Author's response to reviews

Title: Testing assumptions for endophenotype studies in ADHD: Reliability and validity of tasks in a general population sample

Authors:

Jonna Kuntsi (j.kuntsi@iop.kcl.ac.uk)
Penny Andreou (p.andreou@iop.kcl.ac.uk)
Jonathan Ma (spigjma@iop.kcl.ac.uk)
Norbert A Borger (n.a.borger@rug.nl)
Jaap J van der Meere (j.j.van.der.meere@rug.nl)

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Dear BioMed Central Editorial Team

Re: ‘Testing assumptions for endophenotype studies in ADHD: Reliability and validity of tasks in a general population sample’

Thank you for forwarding us the reviewers’ comments on our manuscript. We wish to thank both reviewers for their helpful comments, which we have considered carefully and have revised the manuscript accordingly. Please find below a detailed description of the changes that we have made and our response to each of the queries.

Thank you for considering our manuscript for publication, and we look forward to hearing from you in due course.

Yours sincerely

Jonna Kuntsi PhD
Reviewer: Jeffrey N Epstein

Major compulsory revisions:

1. As requested, we have deleted the analyses that do not directly pertain to the stated study hypotheses: the test-retest inter-class correlations for the WISC data (p.11 and p.15, first version) and the association between IQ scores and ADHD ratings (p.14 and p.16, first version).

2. The reviewer correctly points out that Leth-Steensen et al. (2000) used ex-Gaussian indicators, in addition to mean reaction time (RT) and standard deviation (RT SD), as response variables. However, only RT, RT SD and one of the three ex-Gaussian variables (‘tau’, the degree of positive skew) discriminated between the ADHD and age-matched control groups. Leth-Steensen et al. (2000) found that “(a) both the measures of [tau] and the standard deviations are highly (and equivalently) diagnostic of ADHD, (b) the mean response times are also quite diagnostic of ADHD…, and (c) the measures of both [mu] and [sigma] have very low diagnostic value” (p.183). Given these findings – that RT SD was equivalent to ‘tau’ in its ability to discriminate between the groups and that the other two ex-Gaussian variables were not sensitive to ADHD – the justification for including the ex-Gaussian variables in the analyses is not clear. Recent analyses by Klein et al. (under review) also indicate that whereas RT SD distinguished very well between ADHD and control groups, measures of distributional shape contributed little to group separation. However, if the Editor would like us to include further variables, such as ‘tau’, in our analyses, we are happy to do this once we have discussed the issue in more detail with a statistician.

The two go/no-go task variables that had been transformed were the percentage of false alarms in the incentive condition at time 1 and RT SD in the slow condition at time 2. We now report the results for the untransformed variables (with only slight changes to results) and have revised the manuscript accordingly.

Minor essential revisions:

1. We can confirm that the go/go-no task was not presented in blocks nor were the data analysed in blocks. However, there were three conditions in this task; this is described on p.8 (revised version), including details such as number of trials in each condition.

2. We thank the reviewer for pointing out the sentence that did not read well. We have revised the sentence to clarify that intra-class correlations are recommended only for intra-rater and inter-rater reliability, and not for test-retest reliability (p.10, revised version).

3. We have revised the use of the term ‘improvement’ in the Results section, to clarify that we mean here improvement from a baseline condition to a condition with task manipulations. We now refer to “improved performance
(p<.01) following task manipulations (fast event rate and/or incentives)” (p.11, revised version) and “the extent of improvement from the slow baseline condition to a condition with a faster event rate or incentives (or both)” (p.12, revised version).

Discretionary revisions:

1. We accept the reviewer’s point that the tables present rather a lot of statistical tests. However, our preference would be not to exclude the partial correlations. As we write on p.12 (revised version), the partial correlations are of special interest, given that the main focus is on effects that are independent of age. Presenting both simple and partial correlations enables an easy visualisation of age effects (or lack of such effects) and also enables a direct comparison with data reported previously (eg Kuntsi et al., 2001).

2. We have added a clarification to Discussion (p.17, revised version) that effects of individual manipulations may be open to multiple interpretations. However, we also note that the overall pattern of findings obtained in the present study, including the association between the effects of the two types of manipulations in the go/no-go task, seems most parsimonious with the model of arousal and activation regulation. It is not clear how other models (including the dual pathway hypothesis, which includes a revised delay aversion hypothesis) could account for the combined set of findings. The inhibition deficit and working memory deficit hypotheses are discussed in relation to the data. The Discussion also includes a comment that the possible relationships between different current models need to be investigated in more detail; explicit predictions for task performance following specific task manipulations are as yet lacking for some of the models.

Reviewer: Andreas J Fallgatter

1. Abstract: results and conclusions

These sections have been revised, following the reviewer’s suggestions. Precise range of values are now reported for the correlations and the results section of the abstract includes an additional description of the findings, to help further clarify the sentence in the conclusions section of the abstract that refers to the effects of event rate and incentives. The relevant sentence in the conclusions section has also been revised.

The size of the correlations has also been added to p.13 (revised version).

2. Introduction

The sequence of the tasks was not balanced due to practical considerations. We chose a specific fixed order of task presentation so as to minimise task fatigue and maximise the children’s motivation to complete the tasks throughout the session. For example, the two computer-based tasks were separated and WISC subtests were presented in between these two tasks.
3. Results

The sentence beginning “Rousson et al…” has been revised (see ‘Minor essential revisions’, point 2 of first reviewer’s comments above).

We have added the following sentence to p.12 (revised version): “The model of arousal and activation regulation predicts an association between ADHD symptoms and poor performance in a baseline condition, but lack of (or reduced) association with performance in conditions with such task manipulations.”

4. Discussion

From our testing experience we know that the children found the tasks less interesting during the second testing session (‘retest’), as the novelty had worn off. For this reason we suggest that fatigue during the last tasks of the second testing session may have contributed to the lower reliability coefficient for the reaction time variability in the incentive condition of the go/no-go task. We have added a clarification on this to p.15 (revised version). Importantly, we start the discussion on this by stating that “The reason for this is not clear…” (p.15); we are therefore cautious in our interpretation.

We thank the reviewer for the details of the two papers. The Fallgatter et al. (2002) paper reports excellent long-term reliability for electrophysiological measures, indicating, as the reviewer points out, that higher reliabilities may be obtained for electrophysiological than cognitive measures; this will be especially useful for our planned future ERP work. We have unfortunately been unable to obtain a copy of the Nichols and Waschbusch (2004) paper within this timeframe.

References

