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EDITORIAL

The importance of assessing personality traits and disorders in clinical trials of major depressive disorder

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The heterogeneity of depression itself is often cited as a challenge when designing randomized controlled trials (RCTs) of novel interventions for patients with major depressive disorder (MDD) who do not respond to currently available treatments. Patient characteristics such as illness duration, symptom severity, concurrent substance use, comorbidity (both psychiatric and physical) and socioeconomic factors can all influence treatment outcomes. Personality traits and disorders may also influence treatment response in MDD.

Personality may be dimensionally assessed. For example, the Five Factor Model provides an influential approach.[1] Personality traits could contribute to an individual's susceptibility to developing MDD, and a combination of high neuroticism, low extraversion and low conscientiousness has been associated with a higher risk of MDD.[2] In addition, these personality factors can influence treatment response, and it may be important to consider personality assessment when developing treatment plans for individual patients. For instance, a recent study that compared the treatment response of subgroups with different Five Factor Model personality trait patterns found that depressed patients with high neuroticism and low extraversion were more responsive to specialized treatment than primary care interventions.[3]

While the Five Factor Model is a dimensional model of general personality structure, personality disorders (PDs) are characterized by persistent maladaptive variants of the Five Factor Model personality traits and are diagnosed using either DSM or ICD criteria. PDs commonly coexist with MDD; studies conducted in outpatient settings have estimated that 51.3% have a comorbid PD and MDD.[4] A meta-analysis has shown that a diagnosis of PD is associated with a lower likelihood of response to pharmacological and psychological treatments for MDD.[5] This might not be surprising, since personality factors can influence treatment adherence and therapeutic alliance with treating clinicians. Furthermore, patients with comorbid PD and MDD may have a more severe course of illness and, hence, prove more refractory to treatment. Interestingly, recent studies have contradicted this finding to some extent: a trial of electroconvulsive therapy in patients with MDD and comorbid borderline PD found no difference in treatment response in this patient group.[6] Similarly, in a recent trial of cognitive behavior therapy and interpersonal therapy in patients with MDD and comorbid PD, the presence of a PD had no meaningful impact on treatment response or treatment retention in either modality.[7]

Given the high prevalence of comorbid PD and MDD and the conflicting evidence on whether this contributes to treatment resistance, we propose that a structured assessment of personality traits and disorders could be incorporated in RCTs of interventions for MDD. The study by Kavanagh et al.[8] in the current issue was designed to provide such information. This study presents a post-hoc analysis of the association between PD diagnosis and treatment response in a RCT of the anti-inflammatory tetracycline antibiotic minocycline as an augmenting agent in MDD. The trial included a validated screening tool for assessing PD in all participants, the Standardized Assessment of Personality – Abbreviated Scale, which was administered at week 4 (to decrease participant burden at the baseline interview). This scale is a validated eight-item screening measure used to assess the presence of PDs. Although it is more of a screening tool for PD than a structured diagnostic interview, the authors argue that this scale has shown validity and utility in clinical populations, including patients with MDD. Of note, the authors found a high prevalence of PD (69%) in the recruited sample but found no significant differences in clinical outcomes (Montgomery-Åsberg Depression Rating Scale scores) or functional outcomes between patients with MDD plus PD who were treated with minocycline and patients without PD who were treated with minocycline.

In summary, current evidence regarding the effects of co-occurring PDs on treatment response in MDD remains limited, and the majority of published RCTs have not presented data on this relevant aspect. Although Kavanagh et al.[8] have added to the current evidence base, we suggest that future RCTs of emerging treatments in MDD include a robust assessment of PD in the form of structured diagnostic interviews. In addition, the design of large multicenter RCTs could further elucidate the role of co-occurring personality traits and disorders in MDD treatment outcomes. Moreover, the statistical analysis plan of RCTs should include an analysis to determine the

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moderating and mediating effects of this highly prevalent comorbidity. Such data will determine the ''real world'' applicability of any novel intervention under investigation and improve our understanding of important patient factors that predict response to a variety of treatments for depression. Machine learning algorithms could also be instrumental in elucidating the role of personality traits and disorders in predicting treatment outcomes in MDD. Finally, Kavanagh et al. should be commended for their highly relevant research. Their study provides a rationale for further large-scale trials, which could influence available treatment guidelines for MDD and provide personalized treatment for MDD within the framework of precision psychiatry.

Disclosure

The authors report no conflicts of interest.

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