Reviewer's report

Title: Clinical symptoms and performance on the continuous performance test in children with attention deficit hyperactivity disorder between subtypes: a natural follow-up study for 6 months

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Reviewer: Yehuda Pollak

Reviewer’s report:

The paper describes a longitudinal study of the effect of MPH on clinical symptoms of ADHD and CPT parameters. The paper has several merits including important clinical topic, being longitudinal, use of valid clinical measures, adequate statistical analysis, acceptable writing.

There are, however, some shortcomings which need to be addressed:

Discretionary Recision:

1. One of the main aims of the study was to compare the outcomes of hyperactive (H+) and non-hyperactive (H-) children, as well as aggressive (A+) and non-aggressive (A-) children. The authors conclude that A+/A- subtyping better predicts outcome.

Some problems arise with the methodology by which the authors came to this conclusion.

i. According to both the literature and the data of the current study, aggression and hyperactivity correlate. For example, the factor analysis conducted in this study revealed that opposition and hyperactivity are loaded on the same factor. From a clinical standpoint, despite the overlapping between aggression and hyperactivity, it might be important to know that aggression predicts outcome better than hyperactivity. Nevertheless, from a theoretical standpoint, it is important to control for the overlapping, e.g., by covariating hyperactivity level in the analysis of the effect of aggression.

ii. Surprisingly, baseline differences in clinical hyperactivity between H+/H- is smaller than between A+/A- (see fig. 1B and fig. 2F). I suggest 2 explanations for this: a. Aggression and hyperactivity overlap drastically and in this study aggression provides an extreme operationalization of hyperactivity. Such an explanation hinders the attempt to distinguish between hyperactivity and aggression in prediction MPH outcome. b. The clinical hyperactivity factor includes the opposition subscale of the SNAP-IV. As opposition involves aggression, inclusion of opposition to the factor inflates differences between A+ and A- groups on clinical hyperactivity. Note that clinical hyperactivity was higher across all visits in both H+ compared to H- and A+ compared to A-, but reached statistical significance only in A+ compared to A-. This might be a direct consequence of the inflated differences between aggression groups in clinical hyperactivity. I suggest to repeat the factor analysis without the SNAP-IV.
opposition.

iii. Most importantly, the conclusion regarding the superiority of aggression over hyperactivity is based on the finding that no differences between H+ and H- in clinical and cognitive factor were found, whereas clinical hyperactivity and CPT factors were higher in A+ compared to A-. Along the methods and results sections, the authors report interactions between factors and subtypes. Probably, what they actually mean are interactions between visits and subtypes. Note that on the clinical hyperactivity factor, a main effect of aggression, but no interaction between visits and aggression, was found. Presumably, MPH diminished clinical hyperactivity in both groups in a similar rate, resulting in preservation of baseline differences between aggression groups in hyperactivity level. Therefore, the conclusion of differential effect of MPH on A+ and A- groups is not supported and should be eliminated from the abstract and the discussion.

2. Despite the importance of aggression to the clinical picture of ADHD and the emphasis that was put on this variable as a potential predictor of outcome, the authors did not provide an outcome measure of aggression. This might be overcome by analysis of the opposition measure of the SNAP-IV as an outcome measure.

3. Minor revisions:
   i. The authors may want to provide the number of the H+A+, H+A-, H-A+ and H-A- groups, separately.
   ii. A power analysis justifying the expected effect sizes and the size of N is advisable.
   iii. The CPT first factor is sometimes called "CPT inattention" and sometimes "CPT distraction". Uniformity may make the reading easier.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests