Interest-Activity Dimension and Response to Aripiprazole

To the Editor: A recent study published in JCP by Uher et al[1] presented an important finding of clinical relevance. Although the interest-activity dimension is known as an important predictor of treatment response in major depressive disorder, the report provided the first evidence for its utility as a measure of response to aripiprazole.

The authors thoroughly examined various aspects to establish their findings, but some issues require further attention. Calculation of an interest-activity symptom score using the sum of 6 items is one such issue. Usually, for formulating a composite index, using a weighted sum is preferred and is a statistically more valid approach.[2] In the process of summing items from 2 different scales, there is always a possibility of overrepresentation of a certain variable. Furthermore, the authors could have run a sensitivity analysis by using interest activity scores from individual scales (Montgomery-Asberg Depression Rating Scale and Quick Inventory for Depressive Symptomatology, Self-Report). This, in addition to substantiating their finding, would also have provided insight about which method (self-rated vs clinician rated) better predicts response and should be preferred in clinical settings.

In addition, some clinical variables were not compared between the groups, such as number of prior episodes, number of trials of medication, personality, and plasma level of escitalopram, which could have influenced the results. Although patients with psychotic symptoms were excluded, those with a history of psychotic symptoms are not mentioned. Such patients may respond poorly to an antidepressant trial. Details regarding patients with stable medical conditions such as hypothyroidism, which may affect treatment response and persistence of symptoms, are also missing. It would also have been interesting to know of any association with suicidality, considering the public health importance. If patients with suicidality respond with introduction of aripiprazole, this would strongly favor its early introduction in treatment. Inclusion of partial responders also could have provided a better interpretation of the results as to which group actually benefits, nonresponders or partial responders. Inclusion of patients with up to 3 adequate trials of antidepressants (a deviation from clinical trial registry, which exclude those with 3 trials[3]) suggests that some of the patients can be classified as having "resistant depression." This information could provide some insight regarding differential response.

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Dr Uher and Colleagues Reply

To the Editor: We thank Drs Swami and Mishra for the opportunity to clarify some points about using the interest-activity symptom dimension to personalize treatment for major depressive disorder. Their letter raises several issues on how the interest-activity scale is constructed and used.

First comes the question of whether it is appropriate to use a simple sum of the interest-activity items rather than a more complex and sophisticated method that gives specific weight to each item. Our choice of the simple sum of items method in the Canadian Biomarker Integration Network in Depression trial (CAN-BIND)[1] was based on experience from previous work in the Genome-based Therapeutic Drugs for Depression (GENDEP) and Sequenced Treatment Alternatives to Relieve Depression (STAR*D) studies.[2] The interest-activity was originally derived in GENDEP from 3 depression rating scales using scoring based on item response theory, which estimates weights and thresholds separately for each item and each response option according to a psychometric model.[2] However, when we constructed an alternative interest-activity score as a simple sum of items, it correlated almost perfectly (Pearson product-moment correlation = 0.97) with the score derived using the much more complex method. The STAR*D study used 2 different depression rating scales. The STAR*D interest-activity score was constructed using a simple sum of items with equivalent content, and it predicted outcomes of treatment with undiminished effect size. CAN-BIND applied 2 depression rating scales, of which one was previously used in GENDEP and one in STAR*D. Therefore, prior weights were available for only one of the scales. Given prior experience, we believe that the ease of application of the summed score method outweighs uncertain advantages of more complex scoring procedures with item-specific weights.

The second point that we would like to address concerns the joint use of items from a self-report questionnaire and a clinician-rated scale. Previous work demonstrated that self-report and clinician rating each provide unique information predictive of antidepressant treatment outcome.[3] This is also true of interest-activity symptoms. Self-report and clinician rating contribute evenly to the prediction but are not mutually replaceable. Researchers who plan to replicate or extend our findings and clinicians who wish to use interest-activity symptoms to aid decision making in practice should use a combination of self-report and clinician rating to achieve optimal results. The CAN-BIND publication demonstrates that 3 self-report questions and 3 clinician-rated items are sufficient to obtain meaningful prediction. Together with simple sum rating, this makes interest-activity measures unobtrusive and easy to apply.

Additional points raised by Drs Swami and Mishra include suggestions for other factors that may also be predictive of treatment outcomes. Our published article reports hypothesis-driven analyses focused on the interest-activity dimension.[1] CAN-BIND has collected a wealth of information, and ongoing work uses multivariate methods that consider interest-activity alongside multiple other factors.[4] The results of these analyses, to be reported in the near future, will answer most of these important questions.

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