Editors’ Best of 2019

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There is, in the content of the *Journal*, an embarrassment of riches, and picking a “best” seems to demand a certain qualification: is the “best” the most interesting, most surprising, most educational, most important, most provocative, most enjoyable? How to choose? We are hardly unbiased and can admit to a special affection for the ones that we and the authors worked hardest on, hammering version after version into shape. Acknowledging these biases, here are the 2019 articles that we think deserve your attention or at least a second read.

**New Innovations and Testing Assumptions**

**Double-Blind, Sham-Controlled, Pilot Study of Trigeminal Nerve Stimulation for Attention-Deficit/Hyperactivity Disorder, McGough *et al*.**

**Visiting and Antenatal Depression Affect the Quality of Mother and Child Interactions in South Africa, Christodoulou *et al*.**

It is frequently stated that we keep on implementing old treatment strategies to alleviate the burden of mental health conditions in children and adolescents. Whilst certainly the pace of change is not as quick as we would like, the field is witnessing the emergence of some potentially relevant innovations. An important example comes from a trial on trigeminal nerve stimulation (TNS) for ADHD, published in *JAACAP* by McGough *et al*.1 Currently, there is meta-analytic evidence that stimulants are highly efficacious for the core symptoms of ADHD in the short-term.2  However, a number of patients, parents, and even professionals are reluctant to use ADHD medications in view of their possible side effects and uncertainty regarding long-term effectiveness.3 As such, there is an increasing interest on non-pharmacological strategies for ADHD. Within this context, McGough *et al*. conducted the first double-blind, sham-controlled, randomized pilot trial of TNS for ADHD. After 4 weeks of treatment, compared to children with ADHD assigned to a sham condition, those wearing the active device at night showed a significant reduction in the severity of ADHD symptoms rated by clinicians via the ADHD rating scale, based on parents’ reports and collateral information. No clinically meaningful adverse events during treatment were reported. The authors clearly acknowledged that the effect size (ES) found for the efficacy of TNS on ADHD core symptoms (Cohen d = 0.5) is similar to that of non-stimulants, which is roughly half that of amphetamines. The study supported the marketing authorization from the FDA for TNS as the first medical device for the treatment of children with ADHD (aged 7-12) who are not already taking ADHD medications. The use of TNS for ADHD requires additional research, for instance to understand why teachers ratings of ADHD symptoms did not significantly improve in the trial and, perhaps more importantly, the long term effects and tolerability of the device. However, the McGough *et al.’s* study suggested that TNS might be an effective alternative for patients for which the pharmacological treatment is not an option.

Other examples come from the wealth of innovative papers *JAACAP* published in 2019 designed to advance our understanding of what contributes to the efficacy and effectiveness of psychotherapeutic interventions. This body of work considered important questions about therapeutic response--who benefits most from interventions,4,5 implications of dropping out of therapy early,6 and use of measurement to guide our work in relation to both timing of change as a predictor of outcome or signal to alter treatment approach7 and determining what constitutes reliable change.8 Another set of papers explored changes in response to targeted intervention on both diagnostic specific features as well as effects on other symptom clusters 9 and on general psychopathology or the “p” factor.10 These papers and their authors have informed and enriched our understanding of how/when and for whom therapy may be beneficial—all deserve our thanks and recognition.

The *Journal* also published findings from a number of carefully designed and executed clinical trials. The cluster randomized controlled trial assessing the impact of a home visiting, psychoeducational intervention or standard care on the quality of mother-child interactions among new mothers in 24 Cape Town South African townships represents a particularly innovative example.11 In this trial, Christodoulou and colleagues, used an established therapeutic design to address a question of global importance—how to support positive development of youth in low resourced countries and communities. To this end, they enrolled pregnant mothers and initiated a series of peri-natal home visits using a task-shifting approach by drawing on community women to deliver the intervention. Videotaped observations of M-C interactions were collected to allow ratings of observed behaviors and explored both mother’s behavior and child’s characteristics such as gender, temperament, level of activity, responsiveness to mother. This paper reported on observations when the children were three years of age. Observations revealed more positive parenting and child behavioral in the home visit group compared to those receiving standard care, except for mother’s struggling with depression. The investigators emphasized the positive effects of the intervention on many general health factors while underscoring the need to expand the curriculum to include depression targeted education and intervention elements. This innovative work provides a guide for how to support mothers and children living in high risk circumstances in a way that is effective, culturally sensitive, and sustainable.

