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Reproductive Psychiatry: The Gap Between Clinical Need and Education
Osborne, et al. (*Dr Sarah Nagle-Yang, Associate Residency Training Director, is among the co-authors*)

This commentary is a call to arms regarding the area of reproductive mental health. Even for those who are practicing within the field of psychiatry, there is limited training and education on this particular subject. This article discusses how the current state of limited clinicians practicing and advocating for reproductive mental health education has led women to be influenced more by social media. Unfortunately, the media tends to focus on the risks of medication treatments and not on the risks and consequences of untreated psychiatric conditions during pregnancy and postpartum. As a result, the National Task Force on Women's Reproductive Mental Health is working to define national standards for education on reproductive psychiatry to ensure that all psychiatrists acquire basic knowledge and skills and as a result provide the standard of care for this special patient population.

Ketamine and other NMDA Antagonists: Early Clinical Trials and Possible Mechanisms in Depression
Newport, et al.

This systematic review and meta-analysis of placebo-controlled, double-blind, randomized clinical trials of NMDA antagonists in the treatment of depression found ketamine to produce rapid but transient antidepressant effects along with psychotomimetic and dissociative effects. D-cycloserine and rapastinel, partial agonists at the NMDA co-agonist site also demonstrated a significant reduction of depressive symptoms without psychotomimetic or dissociative effects. These findings suggest glutamate-modulating strategies hold potential in the treatment of depression. However, at this time, their mechanism is still not fully understood and use is still cautioned due to the possibility of abuse and neurotoxicity

Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence from a Four-Decade Longitudinal Cohort Study
Moffit, et al.

This retrospective cohort study of adult ADHD study participants and prospective cohort study of pediatric ADHD study participants found that the two groups had essentially non-overlapping populations sets as 90% of adult ADHD cases lacked a history of childhood ADHD. Additionally, adult ADHD participants did not show the neuropsychological deficits or polygenic risk of their pediatric counterparts, suggesting that adult-onset ADHD may not be a childhood-onset neurodevelopmental disorder and its place within the DSM classification may need to be reconsidered if repeated studies confirm this finding.

Gene-Environment Interaction in Youth Depression: Replication of the 5-HTTLPR Moderation in a Diverse Setting
Rocha, et al.

This large cohort study sought to replicate findings of the 1993 Pelotas Birth Cohort Study on gene-environment interactions (GxE) in youth depression. Findings were consistent with the original study and corroborated the existence of a measured GxE and that a genetic variant in the 5-HTTLPR genotype moderates the link between childhood maltreatment and youth depression.

Psychosis Prevention: A modified Clinical High Risk Perspective from the Recognition and Prevention Program
Cornblatt, et al.

This prospective cohort study of 101 treatment-seeking adolescents at clinical high risk for psychosis were followed for five years with the goal of developing criteria that would have a higher positive predictive value of identifying those who would later develop psychosis and would benefit most from early, aggressive intervention and prevention. The clinical high risk criteria that were found to have a positive predictive validity of 81.8%, consisted of four variables: disorganized communication, suspiciousness, verbal memory deficits and decline in social functioning. Using these criteria compared to attenuated positive symptoms alone has potential to improve predictive accuracy.

Brain Structural Abnormalities in a Group of Never-Medicated Patients with Long-Term Schizophrenia
Zhang, et al.

This cross sectional study compared high resolution T1 images of 25 untreated patients with chronic schizophrenia to 33 matched healthy subjects. Accelerated age-related decline in prefrontal and temporal cortical thickness was noted in never-medicated schizophrenia patients which suggests a neuroprogressive process in some brain regions. Slower age-related cortical thinning of the superior parietal cortex and striatal volumetric abnormalities unrelated to age were also noted which suggest different pathological processes over time in these regions.

Measurement-Based Care Versus Standard Care for Major Depression: A Randomized Controlled Trial with Blind Raters
Guo, et al.

This randomized controlled trial compared time to response and remission of depressive symptoms in a group of study participants who either received measurement-based care (guideline and rating scale based decisions) or standard treatment (clinicians' choice decisions). Findings showed that patients in the measurement-based care group achieved significantly more response compared to the standard treatment group (86.9% compared with 62.7%) suggesting that this approach should be incorporated in the clinical care of patients with major depression.

