Author's response to reviews

Title: Long-term effects of stimulants on neurocognitive performance in Taiwanese children with attention-deficit/hyperactivity disorder

Authors:

Ching-Shu Tsai (jingshutsai@yahoo.com.tw)
Yu-Shu Huang (hu1109s@yahoo.com.tw)
Chen-Long Wu (wu@adm.cgmh.org.tw)
Ming-Horng Tsai (mingmin.tw@yahoo.com.tw)
Shih-Ming Chu (kz6479@adm.cgmh.org.tw)
Fang-Ming Hwang (hwang@yahoo.com.tw)
Kin-Bao Young (young@yahoo.com.tw)

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Author's response to reviews: see over
A cover letter

Reviewer: Margaret H Sibley

Major Revisions:

1. English is not fluent in this report. Many vocabulary and grammatical errors, sometimes preventing the ability to understand the authors' points.
Reply: Thanks for reviewer remind. We will ask expert to edit this manuscript.

1. Significant limitations are not mentioned:
Not a controlled study- inability to rule out practice effects and effects of time should be mentioned.
Reply: We will add the limitation in the paragraph of discussion. The study actually is not a randomized controlled trial and the practice effect is not diminished to be ignored. The two, we would mention in discussion. But we still tried to lessen the influence of practice effect. Such as the interval of two times of WISC test was at least one year to reduce the practice effect which was stand on the report of Manual for the Wechsler intelligence scale for children and Tang’s discourse (reference 40). And we compare the two groups of ADHD children with and without MPH treatment to exclude the possible impact of practice effect of re-test.

1. Why didn't some of the kids take MPH? this was not clear, but it does not seem like this was random assignment.
Reply: Due to the different culture, there is only 5% ADHD that would like to receive medicine treatment in Taiwan. The participants in this study were from the outpatient clinics of medical center in north Taiwan. If patients met the inclusion criteria, they and their parents will be invited to participate in this long term following study. But some parents of ADHD children reject drug treatment, including MPH. So we follow these children as another ADHD group.

1. The non-MPH data should be talked about as exploratory.
Reply: We have tried to discuss the non-MPH data in two sections of results, including difference within ADHD children who received stimulant drugs and who didn’t and the changes of neurocognitive function in ADHD children with/without MPH treatment at the end of one year.

1. May not actually improve construct of IQ as much as it just improves accuracy on the test due to improved attention. This is probably the most likely explanation, but not mentioned by authors.
Reply: Thanks for reviewer’s comment, we will add the explanation “May not actually improve construct of IQ as much as it just improves accuracy on the test due to improved attention” in the manuscript. We tried to investigate the association between the increment of IQ and the improvement of ADHD symptoms. No significant correlation was found (table 5). So the hypothesis that improving attention would secondarily improve Intelligence Quotient scores was not supported in our study.
Reviewer: Augusto Pasini

Some point need to be addressed in the method section:

1. Information about screening for learning disorders (LD) and history of language disorders. These disorders, especially LD often associated with ADHD, can influence performance on WISCIII in alphabetical and nonalphabetical languages.

Reply: We agree with you that learning disorders (LD) and history of language disorders are often associated with ADHD and can influence the performance on WISC III. Additional analysis revealed that there are 19 cases of LD in ADHD children with MPH treatment. However in the study, we did not find any significant difference of the changes of ADHD symptoms and WISC-III intelligence test after MPH treatment within ADHD children comorbid with or without LD (data not shown). And further control with LD in the generalized linear model did not change the effects of age (data not shown). We would mention the finding in the revised article. About history of language disorder, there are only 6 cases in ADHD children in our study, 3 with MPH treatment and 3 not. Due to small sample, we didn’t analyze this data.

2. The Authors should report information about other treatments (i.e. cognitive behavior therapy, parent training, attention training) associated with MPH administration. Furthermore, Authors should discuss different treatment interactions and their possible effect on the results shown in the article.

Reply: Thanks for reviewer’s opinion. We would mention it as our limitation in revised article. This is a long term following study in Taiwan.

3. The authors should update references with following articles:
Reply: Thanks for reviewer offering the update references kindly. We would cite these references in the revised article.