a higher burden of depression and anxiety when compared to the general population and those that relapsed (18%) had significant functional impairments across several domains.

Effects of Cumulative Herpesviridae and Toxoplasma gondii Infections on Cognitive Function in healthy, bipolar, and Schizophrenia subjects
Hamadani, et al.

This study sought to examine the effect of multiple infections on cognitive functioning in patients with schizophrenia and bipolar disorder and in healthy controls. Seropositivity to herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2), cytomegalovirus (CMV), and T gondii was related to cognitive status among 138 patients with bipolar disorder, 105 patients with schizophrenia, and 180 healthy controls. Seropositivity to and antibody levels of HSV-1 were significantly associated with working memory (Wechsler Adult Intelligence Scale). This association was particularly strong in the control group. Cumulative exposure to HSV-1, HSV-2, and CMV viruses and T gondii parasite was also associated with lower scores on working memory as measured by backward digit span in the overall sample.

Metabolic Syndrome and Symptom Resolution in Depression: A 5 year follow-up of older adults
Virtanen, et al.

This study examined whether metabolic syndrome and its components are associated with long-term symptoms resolution in older adults with depressive symptoms. Data from the Whitehall II cohort study was used for analysis. In the reported results metabolic syndrome per se was not associated with symptom resolution. Among the components, low HDL cholesterol (risk ratio [RR] = 0.82) and high triglyceride levels (RR = 0.81) were associated with a lower likelihood of symptom resolution. These findings were replicated in a subpopulation without coronary heart disease and stroke. This suggests that adverse lipid profile may be linked with delayed recovery from depression.

The Lancet Psychiatry
Volume 4, Issue 2

Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial
Goodyer, et al.

This multicenter, randomized controlled superiority trial aimed to assess medium-term effects and costs of psychological therapies on maintenance of reduced depression symptoms 12 months after treatment. The primary outcome was self-reported depression symptoms at weeks 36, 52, and 86. The trial found no evidence of superiority of CBT or short-term psychoanalytical therapy compared with a brief psychosocial intervention in maintenance of reduced depression symptoms 12 months after treatment. Short-term

psychoanalytical therapy was as effective as CBT. Total costs of the trial interventions did not differ significantly between treatment groups.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 56, Issue 2

Mental Health and Self-Worth in Socially Transitioned Transgender Youth
Durwood, et al.

This study examined self-reported depression, anxiety, and self-worth in socially transitioned transgender children compared with 2 control groups: age- and gender-matched controls and siblings of transgender children. In this longitudinal study, children (ages 9-14 years old) and their parents completed measurements of depression and anxiety. Transgender children reported depression and self-worth did not differ from their matched-control or sibling peers; reported level of anxiety was marginally higher. Parents of transgender children confirmed that their children experienced more anxiety than children in control groups. These findings are in contrast to earlier literature on gender-nonconforming children who had not socially transitioned with very high rates of depression and anxiety.

Trajectories of Substance Use Disorder in Youth After Detention: A 12-Year Longitudinal Study
Welty, et al.

This longitudinal study aimed to identify trajectories of substance use disorders in youth during the 12 years after detention and how gender, race/ethnicity, and age at baseline predict trajectories. Youth from detention in Chicago, Illinois were sampled as part of the Northwestern Juvenile Project from 1995 through 1998 and participants were interviewed in the community or correctional facilities up to 9 times over 12 years. Class 1 (24.5%), was a bell-shaped trajectory, peaked 5 years after baseline. Class 2 (41.3%) had a higher prevalence of SUD at baseline, and prevalence decreased over time. Class 3 (14.6%), the most serious and persistent trajectory, had the highest prevalence of comorbid or "other" illicit drug disorders—52.1% at baseline and 17.4% 12 years later. Males, Hispanics, and non-Hispanic whites had the worst outcomes.

Development of Alcohol and Drug Use in Youth With Manic Symptoms
Horwitz, et al.

This analysis examined alcohol and drug use over a 6-year follow-up of children in the Longitudinal Assessment of Manic Symptoms (LAMS) study. Of those >9 years at baseline, 34.9% used alcohol at least once, with 11.9% regular users; 30.1% used drugs at least once, with 16.2% regular users. Predictors of any drug use included single parent, parental substance use, and stressful child life events. Predictors of regular drug use were parental marital status, stressful child life events, and a baseline disruptive behavior disorder diagnosis. Baseline medications decreased the risk of regular drug use.