A Randomized, Double-Blind, Placebo-Controlled Trial of Citicoline for Cocaine Dependence in Bipolar I Disorder
Brown, et al.

This study involved 130 patients with Bipolar I Disorder (depressed or mixed mood state) with comorbid cocaine dependence who were then randomized to receive either citicoline or placebo add-on therapy for 12 weeks. Results of the study showed significant reduction in cocaine use initially in participants who were treated with citicoline. However, these effects diminished over time, suggesting that treatment augmentation is needed to optimize long term-benefits.

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Transcranial Direct Current Stimulation: Theory, Treatment of Major Depressive Disorder, and Other Neuropsychiatric Applications
Siddiqi, et al.

Transcranial direct current stimulation (tDCS) has demonstrated some promise as a treatment for various disorders, including major depressive disorder. However, important questions remain unanswered, including precise mechanisms of action, ideal stimulation parameters for different disorders, optimal dosing schedules, and long-term safety. Cognitive enhancing effects of tDCS have been difficult to predict, but this is limited by methodological variability. Compared to other neuromodulatory treatments, tDCS is safe, well-tolerated, and inexpensive; however, it is likely somewhat less effective. Cognitive effects have been useful for sustaining attention/vigilance and improving cognition in Alzheimer's disease.

Painkillers That Cause Pain: Review of a Rising, Poorly Recognized Complication
Stanciu, et al

Chronic opioid exposure aimed at alleviating pain can paradoxically render some individuals more sensitive to nociceptive stimuli, aggravate underlying pain, and even induce a new pain, a complication termed opioid-induced hyperalgesia (OIH). Clinically, OIH and tolerance both present with worsening pain despite dosage escalation. Management of OIH involves reduction in the opioid dose, tapering with the aid of an adjuvant analgesic, or supplementation with N-methyl-D-aspartate modulators.

Prevention of Dementia
Jerath AU

Epidemiological studies suggest that reducing substance use, dietary modification, control of diabetes and metabolic syndrome, treatment of depression, and maintaining an active lifestyle may help reduce the prevalence of dementia. Randomized controlled studies examining these factors have been few in number and have yielded inconclusive results.

Delusional Memory in First-Episode Psychosis
Aftab A (*PGY2*)

The case report discusses the psychopathology of psychosis with a focus on delusional memory. Delusional memory can be a delusional interpretation of real memory or a delusion that is experienced as a memory. Delusional interpretation of real memory is the memory analogue of delusional perception and therefore a Schneiderian first-rank symptom. Studies utilizing the Deese-Roediger-McDermott paradigm have shown that in individuals with schizophrenia, especially in those with active psychosis, there is an increased percentage of inaccurate but confidently held memories (increased knowledge corruption index).

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Meta-Analysis of Functional Neuroimaging of Major Depressive Disorder in Youth
Miller, et al.

This meta-analysis aimed to identify the most reliable neural abnormalities reported in existing functional neuroimaging studies in youth diagnosed with major depressive disorder, and characterize their relations with specific psychological dysfunctions. Reliable patterns of abnormal activation, including task-general and task-specific effects in several distributed brain networks were found, which may explain seemingly disparate symptoms of MDD in youth. See paper for details.

Symptom-Onset Dosing of Sertraline for the Treatment of Premenstrual Dysphoric Disorder - A Randomized Clinical Trial
Yonkers, et al.

This double-blind, placebo-controlled sought to determine the efficacy of symptom-onset dosing with the Sertraline for treatment of premenstrual dysphoric disorder (PMDD). Premenstrual Tension Scale (PMTS) score was the primary outcome measure, with 3 other scales used as secondary outcome measures (IDS-C, DRSP, CGI). No significant differences between sertraline and placebo were found on PMTS, however significant results were found on secondary outcome measures. Depending on the symptom scale, women with PMDD may or may not benefit from symptom-onset treatment with SSRIs.

Antidepressant Response Trajectories and Associated Clinical Prognostic Factors Among Older Adults
Smagula, et al.

This study aimed to assess typical patterns of response to an open-label 12 week trial of Venlafaxine XR for late-life depression and to evaluate clinical factors associated with response patterns. Factors associated with having a nonresponsive trajectory included greater baseline depression severity, longer episode duration, less subjective sleep loss, more guilt, and more work/activity impairment. Higher delayed memory (list recognition) performance was associated with having a rapid response.

