Reviewer’s report

Title: Relationships Among Neurocognition, Symptoms and Functioning in Patients with Schizophrenia: A Path-Analytic Approach for Associations at Baseline and Following 24 Weeks of Antipsychotic Drug Therapy

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Reviewer: Michael Minzenberg

Reviewer’s report:

The paper by Lipkovich et al describes an analysis of the relationships between cognition, symptoms, and functioning in a large sample of stable chronic schizophrenia patients during the course of a randomized, one-year antipsychotic medication trial. They found that at baseline, “processing speed” predicted function via negative symptoms, and that at 24 weeks, changes in processing speed were related to changes in function both directly and indirectly through changes in negative symptoms. Working and verbal memory did not contribute significantly to these path models, and positive symptoms contributed to function only at baseline.

This is a well-designed study that adds to an important literature addressing the relationships of cognition and symptoms to functional outcome. I have only a few concerns and queries about the study. All are discretionary in nature.

1. Because this is a medication treatment study, can the 3 treatment groups be added to the models, or somehow otherwise considered as a factor in these relationships? It would be quite interesting to know if these relationships varied by treatment.

2. Digit-symbol and verbal fluency are both complex tasks that draw on a variety of discrete cognitive processes, and this is obscured by grouping them together simply as measures of “processing speed.” How do these 2 measures perform when considered separately in the models?

3. Can some measurement properties (e.g. internal and test-retest reliability) be provided for the function measure, since the hypotheses are so dependent on them?

4. It would be helpful and interesting to know what those change scores were, for symptoms, cognition and function, both to get a feel for the treatment response, and to consider if there were some restricted change scores that may limit the power of the models.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.