Author’s response to reviews

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

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Author’s response to reviews:

Date: 6 June 2019

TO: “BMC Pharmacology and Toxicology Editorial Office”

From: Rui Tao

Subject: Revised submission to BMC Pharmacology and Toxicology-PHAT-D-18-00243R2

Differential role of dose and environment in initiating and intensifying neurotoxicity caused by MDMA in rats Ibrahim M Shokry; Connor J Shields; John J Callanan; Zhiyuan Ma; Rui Tao

Dear Dr. Bowman,

We would like to thank you and the reviewers for your time and your constructive feedback. The entire manuscript has been edited. We have addressed the reviewers’ specific comments as follows:
P4 L 15: flattened
  Reply: Changed to flat

L20: in combination with a monoamine
  Reply: With replaced of

L22: Despite difficulty in behavioral measurement
  Reply: behavioral replaced behavior

L58: both are used ('s & s) but "2000s" is somewhat more common P 5 L12: course of a serotonin syndrome involved at least two
  Reply: Changed to “2000s”

P5 L12: course of a serotonin syndrome involved at least two
  Reply: involved replaced Is involved

L16: Delete R in 5-HT2AR throughout
  Reply: deleted

L22: mediating molecules differ from those for the serotonin syndrome L 50: In the present study, we decided to utilize the … to elicit the
  Reply: Differ replaced different

L55: relatively high efficacy with the
  Reply: With replaced in
L56/57: this is hard to follow, consider "we reduced the low dose (LD) to 2mg/kg in the present study"

  Reply: This sentence replaced the old sentence

P6 L23: to intensify the effects

  Reply: to intensity the effect replaced intensify effects

L29: administered the low dose

  Reply: with is removed

L31: Are there any raves in the US anymore? Though that was just a 90s thing.

  Reply: Yes

L39: under a normal environmental

  Reply: under a normal replaced under the normal

L41: experiments were performed

  Reply: experiments were performed replaced experiments performed

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

  Reply: SERT immunochemistry is used

P10 L26: based on results of a power analysis

  Reply: a is added before power
P13 L38: However, the molecules mediating the serotonin syndrome may be distinctly different from those for processing

Reply: the molecules replaced molecules

L48: are different from those

Reply: from replaced in

P14 L7: consider: "and likely prevent harmful actions and further deterioration."

Reply: This sentence replaced the old one

L17: in adaptation to the drug environment. At warm temperatures,

Reply: to the drug replaced for the drug., and temperatures replaced temperature

P15 L14: have impact on the activity

Reply: have impact on replaced have impacts on

P16 L13: although environments have an impact on the activity

Reply: have an impact on replaced have impacts on

L35: This section should we written in the past tense.

We found that the low-dose of MDMA was

Reply: was replaced is in this sentence

L39: extracellular 5-HT was the determinant Ref #16. Non-proper nouns in the article title should be in lower-case. #21, 22 too.

Reply: was replaced is in the sentence
The term "abuse" has fallen out of favor (at least in psychiatric circles post 2013 and DSM5). Consider spritzing in some "ecstasy misuse" instead.

Reply: “ecstasy misuse” replaced “ecstasy abuse”

Question: 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.

Reply: the resolution at 300 increased to 600