Author's response to reviews

Title: Effects of Microcurrent Stimulation on Hyaline Cartilage Repair in Immature Male Rats (Rattus norvegicus)

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Author's response to reviews: see over
To
Professor
Tom Rowles PhD
Executive Editor
BMC Complementary and Alternative Medicine

Dear Professor,

Enclosed is the revised version of *Effects of Microcurrent Stimulation on Hyaline Cartilage Repair in Immature Male Rats (Rattus norvegicus)* manuscript, after the referee’s considerations, for your final evaluation.

In relation to editor and referees indications will clarify below, point-by-point, the changes made:

**Editorial comments:** Thank you for including an ethics statement in your manuscript. However, we would ask you to include the full name of your ethics committee in this statement. Answer: Suggested included on page 05 of the revised manuscript.

**Referee 1:** No comments enclosed.

**Referee 2:**

Comment 1: Microcurrent stimulation: there is no indication with regards the detailed parameters of the applied current. You have said that it is of 20 microamps and pulsed but there is nothing with regards the pulse frequency, pulse duration, interpulse interval, whether the pulse nature in monophasic or biphasic, whether symmetrical or asymmetrical or whether the 20 microamps relates to the mean current intensity or the peak. There is additionally no information with regards electrode placement relative to the deficit or whether there was an electrode polarisation consideration. The lack of this information makes it impossible to replicate this work unless one had an identical machine and there were no treatment options. It also makes
it almost impossible to compare your results with those obtained by others in previous work. You state that a continuous electrical current was applied, but then you say that this was delivered at low frequency - which is contradictory. Answer: Suggested included on page 06 of the revised manuscript.

Comment 2: You results lack specific information with regards statistical significance - you say there are differences or that one group had 'more cells' for example, but do not cite your results with sufficient detail. Answer: The data related to morphometric analysis are summarized in Table 1. The authors believe that the citation of numbers in the text would make it redundant.

Comment 3: Several authorities have question the capacity of Excel to carry out robust (statistically) analyses beyond simple t tests, and even they do not provide results which are equivalent to dedicated statistics packages (e.g. SPSS). Do the results come out with the same level of significance when a dedicated statistics package is employed? In your Table 1, you do not cite the actualy p value obtained - just that it is lower (or not) then p=0.05. It is normal to quote the exact p value. Answer: Suggested included on pages 09 and 22 of the revised manuscript.

Comment 4: You make no mention of what happened to your control group. It could be that they were simply not treated at all (which is what one would assume) or that they were handeled in the same way as the treatment group with electrodes attached but with no current applied. This needs clarification. Answer: Suggested included on page 06 of the revised manuscript.

Comment 5: Your abstract needs clarification with regards statistical significance. Answer: Suggested included on page 02 of the revised manuscript.

Comment 6: Your reference (30) has an error in the author name Answer: Error corrected.

Comment 7: In your discussion (page 13 my copy) you suggest that your study showed that low amperage currents reduce the early stage of inflammation whereas higher amperage currents tends to control the final stages of the inflammatory process. Given that the current applied in this work was the same for all animals (so far as I can tell), how can you make this observation based on your data? Answer: Suggested included on page 13 of the revised manuscript.
Comment 8: Also on page 13 you state that sub sensory stimuli are KNOWN to generate microcurrents that can penetrate cells, restoring the natural bioelectricity after injury. There are no specific references attributed to this statement which is somewhat critical. There are 4 references at the end of the paragraph and I can not recall any of them establishing such an effect. The paper by Kirsch suggests such a phenomenon, but it is not supported by any research evidence. Clarification is essential, as it would be for several other similar statements in the discussion, many of which are attributed to multiple papers rather than specific research evidence. It is unclear which of your statements are based on common concept or hearsay and which on evidence. The reader who does not intimately know the literature would assume that all are based on research findings which is not entirely true.

Answer: Corrections included on pages 12, 13 and 14 of the revised manuscript.

We look forward to hearing from you soon.

Sincerely yours,

Carla de Campos Ciccone, Denise Cristina Zuzzi, Lia Mara Grosso Neves, Josué Sampaio Mendonça, Paulo Pinto Joazeiro and Marcelo Augusto Marretto Esquisatto