Author’s response to reviews

Title: Upper airway stabilization by osteopathic manipulation of the sphenopalatine ganglion versus sham manipulation in OSAS patients: a proof-of-concept, randomized, crossover, double-blind, controlled study

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We thank Heidemarie Haller. We have taken her comments into account (see below). We hope that the manuscript will be deemed acceptable in its revised form 

Heidemarie Haller (Reviewer 1):

Question 1: I would like to thank the authors for considering my comments. However, the added information about the random sequence generation and allocation concealment is still lacking. How was the random sequence generated? Do the authors use block randomization with random block lengths or one block only? How was the allocation concealment secured? Which method did the authors use?

Answer: We have modified the “randomization and blinding” section:
"The order of administration of AM and SM was randomized. The random sequence was generated using the R statistical software. It consisted in a single block of ten (five allocations to AM at visit 1 then SM at visit 3 and five allocations to SM at visit 1 then AM at visit 3). The allocation concealment was secured as follows. A research nurse not participating in the study itself was responsible for the random sequence generation and for treatment allocation. After the physician responsible for the clinical investigation ("investigator") had confirmed the eligibility and collected baseline data of a given patient during visit 1, the research nurse provided the osteopath performing the AM and SM maneuver with this patient's allocation, outside the knowledge of the investigator. The osteopath was himself ignorant of the randomization list as a whole. The investigator was not present when the osteopath performed the maneuvers, and was therefore blinded to the allocation when subsequently analyzing the data. As a result, both the patient and the investigator analyzing the data were blinded to the allocation. The osteopath was not involved in any manner in the data analysis”.

Question 2: I have a further concern about the trial registration. The authors should explain why outcome measures and number of included patients differ between trial registration and manuscript!
Answer:
Number of patients: in clinicaltrials.gov we have included 10 patients in the “enrollment” section, and we have presented the results of 9 patients in this publication. The tenth patient consented to participate, and the first visit was planned a few days later, but this patient was lost to follow-up before this screening visit. Insofar as there was no baseline evaluation in this case, this patient does not appear in the analyzed population. He however appears in the trial registration process because he did sign the inform consent form.
Outcome measures: primary endpoint (pharyngeal critical pressure = Pcrit), secondary efficacy endpoints (OSA symptoms = snoring and sleepiness) and adverse events, were only required by clinicaltrials.gov at the time we registered the study, and are registered. Endpoints for evaluation of AM and SM (that were not efficacy endpoints, such as sensation questionnaire, lacrimation, pain), were not required by clinicaltrials.gov and were not included in the template.