Early Cannabis Use, Polygenic Risk Score for Schizophrenia and Brain Maturation in Adolescence
French, et al.

Study reveals that a negative association was observed between cannabis use in early adolescence and cortical thickness in male participants with a high polygenic risk score (risk for schizophrenia determined across 108 genetic loci). This observation was not the case for low-risk male participants or for the low- or high-risk female participants.

The Lancet Psychiatry
Volume 2, Issue 10

Psychiatric disorders and violent reoffending: a national cohort study of convicted prisoners in Sweden
Chang, et al.

This longitudinal cohort study of prisoners in Sweden revealed that diagnosed psychiatric disorders were associated with an increased hazard of violent reoffending in male (adjusted HR 1·63 [95% CI 1·57–1·70]) and female (2·02 [1·54–2·63]) prisoners. Risk was higher with substance use disorders and bipolar disorder compared to other psychiatric disorders. The hazard of violent reoffending increased in a stepwise way with the number of diagnosed psychiatric disorders.

Mortality risk of opioid substitution therapy with methadone versus buprenorphine: a retrospective cohort study
Kimber, et al.

This is a retrospective cohort study from Australia. Patients who initiated with buprenorphine had reduced all-cause and drug-related mortality during the first 4 weeks of treatment compared with those who initiated with methadone (adjusted all-cause MRR 2·17, 95% CI 1·29–3·67; adjusted drug-related MRR 4·88, 1·73–13·69). For the remaining time on treatment, drug-related mortality risk did not differ.

Prevalence of autism spectrum disorder phenomenology in genetic disorders: a systematic review and meta-analysis
Richards, et al.

ASD phenomenology varied between genetic syndromes, but was consistently more likely than in the general population. Relative risks and the odds ratio compared with the general population were highest for Rett's syndrome and Cohen's syndrome.

Journal of the American Academy of Child and Adolescent Psychiatry
Volume 54, Issue 10

Physical Activity, Sadness, and Suicidality in Bullied US Adolescents
Sibhold, et al.

Objectives of this study included assessing the relationship between physical activity, sadness, and suicidality in bullied US adolescents. The authors hypothesized that physically active students would be less likely to feel sad or to report suicidal ideation or attempts. The authors used the 2013 National Youth Risk Behavior Study to assist with stratification. Bullied students were twice as more likely to report feelings of sadness and 3 times as likely to report suicidal ideation or attempt. Students who exercised 4-5 times a week had lower adjusted odds of sadness, suicidal ideation, or suicide attempts than students

who exercised less than or equal to 1 day a week. Furthermore, exercise for 4 or more days a week was associated with an approximate 23% reduction in suicidal ideation and attempts in bullied students.

Antecedents of the Child Behavior Checklist-Dysregulation Profile in Children Born Extremely Preterm
Frazier, et al.

This study aimed to evaluate the antenatal and early postnatal antecedents that might influence the association between extreme preterm birth and emotional and behavioral dysregulation at 2 years of age. This multi-site prospective study of 826 infants born prior to 28 weeks gestational age consisted of parents completing the Child Behavior Checklist when the child was at 2 years corrected age. Maternal, pregnancy, placenta, delivery, and newborn characteristics were compared to those of healthy peers. Model with antenatal variables including low maternal education achievement, passive smoking, and recovery of Mycoplasma from the placenta were associated with increased risk of developing emotional and behavioral dysregulation.

Normal Variation in Early Parental Sensitivity Predicts Child Structural Brain Development
Kok, et al.

This study observed the prospective relation between mothers' and fathers' sensitive caregiving in early childhood and brain structure later in childhood. Maternal and paternal sensitivity was repeatedly observed during age 1 - 4 years. Head circumference was measured at 6 weeks and MRI was performed at 8 years of age to evaluate brain structure. Larger total brain volume and gray matter volume correlated with higher levels of parental sensitivity at 8 years, controlling for infant head size. No significant difference was noted between paternal and maternal sensitivity.

Subthreshold Depression and Regional Brain Volumes in Young Community Adolescents
Vulser, et al.

This study utilizing a community based sample examined the differences in brain structure on MRI scans at age 14 years in adolescents with subthreshold depression (vs healthy controls) and their relation to depression at age 16 years. Adolescents with subthreshold depression had smaller gray matter volume in certain parts of the brain, particularly the frontal-striatal-limbic affective circuits.

