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RECOMMENDED ACADEMIC READING

In this issue, we would like to recommend several recent psychopharmacology publications relevant to child psychiatry.

Dr. Dean Elbe recommends an article by DeVane et al. (2019). This article reports on a rarely conducted study format, a rigorous head-to-head pharmacotherapy randomized controlled trial in child psychiatry. The study examined and contrasted the beneficial and adverse effects of the two US FDA approved/established first-line treatments for irritability of autism. The study was conducted in South Carolina, and ran from 2011-2015, so the DSM-IV-TR criteria for autistic disorder was used, rather than DSM-5 autism spectrum disorder criteria. The primary outcome measure used was reduction of the Aberrant Behavior Checklist irritability (ABC-I) subscale after 10 weeks of treatment, and metabolic testing (fasting glucose, lipid panel, prolactin) was completed at baseline and at week 10. Patients were able to enroll in an open-label extension phase for an additional 12 weeks of treatment.

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Reference

DeVane, C. L., Charles, J. M., Abramson, R. K., Williams, J. E., Carpenter, L. A., Raven, S., ... & Bragg Jr., J. E. (2019). Pharmacotherapy of Autism Spectrum Disorder: Results from the Randomized BAART Clinical Trial. *Pharmacotherapy, 39*(6): 626-635. doi: 10.1002/phar.2271.

https://pubmed.ncbi.nlm.nih.gov/31063671/

Dr. Dean Elbe recommends a pair of phase III registration randomized controlled trials (RCTs) of vilazodone, a serotonin partial agonist reuptake inhibitor (SPARI) as a possible treatment for major depressive disorder in adolescents. Durgam et al. (2018) examined fixed-dose vilazodone vs. placebo in adolescents while Findling et al. (2020) looked at flexibly-dosed vilazodone vs. placebo with fluoxetine as an active comparator in both children and adolescents, and also included a 26-week open label extension. Consistent with large phase III trial designs, the methodology used was relatively straightforward, with change in Children's Depression Rating Scale-Revised (CDRS-R) score as the primary outcome measure. Did high placebo response rates as seen in other multi-center pediatric depression trials overwhelm the ability of vilazodone to show a difference compared to placebo? Did even the active comparator and *de facto* first-choice medication fluoxetine separate itself from placebo? No matter the outcome, via completion of these RCTs, the manufacturer achieved a 6-month US Food and Drug Administration (FDA) pediatric extension to vilazodone patent protection.

References

Durgam, S. Chen, C., Migliore, R., Prakash, C., Edwards, J., & Findling, R. L. (2020). A Phase 3, Double-Blind, Randomized, Placebo-Controlled Study of Vilazodone in Adolescents with Major Depressive Disorder. *Pediatric Drugs, 20*(4), 353-363. doi: 10.1007/s40272-018-0290-4

https://pubmed.ncbi.nlm.nih.gov/29633166/

and

Findling, R. L., McCusker, E., & Strawn, J. R. A. (2020). A Randomized, Double-Blind, Placebo-Controlled Trial of Vilazodone in Children and Adolescents with Major Depressive Disorder with Twenty-Six-Week Open-Label Follow-Up. *Journal of Child and Adolescent Psychopharmacology, 30*(6), 355-365. doi: 10.1089/cap.2019.0176

https://pubmed.ncbi.nlm.nih.gov/32460523/

Dr. Daniel Gorman recommends a recent publication in the ADHD field. Arguably the most important clinical trial in the history of child psychiatry, The Multimodal Treatment Study of Attention-Deficit/Hyperactivity Disorder (MTA) has had a profound influence on management of this common condition. For ADHD nerds, however, the MTA is also a riveting Netflix series, with new instalments released every couple of years. After the initial 14-month randomized phase, naturalistic assessments were performed at 2, 3, 6, 8, 10, 12, 14, and 16 years after baseline. An intriguing storyline has been the effect of stimulant treatment on growth. Data at 3 years after baseline, when the children were 10-12.9 years old, suggested that stimulants reduced height by 2 cm on average. The cliffhanger, though, was the implication of this finding for final height. The thrilling denouement is finally revealed in an article by Greenhill et al. (2020). There's even a plot twist involving stimulant effects on weight!

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Reference

Greenhill, L. L., Swanson, J. M., Hechtman, L., Waxmonsky, J., Arnold, L. E., Molina, B. S. G., … & MTA Cooperative Group. (2020). Trajectories of growth associated with long-term stimulant medication in the Multimodal Treatment Study of Attention-Deficit/Hyperactivity Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 59*(8):978-989. doi: 10.1016/j.jaac.2019.06.019

https://pubmed.ncbi.nlm.nih.gov/31421233/

Dr. Tamara Pringsheim recommends a clinical trial published in the Journal of Intellectual Disability Research. Ramerman and colleagues (2019) performed a placebo-controlled, randomized, double-blind discontinuation trial of risperidone for challenging behaviours in children and adults with intellectual disabilities (IQ<70) after 1 year or longer use. In this trial of 25 participants, continued use of risperidone at the same maintenance dose was compared with gradual discontinuation to placebo over six months. The primary outcome measure of the study was the irritability subscale of the Aberrant Behaviour Checklist. Important secondary outcomes included weight, body mass index, waist circumference, laboratory testing of metabolic markers and prolactin, extrapyramidal symptoms and renewed use of antipsychotic drugs within 18 weeks of de-blinding. While this trial had a small sample size and a mixed population of children and adults, it provides important information on the benefits and risks of risperidone discontinuation for behavioural problems associated with intellectual disability.

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Reference

Ramerman, L., de Kuijper, G., Scheers, T., Vink, M., Vrijmoeth, P., & Hoekstra, P. J. (2019). Is risperidone effective in reducing challenging behaviours in individuals with intellectual disabilities after 1 year or longer use? A placebo-controlled, randomised, double-blind discontinuation study. *Journal of Intellectual Disability Research, 63*(5), 418-428. doi: 10.1111/jir.12584.

https://pubmed.ncbi.nlm.nih.gov/30609152/