We are proud that *JAACAP* is at the forefront in the scientific dissemination of treatment innovations in child and adolescent psychiatry.

**Samuele Cortese**

**Elizabeth A. McCauley**

**Bringing Hope and Identifying Hopelessness**

**Characteristics and Precipitating Circumstances of Suicide Among Incarcerated Youth, Ruch *et al*.**

**LGBT Youth, Mental Health, and Spiritual Care: Psychiatric Collaboration With Health Care Chaplains, Adelson *et al*.**

**The Suicide Crisis in Our Detention Facilities**

 Youth suicide rates are rising in the United States and preventing suicide is an imperative for research, practice, and policy. There is no way we could overstate this imperative, or the attention *JAACAP* has and will give to these issues with no less than 11 of the articles we published in 2019 focused on suicide, covering translational neuroscience,12 epidemiology,13 prevention,14 treatment,15 and policy.16 All are these articles – with the exception of this one – focus on what is euphemistically referred to as “non-institutionalized” populations. Yet incarcerated youth are at particularly high risk of suicidal behavior, with more dying by suicide than by any other cause.17

Ruch *et al*.18 analyzed data from the National Violent Death Reporting System with supplemental information from coroner/medical examiner and law enforcement reports. This approach enabled the authors to include 213 youth ages 10-24 years who died by suicide while in custody and compare them to 9,913 of their non-institutionalized counterparts. The authors found that many of the characteristics of incarcerated and non-incarcerated youth were similar, including the presence of mental health problems. Unique characteristics of youth who died by suicide while incarcerated included that they were more likely to die by hanging and less likely to leave a suicide note. Most youth who died by suicide did so within a week of incarceration.

In addition to the population focus, what also makes this article noteworthy is the inclusion of 5 chilling case descriptions from coroner/medical examiner and law enforcement reports in the article’s supplementary materials. For example, “*Victim is a 16-year-old white boy who was found inside his jail cell hanging by a bedsheet around his neck. The victim tied a bedsheet over bars above the door. The victim had been arrested 2 days previously for assault. The victim had been placed in isolation. There was no evidence of a mental health diagnosis or treatment. The victim had never attempted or threatened suicide*.”

As Ruch *et al*. note, interventions that address both the unique circumstances for suicide among incarcerated youth as well as those that are common among all youth who died by suicide must be consistently implemented in youth and adult detention facilities, jails, and prisons. These youth deserve the best we can offer them, and research like shows us how we can do better.

**A Child Psychiatrist, Priest and Rabbi walk into a room…**

Those of us who object to “Gifted and Talented” designations in school systems on account of a belief that *all* children are gifted and talented may also object to the notion of “Special Populations” in childhood: *all* children are special. But not all children are treated the same. They do not all have the same exposures. They do not share the same risks. It is not their fault, though they may be blamed, stigmatized and further abused for these vulnerabilities in a cruel cycle of victimization. Recognizing that increased vulnerability, increased targeting, and increased psychiatric morbidity and psychosocial stress do not make children less valuable, but instead require something “more” is what makes the designation “Special” more meaningful.

In taking a look at all the clinical papers and Book Forums published throughout 2019, it is tempting to see themes. Identifying and protecting vulnerable youth in Special Populations is certainly one of them. In 2019, three letters and a Clinical Perspectives directly addressed clinicians’ concerns about current immigration policies and their effects on children and families (see for example two letters in our January issue).19,20 At a time when professionals across many disciplines are asking whether and how their views are relevant, we at least have not been silent, even if we have to continue to ask ourselves how to become more efficacious in our advocacy for children and families, especially Special Populations.

 Clinical material in the *Journal* over the past year has run the gamut from sleep and prevention to autism, violent radicalization, inpatient psychotherapy and computational modeling, and picking a “best” is always a mug’s game. There are a number of reasons why we would pick *LGBT Youth, Mental Health, and Spiritual Care: Psychiatric Collaboration With Health Care Chaplains* by Adelson, Walker-Cornetta and Kalish21 as our “Best of” 2019.