Current Psychiatry
Volume 14, Issue 10

What to do when your depressed patient develops mania
Goldberg and Ernst

This article provides a systematic approach on how to evaluate a patient with depression who now presents with manic symptoms. In addition to assessing for both manic and depressive symptoms,

evaluate for elicit substances and stop any antidepressant. Antidepressants have been shown to harm presentations involving mixed states and show no evidence in preventing post-manic depression. It is also advised to start anti-manic pharmacotherapy (see article for discussion of mood stabilizers and antipsychotics) as well as normalizing the sleep-wake cycle. This article also provides recommendation of medical evaluation for first episodes of mania. Additional the article provides guidance on length of treatment with mood stabilizer and future addition of antidepressants once mania is stabilized.

How coffee and cigarettes can affect the response to psychopharmacotherapy
Narahari, et al. *(PGY2 Amandeep Bains is among the co-authors)*

CYP1A2 hepatic enzymes detoxify a variety of environmental agents such that they can be excreted in the urine and metabolizes 20% of all drugs handled by the CYP system. Tobacco increases the activity of these enzymes (CYP1A2 and CYP2B6) resulting in lower blood drug concentrations and decreased clinical response. However, pure nicotine found in nicotine replacement therapies do not induce CYP enzymes. Because of these effects, patients in a smoke-free facility could have drug toxicity if the outpatient dose is maintained on admission. Caffeine is metabolized by CYP1A2 such that forced smoking cessation in the hospital and continued caffeine consumption could lead to caffeine toxicity. It can also form an insoluble precipitates with antipsychotics in the intestines, decreasing absorption.

Urine drug screens: When might a test result be false-positive?
Pawlowski and Ellingrod

Most in office urine testing is POC, which is an immunoassay and can quantitatively detect agents for only 3 to 7 days after ingestion. False positive occur due to cross-reactive binding of a similarly shaped molecule. Additionally, with POC testing, synthetic substances require a higher dosage in order to be detected, for example, synthetic opioids. Amphetamine and opiate false positives are more common than cocaine and cannabinoid false positives. Gas chromatography-mass spectrometry (GC-MS) is a good tool to confirm positive or negative screens. It breaks down a specimen into fragments prior to separation such that it can identify a specific drug (oxycodone) instead of a large class (opioid). One down fall of GC-MS, is that depending on specimen collection, the sample may be broken down into metabolites such that the parent compound is no longer detectable (heroin is metabolized into morphine).

International Journal of Psychoanalysis
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Shame, Hatred, and Pornography: Variations on an Aspect of Current Times
Janin C; DOI: 10.1111/1745-8315.12417

Claude Janin has produced an elegant article that integrates shame, hatred, and pornography. Drawing on clinical vignettes as well as various psychoanalytic perspectives, Janin offers an insightful study placing these themes in a contemporary context.

Intersubjectivity, Otherness, and Thirdness: A Necessary Relationship
Fiorini LG; DOI: 10.1111/1745-8315.12432

Fiorini delivers a concise survey of the concepts of intersubjectivity, otherness, and thirdness as it applies to analytic work. She explicates clinically relevant considerations of these concepts and illuminates future directions for inquiry.

The American Journal of Psychoanalysis
Volume 75, Issue 3

Some Psychoanalytic Reflections on the Concept of Dignity
Akhtar S

Drawing from diverse perspectives, Salman Akhtar reviews philosophical and psychoanalytic writings regarding dignity. He classifies these conceptualizations in metaphysical, existential, and characterological categories. Furthermore, Akhtar considers the clinical implications of the various concepts of dignity.

Seeing Double, Being Double - Longing, Belonging, Recognition, and Evasion in Psychodnamic Work with Immigrants
Boulanger G

Ghislaine Boulanger proposes that people who are immigrants live double lives – one identified with their place of origin and another identified with their adopted setting. She argues that successful treatment allows people who are immigrants to take doubleness for granted – thus seeing and being double. She integrates these observations with clinical information.

