Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Applying (or Not?) CAR-T Neurotoxicity Experience to COVID-19 Delirium and Agitation

TO THE EDITOR: The natural history of severe COVID-19 has been likened to that of a cytokine release syndrome (CRS), leading some to ask whether or not countering excess cytokine release would be therapeutic generally.[1] At the same time, anecdotal reports have indicated that the confusion, agitation, or delirium in COVID-19 has been idiosyncratic or difficult to treat, despite the importance of continuing to address delirium and other neuropsychiatric symptoms in these patients.[2] With most experience about CRS arising from the care and outcomes of CAR-T immune therapy for cancers, this constellation of facts might suggest that the lessons learned from CAR-T neurotoxicity can be applied to the care of the COVID-19 patient. However, this application should be done with caution with regard to the neuropsychiatric aspects of COVID-19.

First, an appropriate degree of caution is needed because the pathophysiology of CAR-T neurotoxicity remains unclear. At the present time, it is unclear whether neurotoxic symptoms occur as a direct effect of CAR-T cells on the central nervous system (termed immune effector cell–associated neurotoxicity syndrome [ICANS]) or as a systematic CRS.[3] For example, multiple studies have supported the finding that patients receiving CAR-T who developed early CRS were more likely to develop neurotoxicity and severe neurotoxicity.[4,5] However, the specific role of cytokines in CAR-T neurotoxicity is not precisely understood at the present time.

In addition, there is evidence that the application of therapies for CRS to the overall medical approach to COVID-19 may be problematic. There is interest in care that includes blockade of cytokines and the human inflammatory response, possibly with tocilizumab, an interleukin-6 receptor antagonist which was approved by the US Food and Drug Administration (FDA) for the treatment of CAR-T cell–induced CRS.[1,6] However, there are questions as to whether tocilizumab actually penetrates the blood-brain barrier. A further complication is that there is indication that use of tocilizumab tended to worsen depression, anxiety, pain, and sleep when given to adult patients who received CAR-T.[7]

The growth of interest in the immunologic aspects of psychiatric illness and therapeutics has been welcome within psychiatry. In this context, it is important that workers around the nation have been considering the similarities between the CAR-T CRS and COVID-19. Indeed, there is every reason to prepare for short-term and long-term neuropsychiatric effects of the novel coronavirus (one should not forget the acute and chronic effects of *Encephalitis lethargica* that arose after the influenza pandemic of 1918–19).[8] However, until we clearly understand the actual interaction of inflammatory molecules on the brain in CAR-T and other CRS-inducing conditions (which we continue to study in our institution), it will be important to pursue immune-based explanations of pathophysiology and therapies with caution and by utilizing the widest range of medical literature.

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Importance of Heterogeneity in Bariatric Surgery Candidates—Comment on: Psychiatric Medication Use and Weight Outcomes 1 Year After Bariatric Surgery

TO THE EDITOR: The impact of psychiatric disorders on outcomes in candidates for bariatric surgery are often underestimated and rather neglected.[1] Nevertheless, the link between psychiatric health and surgical outcomes has increasingly been demonstrated after a variety of surgical procedures.[2] Therefore, we read the article by Hawkins et al.[3] entitled "Psychiatric Medication Use and Weight Outcomes One Year After Bariatric Surgery" with great interest. In this article, the authors investigated the influence of psychotropic medication use on weight loss after Roux-en-Y gastric bypass surgery. No significant effects of psychotropic medication on weight loss were observed, except for an increased weight loss in patients treated with serotonin-norepinephrine reuptake inhibitors in the secondary analysis.

Notably, in April 2019, we already published our observations concerning the effects of antidepressants and psychotropic drugs on outcomes up to 24 months after bariatric surgery.[4] In this study, which included 751 patients, we observed a significant effect (−5.52 percent excess body mass index loss [%EBMIL]) of antidepressants, which was largely caused by tricyclic antidepressants (−11.01 %EBMIL) and serotonin-norepinephrine reuptake inhibitors (−12.47 %EBMIL). Clearly, our results are conflicting with those reported by Hawkins et al.[3] Guided by our own experiences with this topic, we would like to further comment on the issues inherent to studying outcomes in bariatric surgery, especially when determining the influence of psychotropic medications and how these should be taken into consideration when interpreting such results.

Bariatric surgery candidates are very diverse and frequently have different reasons and motivations for seeking surgical assistance. Some patients, for example, suffer from obesity-related comorbidities, while others undergo the procedure to prevent medical complications. Many patients also hope to improve their mental health and self-esteem. Moreover, the etiology of obesity also significantly differs between patients. Add the large number of variables after the procedure, such as dietary compliance, physical activity, medication use, and so on. to the picture, and studying this heterogeneous population becomes a worrisome challenge. This is not different when investigating the outcomes in patients treated with psychotropic medications, who frequently receive combination therapy together with other classes of drugs such as antipsychotics, have variable therapy compliance, and postoperatively often require therapy modifications such as therapy cessation.

Taking the important heterogeneity in this population into account, in our view, a multivariate approach should be adopted when examining the effects of psychotropic drugs on bariatric surgery