Reviewer’s report

Title: The effect of Spinal Manipulative Therapy on Heart Rate Variability and pain in patients with chronic neck pain: A Randomized Controlled trial

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Reviewer: David William Evans

Reviewer's report:

This manuscript left me disappointed and somewhat confused. Despite the promise given by the title, I feel that the authors lacked clarity with their aims, objectives, research questions and methodology. There was also insufficient detail throughout.

The idea of the study was good; the field of musculoskeletal healthcare sorely needs data that investigate mechanisms within interventions that have now been established as having a beneficial therapeutic effect (e.g. spinal manipulation). However, this requires explanatory trials of an intervention that contain nested measures (and possibly interruption) of mechanisms, such as those related to the autonomic nervous system. This is where the current study protocol begins to lose its way. The authors state (page 3, line 22) that "the aim of the study is to examine the effects of SMT on HRV and pain to test if a CPM test can be used to predict treatment response, in a population of patients with recurrent and persistent NP." The authors then describe how they will allow practitioners to choose from an array of treatments (HVLAT or mobilisation) and additionally introduce another intervention across both groups of the study (stretching exercises) without any explanation or justification for this. Using multiple interventions constitutes a pragmatic trial design, thus introducing multiple confounders that hinder any explanatory power for investigating mechanisms.

The measure used to assess susceptibility for pain modulation, CPM, is by its very nature painful. It is therefore highly likely to affect the primary outcome, heart rate variability (HRV). It must therefore be used very carefully to avoid inadvertently changing outcome and conflating any effect of treatment. Insufficient detail was given in the text to make a judgement on this. At no point could I find detail about when measures were taken; before, during or after treatment. This is not acceptable for a protocol paper, which should leave the reader in no doubt whatsoever, and should allow perfect replication of the study.

Throughout the manuscript, I found myself having to search through the text for information relating to the chronology of screening, recruitment, assessment and intervention. The figures provided did not provide enough detail and the text did not make up for this lack of detail sufficiently. Arguably, the most concerning sentence of the manuscript was (page 5, lines 24-25) "Logistical details of this recruitment stage will be adapted to individual clinic routines." This introduces enormous potential bias; if unavoidable, much more detail is required so that the reader can assess the potential for bias. I also could not find any detail of how potential participants were approached, screened for eligibility, recruited, etc. Nor was any detail of how data were collected (paper or electronic), transferred to
database, and stored (data protection) prior to analysis.

One further concern is that data collection apparently began 6 months ago; hence, it may be too late to improve the methodological flaws highlighted above. These apparent deficiencies may be just due to poor reporting, but I fear this is unlikely to be the case.

I have uploaded an annotated copy of the manuscript, which provides further comments; in its current state, I cannot recommend publication of this manuscript.

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