Miscellaneous Studies

Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescents
LeNoury, et al. *BMJ* 2015;351:h4320

This study was a reanalysis of the 2001 SmithKline Beecham Study 329 that was published by Keller et al. The goal of the original study was to compare the efficacy and safety of paroxetine and imipramine with placebo in the treatment of adolescents with a unipolar major depressive disorder. The study was a double blind randomized placebo controlled trial that involved 12 psychiatric centers in North America from the years 1994-1998. It assessed 275 adolescents with major depression of at least eight weeks in duration and participants were randomized to eight weeks double blind treatment with paroxetine, imipramine, or placebo. Based on analysis of primary and secondary outcomes, it was determined that the efficacy of paroxetine and imipramine was not statistically different or even clinically different from placebo.

Furthermore, use of paroxetine or imipramine had risk of clinically significant harm. Furthermore, this reanalysis suggests the importance of making primary data accessible and the value of reanalysis.

Long-term outcome in the prevention of psychotic disorders by the Vienna omega-3 study
Amminger, et al. Nat Commun. 2015 Aug 11;6:7934.

This study was a retrospective analysis of a previous double-blind placebo-controlled trial of ultra-high-risk children (41 treatment vs. 40 placebo) where 13-25 year olds were given a 12 week course of 700mg EPA/400mg DHA. The authors looked at whether the two groups were different in their conversion to a psychotic disorder (primary outcome) and psychosocial functioning (secondary outcome) 6.7 years later. They showed that 4/41 of the treatment from the treatment group and 16/40 placebo group developed a psychotic disorder. The secondary outcome was less dramatic where the treatment group had a mild, but statistically significant, higher level of functioning as compared to the placebo group.

Research Watch Bonus Materials

An Overview of Cariprazine (Vraylar)

Black Box Warning: Increased mortality in elderly patients with dementia-related psychosis
Indications: Treatment of schizophrenia and acute treatment of manic or mixed episodes associated with Bipolar I Disorder
Dosage:
Schizophrenia: Starting Dose 1.5 mg once daily, Recommended Dose: 1.5 mg to 6 mg once daily
Bipolar Mania: Starting Dose 1.5 mg once daily, Recommended Dose: 3 mg to 6 mg once daily
Common Adverse Reactions: Extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence, restlessness
Drug Interactions: With strong CYP3A4 inhibitors and inducers
Mechanism of Action: Partial agonist at D2 and D3 receptors (with high selectivity towards the D3 receptor) and 5HT1A receptors, and antagonist at 5-HT2A receptors.
Metabolites: Cariprazine has active metabolites with long half-lives (in weeks).
Effect on QTc: No clinically significant prolongation of the QTc interval up to 3 times maximum recommended dose.
Unique Features: High selectivity towards D3 receptor; has been noted to produce pro-cognitive effects in animal studies

An Overview of Aripiprazole lauroxil (Aristada)

Aripiprazole lauroxil (Aristada) is an extended-release injectable suspension for intramuscular use, approved by FDA for the treatment of schizophrenia. It can be administered every four to six weeks using an injection in the arm or buttocks.

Aristada can be initiated at a dose of 441 mg, 662 mg or 882 mg administered monthly or 882 mg dose every 6 weeks. In conjunction with the first Aristada injection, administer treatment with oral aripiprazole for 21 consecutive days.

FDA changes to Clozapine monitoring and prescribing guidelines

Starting Oct 12, 2015, ALL clozapine products are only available through the Clozapine Risk Evaluation and Mitigation Strategy (REMS) program.

1. How to monitor patients for neutropenia and manage clozapine treatment:
    a. Neutropenia will only be monitored by Absolute Neutrophil Count (ANC). WBC counts are no longer expected.
        i. If outpatient, ANC must be reported to REMS before medication is dispensed
        ii. If inpatient, ANC must be reported within 7 days
    b. Patients will be allowed to continue on Clozapine at a lower ANC. Patients with benign ethnic neutropenia (BEN) are now eligible.
    c. 2 monitoring algorithms
        i. Without BEN, stop clozapine if ANC <1000/uL
        ii. With BEN, stop clozapine if ANC <500/uL
    d. Prescribers now have more flexibility to “re-challenge” patients
    e. Prescribers can continue clozapine treatment with ANC <1000/uL if the benefits of clozapine treatment outweigh the risk of severe neutropenia.
2. REMS: a shared risk evaluation and mitigation strategy (shared monitoring system-replaces the 6 existing registries)
    a. Patients currently under treatment will be automatically transferred to REMS program
    b. Prescribers and pharmacies must be certified with REMS starting Oct 12, 2015