Author’s response to reviews

Title: Case Report of Vasovagal Syncope Associated with Single-Pulse Transcranial Magnetic Stimulation in a Healthy Adult Participant

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Author’s response to reviews:

Dear Editor and Reviewers for BMC Neurology,

Thank you for your efforts and expertise in review of our manuscript “Case Report of Vasovagal Syncope Associated with Single-Pulse Transcranial Magnetic Stimulation in a Healthy Adult Participant”. We appreciate the opportunity to respond to the reviewer’s comments and resubmit our findings to your journal. We agree that reporting rare adverse events is needed, and essential to continue appropriate and guided investigation of neuromodulation in human trials.

The editor and reviewers raise important points that we have directly addressed below, with the Line referenced to the “edited” version. We have ensured that our revised manuscript conforms to your journal style, and have again referred to the Instructions for Authors on the journal homepage. We appreciate your ongoing consideration and efforts in review of our work, and look forward to hearing from you.
Reviewer #1.

“Was the glucose blood test performed after the rTMS session?”

RESPONSE: The session was single-pulse TMS, and a blood glucose test was not performed. The subject reported adequate and normal ingestion of liquid and food before the session, and the physician evaluation did not indicate evaluation of blood-glucose. We have now included this statement within the manuscript. Lines 189-191

“Even this case report is very suggestive of a convulsive syncope, rather than a seizure, an electroencephalography should recommend in future studies. Please add.”

RESPONSE: This recommendation has been added to the manuscript. Lines 224-226

“I noted that the subject under investigation suffered of hypo-thyroidism. Therefore, I suggest warranting potential readers to check for subtle thyroid problems, chiefly hypo-thyroidism, in future studies. In fact, in a previous paper, some observed abnormalities of several TMS parameters in adult hypothyroidism (Rizzo et al., 2008). There patients should not be considered as healthy subjects in studies of nervous system.”

RESPONSE: We respect the point that a “healthy subject” serving as a pure control should have an absence of any/all medical diagnoses, and the reference provided. We have now included this added statement in the manuscript to provide additional guidance for future investigations. This pertinent reference has also been added. Lines 220-224

“As stated in Tamijani et al., 2015, though the underlying molecular mechanisms still remain unknown, the effects of thyroid hormones on inhibitory and excitatory neurons may affect brain seizure activity, mostly as predisposing factor. This point should be discussed.”

RESPONSE: This point is respected, and an additional statement in the manuscript has been added not only to address thyroid hormones but also all centrally-acting medications and the influence on cortical excitability and potential for seizure activity. This pertinent reference has also been added. Lines 220-224
“Ethics: If your study involves humans, human data or animals, then your article should contain an ethics statement which includes the name of the committee that approved your study. If ethics was not required for your study, then this should be clearly stated and a rationale provided.”

“Consent:

If your article is a prospective study involving human participants then your article should include a statement detailing consent for participation.

If individual clinical data is presented in your article, then you must clarify whether consent for publication of these data was obtained.”

RESPONSE: This protocol was not deemed, by our University IRB, in need of ethical committee approval as the session was part of a neurophysiological testing session with a healthy control. However, informed consent was obtained by the subject including review of potential adverse events. These statements are now included. Lines: 63-68.

“Availability of supporting data:

BioMed Central strongly encourages all data sets on which the conclusions of the paper rely be either deposited in publicly available repositories (where available and appropriate) or presented in the main papers or additional supporting files, in machine-readable format whenever possible. Authors must include an Availability of Data and Materials section in their article detailing where the data supporting their findings can be found. The Accession Numbers of any nucleic acid sequences, protein sequences or atomic coordinates cited in the manuscript must be provided and include the corresponding database name.”

RESPONSE: Data, as it would pertain to this case report, would be the physician report for the individual who participated in the study. Through participant consent, this report was formally obtained. However, in order to maintain confidentiality, this report has not been included in this manuscript.
“Authors Contributions:

Your 'Authors Contributions' section must detail the individual contribution for each individual author listed on your manuscript.”

RESPONSE: We have now divided each author and their individual contribution in the Authors’ Contribution Section. Lines: 250-255