A joint authorship by a child psychiatrist, priest and rabbi, the article explores the clinical role of “critical theological reflection”, “affirming traditions”, and “adaptive spiritual possibilities” for LGBT youth. Addressing but without being shackled by the painful social and political prejudices that make LGBT youth a “Special Population”, the authors provide a pragmatic and spirited model for clinical collaboration and engagement but, most of all, describe this collaboration and engagement with a meaningful optimism. Not just hope, but a path towards hope; not just an ideal, but a way of achieving that ideal. At times like these, it can be hard to find that optimism, but Adelson, Walker-Cornetta and Kalish did just that.

**Schuyler W. Henderson**

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**Developmental Brain Changes Related to Early Exposures**

**Structural Brain Alterations in Youth with Psychosis and Bipolar Spectrum Symptoms, Jalbrzikowski *et al*.**

**Early Trauma Exposure and Neural Response Inhibition in Adolescence and Young adults: Trajectories of Frontal Theta Oscillations During a Go/NoGo Task, Meyers *et al*.**

We have selected two neuroimaging articles that are examples of some of the best published in *JAACAP* in 2019. The first article by Jalbrzikowski and colleagues, “Structural Brain Alterations in Youth with Psychosis and Bipolar Spectrum Symptoms”,22 described a study that contrasted groups using anatomic imaging and a cross-sectional design. We selected this particular article for this years “best” category for a number of reasons. First, its large sample size allows for adequate power to compare the four groups (typically developing (TD), N=376; psychosis spectrum, N=113; bipolar spectrum, N=117; bipolar with psychosis spectrum, N=109). The study design also allowed for a dimensional investigation of symptoms at earlier stages of illness and in those with subclinical symptoms who were free from the confounds of medications and chronic illness. The investigators used a community based, non-help seeking sample (ages 9-22 years). In addition, this study allowed for determining which age epoch certain neuroimaging findings emerged during development (eg, late childhood, early adolescence, late adolescence etc.). Finally, the authors found a number of brain areas that could serve as specific psychosis-spectrum biomarkers [reduced cortical surface area in orbitofrontal, posterior cingulate and pre-and post-central regions (Cohen’s *d* effect sizes compared to TD ranged from 0.2-0.4) and reduced thalamic volume (compared to the three other groups, *p* values ranged from 0.04 to 0.005)].

 This study did not replicate the reduced cortical thickness (CT) findings that have been reported in adults with schizophrenia, suggesting that CT reductions may be markers that appear after illness onset, or may be due to medication effects, neurotoxic effects, or effects of chronic illness. In addition, across all groups, the authors found that better global functioning was associated with increased surface area in the lateral orbital frontal cortex and better executive cognition and less negative symptom severity were associated with increased postcentral surface area. These findings suggest that structural brain abnormalities may reflect functioning of youth in the real world. The cortical SA and thalamic volume reductions seen here might represent very early risk biomarkers for psychosis spectrum that could aide in early identification efforts. Given these findings, future studies would benefit from longitudinal designs to help elucidate when specific brain differences emerge in youth who are at risk for serious mental illness and the extent to which these brain differences deviate from the normative neurodevelopmental trajectory.

The second article by Meyers *et al*., “Early Trauma Exposure and Neural Response Inhibition in Adolescence and Young adults: Trajectories of Frontal Theta Oscillations During a Go/NoGo Task”23 used a longitudinal design to explore the relationship between early life trauma and downstream brain development. The study was embedded within the Collaborative Study on the Genetics of Alcoholism (COGA), which is a longitudinal study of children of families with high rates of alcohol use problems and a control sample drawn from the community. The authors assessed three forms of trauma, including non-assaultive, assaultive, and sexual-assaultive experiences that occurred prior to ten years of age. The sample was drawn from 2,625 children from 2,413 families who had at least one follow-up interview. Sample size is important in a study that includes three different types of trauma with relatively low base-rates of trauma exposure: 16.6% (non-assaultive), 4.6% assaults, 6.6% sexual assaults). Sample size is also important in such studies to control for potential confounding factors, as children who have such experiences may have different baseline underlying neurobiological factors compared to those who do not experience such events. The brain-based metric consisted of EEG frontal theta wave activity obtained during a Go/NoGo task. The Go/NoGo task was selected based on prior work showing that early life stress can impact neural networks associated with cognitive and behavioral control and reward processing. Further, alterations in theta activity have been shown to be associated with early-life stress and deprivation. The authors found that those exposed to sexual assault prior to ten years of age had a decrease in the rate of change of frontal theta measures, suggesting an alteration of neurodevelopmental trajectories as a result of sexual trauma, although the study design was unable to infer causality. Further, the change in frontal theta wave measures was associated with an increase in alcohol use and internalizing symptoms. Since neurodevelopment follows non-linear trajectories, future studies within this interesting ongoing cohort will be beneficial to not only better define the differences in neurodevelopmental trajectories in those exposed to trauma, but also to tap other aspects of the cohort and derive both risk and resilient factors that influence the neurodevelopmental trajectories.

