PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Study protocol for a randomized controlled trial examining the association between physical activity and sleep quality in children with autism spectrum disorder based on the melatonin-mediated mechanism model
AUTHORS	Tse, Choi Yeung Andy; Lee, Paul; Zhang, Jihui; Lai, Elvis, W.H.

VERSION 1 – REVIEW

REVIEWER	David Wachob Indiana University of Pennsylvania, U.S.A.
REVIEW RETURNED	13-Dec-2017

GENERAL COMMENTS	Have you considered a cheek swab to test Melatonin levels instead of urine sample? This might be logistically more viable to manage with this population. Why are you using 12-week as the time frame for each phase? For example, waiting 12 weeks for T3 (follow-up) doesn't seem to make sense from a physiology standpoint. The impact from any exercise intervention will diminish drastically over 3 months. Have you considered breaking T3 (follow-up) into two parts, such as a 6-week follow-up, then a 12-week? That way you could monitor how much, and how fast, the intervention's benefits diminish. Page 4, line 10: That bullet point reads "…melatonin-medicated", but I believe you mean "melatonin-mediated…" Page 5, line 32: Should be "drowsiness", not downiness. The intervention: You identify that the participants will be engaged in the intervention for 20 minutes of jogging. And will maintain MVPA throughout. You need to set parameters for MVPA to determine if the intervention was completed successfully. For example, you might determine "out of the 20 minute jogging phase of the intervention, participants must maintain their target heart rate (THR) for at least 15 out of the 20 minutes (75%) in order to count the intervention as acceptable". It's very unlikely that the children will maintain MVPA for the entire time, especially at first. The Polar devices can calculate how long the user is within their pre-set THR (50-80% of max HR). The control group: You state that the control group will not participate in any additional PA/exercise. Does that include physical education (PE) class? If not, specify that, and include how often students receive PE (i.e. they receive PE once per week for 40

	minute periods, et…). Great project. It was a pleasure reviewing it. Best of luck!

REVIEWER	Dr Jane McCarthy King's College London, UK
REVIEW RETURNED	30-Dec-2017

GENERAL COMMENTS	Very worthwhile study as sleep disturbance in children with autism has a major impact on quality of life of families for many years. I am not sure of the requirements for consent from children with low IQ in Hong Kong if the child is not able to give written consent which may need further clarification. This may be addressed through the process for obtaining ethical approval. Also end of abstract indicates data will be collected from January 2017 presumably meant January 2018.

VERSION 1 – AUTHOR RESPONSE

Editorial Comments and Requests:

- Please carefully proofread the paper. There appears to be some typographical/ grammatical errors in the manuscript e.g. the title: “using melatonin-mediated mechanism model” should be “using A melatonin-mediated mechanism model”
Response: The manuscript has been proofread carefully and the typographical/grammatical errors have been revised, including the title.

In the introduction you say “In Hong Kong, an estimate of 90 per 10,000 individuals suffered from ASD.” Why is this in the past tense?
Response: The typo has been corrected.

- Please ensure that the abstract is formatted according to journal guidelines for study protocols. See: http://bmjopen.bmj.com/pages/authors/#study_protocols Currently there is no 'ethics and dissemination' section.
Response: The section has been added.

- The 'strengths and limitations' section needs revising. The first 3 points are not clearly strengths or limitations of your study. It shouldn’t be a summary of the study and its findings. As a reminder, this section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods or design of the study reported (see: http://bmjopen.bmj.com/site/about/guidelines.xhtml#articletypes).
Response: The section is significantly revised.

- Please ensure that the intervention is reported in sufficient detail. We suggest going through the TiDer checklist: http://www.equator-network.org/wp-content/uploads/2014/03/TIDieR-Checklist-PDF.pdf
Response: More details (e.g., set up of activity circuit, rationale of 24 sessions of jogging, MVPA parameters) are provided according to the TiDer checklist.

- Please clarify in the paper which outcomes are primary and which are secondary.
Response: Clarification is made.

- Along with your revised manuscript, please provide a completed copy of the SPIRIT checklist (http://www.spirit-statement.org/). Please remember to include the relevant page number(s) from the manuscript next to each reporting item or state 'n/a' next to items that are not applicable to your study. For help and guidance completing the checklist see: http://www.bmj.com/content/346/bmj.e7586
Response: A completed copy of the SPIRIT checklist has been provided.

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: David Wachob
Institution and Country: Indiana University of Pennsylvania, U.S.A.
Competing Interests: None declared

Have you considered a cheek swab to test Melatonin levels instead of urine sample? This might be logistically more viable to manage with this population.
Response: Yes we have thought about this idea. We have done a pilot study and we found that collection of urine sample is manageable in this population. Therefore, to enhance internal validity, we prefer to collect urine sample.

Why are you using 12-week as the time frame for each phase? For example, waiting 12 weeks for T3 (follow-up) doesn't seem to make sense from a physiology standpoint. The impact from any exercise intervention will diminish drastically over 3 months. Have you considered breaking T3 (follow-up) into two parts, such as a 6-week follow-up, then a 12-week? That way you could monitor how much, and how fast, the intervention's benefits diminish.
Response: Thanks the reviewer for mentioning this very good point. A 6-week follow-up has been added to the protocol.

Page 4, line 10: That bullet point reads "…melatonin-medicated", but I believe you mean "melatonin-mediated…"
Response: The typo has been corrected.

Page 5, line 32: Should be "drowsiness", not downiness.
Response: The typo has been corrected.

The intervention: You identify that the participants will be engaged in the intervention for 20 minutes of jogging. And will maintain MVPA throughout. You need to set parameters for MVPA to determine if the intervention was completed successfully. For example, you might determine "out of the 20 minute jogging phase of the intervention, participants must maintain their target heart rate (THR) for at least 15 out of the 20 minutes (75%) in order to count the intervention as acceptable". It's very unlikely that the children will maintain MVPA for the entire time, especially at first. The Polar devices can calculate how long the user is within their pre-set THR (50-80% of max HR).
Response: The authors acknowledged the reviewer's concern and followed the suggestion. The parameters for MVPA are set.

The control group: You state that the control group will not participate in any additional PA/exercise. Does that include physical education (PE) class? If not, specify that, and include how often students receive PE (i.e. they receive PE once per week for 40 minute periods, et…).
Response: The information of PE class is provided.

Great project. It was a pleasure reviewing it. Best of luck!

Response: Thank you.

Reviewer: 2
Reviewer Name: Dr Jane McCarthy
Institution and Country: King's College London, UK Competing Interests: None

Very worthwhile study as sleep disturbance in children with autism has a major impact on quality of life of families for many years.
Response: Thank you.

I am not sure of the requirements for consent from children with low IQ in Hong Kong if the child is not able to give written consent which may need further clarification. This may be addressed through the process for obtaining ethical approval. Also end of abstract indicates data will be collected from January 2017 presumably meant January 2018.
Response: The authors acknowledged the reviewer's concern and it is addressed through ethical approval. In case the children with too low IQ that they cannot give written consent, he or she will not be recruited for this study. Meanwhile, the first enrollment of the study will be started in February 2018 and we have revised the abstract accordingly.