Author’s response to reviews

Title: Peripheral Vascular Responses to Acetylcholine as a Predictive Tool for Response to Cholinesterase Inhibitors in Alzheimer's Disease

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Version: 2 Date: 18 Apr 2019

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Editors Comments

1. It is noticed that you are missing your Consent for publication subsection in the Declarations, and that several of the subsections are labelled incorrectly. Please revise and add to your Declarations subsections so that each of the following are presented:

2. Thank you for including a statement in the Authors’ contributions that the authors agreed to have performed duties in line with the ICMJE guidelines for authorship. However, we ask that you detail each author’s individual contributions to the study rather than an encompassing statement.

3. In your Funding section, please also state the role of the funding body in the design of the study; collection, analysis, and interpretation of data; and in writing the manuscript.

On page 12 under Declarations we have added details regarding consent to publish, details on authors' contributions and the role of the funding body in the design of the study, collection, analysis, and interpretation of data; and in writing the manuscript.

Reviewer 2:
Thank you for the response to the comments, which has indeed added to the value of this manuscript. However, one key point remains which calls for correction: the agents which affect cholinergic signaling far exceed anti-cholinesterases, and include simple over-the-counter approachable anti-allergy pills like Benadryl or anti-muscarinic agents for controlling incontinence etc. Numerous leading articles reflect a major impact of these treatments on the risk for cognitive decline. It is important to add those agents to the list of tested details and cite the papers reporting their impact.
On page 1, paragraph 1 we have added the following information:
Patients were excluded if they had medical conditions known to interfere with acetylcholine metabolism or were likely to react adversely to skin stimulation. Additionally, we excluded patients if they were taking medication whose primary action was anti-cholinergic and was being used for a medical condition in which anti-cholinergic action was the desired intervention e.g. oxybutynin for irritable bladder.

On page 12, paragraph 4 we have also added the following information and supported the statement with 3 references as suggested by the Reviewer:
We recognise that many drugs have anticholinergic actions of differing potency [25-27] and that some of these were used for concomitant medical disorders, but given the sample size in our pilot study it is unrealistic to use potency as a variable in our analyses. In our larger planned study we will address this issue more closely. Participants who had previously been treated with cholinesterase inhibitors or who had medical conditions known to interfere with acetylcholine metabolism were excluded.