**Jean A. Frazier**

**Tonya J.H. White**

**Sex Differences in Development**

**Common Polygenic Variations for Psychiatric Disorders and Cognition in Relation to Brain Morphology in the General Pediatric Population, Alemany *et al.***

**Beyond a Binary Classification of Sex: An Examination of Brain Sex Differentiation, Psychopathology, and Genotype, Phillips *et al*.**

For another year, we found ourselves smitten with papers that used a multimethod approach to answer novel and important research questions. However, this year our picks tackle an ancient question at the level of the brain and the genome - why are boys and girls so different? Both papers we chose integrated polygenic risk scores and brain morphology to enhance our understanding of how brain and genes are associated with sex differences in psychopathology. Both address a straightforward question related to well-established sex biases in psychopathology but leverage large data sets and integrated models in unique ways. As such, they end up being “the best of” in that they challenge us to not just accept the simple answers but instead delve deeper into the increasing expanse of neuroscience and molecular genetic data to enhance our understanding of the developmental trajectories of our most common psychopathologies and how these patterns differ by sex.

The paper “Common Polygenic Variations for Psychiatric Disorders and Cognition in Relation to Brain Morphology in the General Pediatric Population” by Alemany and colleagues24 is an analysis of the large and influential Generation-R dataset in Rotterdam, The Netherlands. This particular study examined MRI and genetic data from over 1000 children at age 10. Rather than using single nucleotide polymorphisms or genome-wide association, this study used well-defined polygenic risk scores from previous studies and combined them with structural magnetic resonance imaging (MRI) data to determine the brain regions associated with the additive genetic effects tied to specific psychiatric disorders and general cognitive ability. They found that the ADHD polygenic risk score was not only associated with caudate volume, but also that caudate volume mediated the relation between genetic susceptibility and attention problems, with one important caveat. This relation was observed only in boys. On the flip side the polygenic risk scores for intelligence and educational achievement were also associated with total brain volumes, but here the effect did not differ by sex. This work adds to the growing body of literature suggesting that the prevalence differences for ADHD in boys versus girls may have neurobiological underpinnings that are not simply an artifact of the way in which ADHD is measured. Our second “best of 2019” complements these findings.

The second article, “Beyond a Binary Classification of Sex: An Examination of Brain Sex Differentiation, Psychopathology, and Genotype” by Phillips et *al*.25 also examines brain, genes, and sex differences, but tackles the question of what is and is not the same in the developing brain between boys and girls. As with our first choice, this study looks at psychological disorders that exhibit sex differences at the level of the brain and genome. However, focusing on our established knowledge of sex differences in psychopathology this study goes in the other direction, testing how sex differences in brain morphology predicted sex-biased psychopathology. Consistent with our love of the “not-so-simple”, the authors used sex as a continuous measure, rather than a binary classification and took the analyses one step further to include links to polygenic risk scores linked to these same sex-biased psychopathologies. As with the Alemany et al. study,24 in this study25 male brain morphological traits were significantly associated with externalizing, particularly disruptive, behaviors. In addition, the study found that this male-biased difference in brain regions was associated with different genes based on sex, providing a first hint at the genetic architecture underlying sexual dimorphism in the brain. The authors acknowledge the limitations of this study and note the need for additional studies and greater attention to how sex-specific brain region differentiation varies across development.

Taken together, these papers make it clear that 2019 *JAACAP* has much to offer our readership in terms of thinking about the developmental trajectory of psychopathology and the influence of sex in these pathways. We have known boys and girls are different for a long time, but how sex factors in the risk for psychopathology and the treatment implications of these differences are areas we hope to see as highlights of 2020.

**Robert R. Althoff**

**Stacy S. Drury**

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