RECOMMENDED ACADEMIC READING (RAR)

A focus on adult depression

In this issue, RAR focuses on recent important findings from studies of adult depression that may have relevance to work in child and adolescent depression. Thanks to our mood disorder experts from adult psychiatry in identifying and describing some of the publication highlights.

Dr. Valerie Taylor’s recommended reading is an article by Chin Fatt et al. (1). This article provides further support for what the authors describe as “the potential of the microbiome for precision medicine approaches in psychiatry.” This study applied advanced bioinformatics tools to perform unique analysis of a clinical sample of 179 participants with major depressive disorder in the Texas Resilience Against Depression (T-RAD) study. This study recruited participants 10 years of age and older, and while this particular analysis was of the adult cohort, there are interesting observations that may impact all ages. Using sophisticated data driven approaches, this study identified bacterial taxa that were associated with depression and anxiety, as documented using validated self-report scales. Based on the results, the authors propose that reduced abundance of butyrate producing taxa and increased abundance of inflammatory-related taxa may drive increased anxiety and depressive symptoms in depression. I think this paper is interesting as it provides a critical step toward understanding the association between the microbiome and depression, and how a community-driven approach may facilitate effective precision medicine to improve clinical outcomes. This could help in the development of novel treatment approaches for mental illness.

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References

“Can I stop my antidepressants now?”

Patients often ask that question after feeling better. Studies have looked at relapse for people with depression who go off their medications, of course, but overwhelmingly such work has focused on patients recruited from specialty care (who are, perhaps, more ill).

That’s why Dr. David Gratzer’s recommended reading is Lewis et al. from The New England Journal of Medicine (1). This study on antidepressant discontinuation is well designed and thoughtful, adding nicely to the literature. A quick summary of the methodology: 606 adult patients from family practices in the United Kingdom, who had a history of major depressive disorder but “felt well enough to consider stopping antidepressants…”, were randomized to continue the antidepressant treatment or be tapered off but given placebo. What did they find? “Relapse of depression occurred in 92 of 238 patients (39%) in the maintenance group and in 135 of 240 (56%) in the discontinuation group during the 52 weeks of the trial (hazard ratio, 2.06 [95% confidence interval: 1.56-2.70, p<0.001]).” (p.1261)(1). In fact, 39% of the patients in the discontinuation group restarted antidepressants.

This paper shows the challenges faced by patients who stop their medications even if in a good place with their illness. But two cheers for antidepressants: people did better by continuing medications, yes, but many patients relapsed on antidepressants. Clinical take-away: patients need to be monitored carefully even if they are taking their medication.

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References


Dr. Raymond Lam’s recommended reading is an article by Jefsen and colleagues, published in JAMA Psychiatry in May, 2023 (1). This study utilized a cohort (n = 6.65 million) from the Danish nationwide registry of individuals born in Denmark before 2005 and who were alive and at least 16 years old between 1995 and 2021. The authors examined the association between a registry-based diagnosis of cannabis use disorder (CUD) and risk of subsequent unipolar major depressive disorder (MDD) and bipolar disorder (BD). CUD was associated with increased risk of both unipolar MDD and BD, for both psychotic and non-psychotic subtypes of these conditions. I found this study to be important because there are only limited data about the relationship of CUD with mood disorders, especially non-psychotic subtypes. Another interesting finding was that the risk was higher for psychotic BD than non-psychotic BD.

In tandem with results from other studies (2) with similar methods reporting higher risk estimates for developing schizophrenia compared to BD, this suggests that effects of cannabis are primarily psychotogenic in nature. The study had several strengths. It was a representative sampling of individuals born in Denmark before 2005 and who were alive and at least 16 years old between 1995 and 2021. The authors examined the association between a registry-based diagnosis of cannabis use disorder (CUD) and risk of subsequent unipolar major depressive disorder (MDD) and bipolar disorder (BD). CUD was associated with increased risk of both unipolar MDD and BD, for both psychotic and non-psychotic subtypes of these conditions. I found this study to be important because there are only limited data about the relationship of CUD with mood disorders, especially non-psychotic subtypes. Another interesting finding was that the risk was higher for psychotic BD than non-psychotic BD.

Dr. Alexander McGirr’s recommended reading is an article by Cole et al published in *The American Journal of Psychiatry* in February 2022 (1). This randomized, double-blind, sham-controlled study built on previous open-label data utilizing a novel transcranial magnetic stimulation protocol for treatment resistant major depressive disorder in adults. This protocol, known by the acronym SNT (Stanford Neuromodulation Therapy), has been granted Breakthrough Device Designation by the US FDA based in part on the data presented in this article. The SNT protocol cleverly combines two important factors in transcranial magnetic stimulation treatment for depression to accelerate or condense what is typically a six week treatment into five days: 1) precision medicine targeting using functional magnetic resonance imaging, and 2) harnessing fundamental principles of synaptic plasticity. The precision medicine approach builds on data suggesting that the optimal stimulation target within the dorsolateral prefrontal cortex is functionally anti-correlated to activity in the anterior cingulate cortex. Then, informed by spaced learning theory and repeated spaced long-term potentiation experiments, they deliver 10 daily treatments separated by an hour to this target, which is important because that leaves sufficient time for protein transcription to occur and adaptation to the stimulation to stabilize. This sham controlled RCT was prematurely terminated after a midpoint interim analysis with only 29 participants showed very robust separation and superiority of active-SNT over sham-SNT, with high rates of response (71.4% active versus 13.3% sham) and remission (57.1% active versus 0% sham) after the conclusion of treatment. Moreover, these benefits were sustained four weeks after completing treatment with 69.2% response and 46.2% remission in the active-SNT group.

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