Reviewer's report

Title: Differential role of dose and environment in initiating and intensifying neurotoxicity caused by MDMA in rats

Version: 2 Date: 13 May 2019

Reviewer: BRIAN PIPER

Reviewer's report:

The authors have sufficiently revised this paper. From a purely technical perspective, this multi-level dataset will have an enduring contribution to the field.

However, there are many, mostly minor, language issues.

P4 L 15: flattened
L20: in combination with a monoamine
L22: Despite difficulty in behavioral measurement
L58: both are used (‘s & s) but "2000s" is somewhat more common

P 5 L12: course of a serotonin syndrome involved at least two
L16: Delete R in 5-HT2AR throughout
L22: mediating molecules differ from those for the serotonin syndrome
L 50: In the present study, we decided to utilize the … to elicit the
L55: relatively high efficacy with the
L56/57: this is hard to follow, consider "we reduced the low dose (LD) to 2mg/kg in the present study"

P6 L23: to intensify the effects
L29: administered the low dose
L31: Are there any raves in the US anymore? Though that was just a 90s thing.
L39: under a normal environmental
L41: experiments were performed

P9 L32: Why is this labeled "DAB immunohistochemistry"? Consider SERT immunohistochemistry.

P10 L26: based on results of a power analysis

P13 L38: However, the molecules mediating the serotonin syndrome may be distinctly different from those for processing
L48: are different from those

P14 L7: consider: "and likely prevent harmful actions and further deterioration."
L17: in adaptation to the drug environment. At warm temperatures,
P15 L14: have impact on the activity

P16 L13: although environments have an impact on the activity
L35: This section should we written in the past tense.
We found that the low-dose of MDMA was
L39: extracellular 5-HT was the determinant

Ref #16. Non-proper nouns in the article title should be in lower-case. #21, 22 too.

The term "abuse" has fallen out of favor (at least in psychiatric circles post 2013 and DSM5). Consider spritzing in some "ecstasy misuse" instead.

The resolution of all Figures still looks pretty grainy. This is especially true for the bar graphs. Please work with journal staff at exporting with a better resolution.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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I am able to assess the statistics

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