Comments on Tao et al. (2017), "Multiple-Frequency Matching Treatment Strategy for Tinnitus"

Dear Editor

"Multiple-frequency matching treatment strategy for tinnitus" by Tao et al. [1] provides pilot study outcomes for a sound-based tinnitus therapy and was published recently in the Journal of International Advanced Otology. It is recommended by guidelines such as the consolidated Standards of Reporting Trials (CONSORT) statement [2] endorsed by this journal, that research be reported in a manner that supports transparency and future reproducibility. Accordingly, our reading of this publication revealed several fundamental methodological issues and factual errors. Our concerns regard potentially inaccurate study conclusions, likely the result of unclear study rational and methodology reporting.

Study aims: The study aim in the abstract has two parts, as stated by the authors: (1) integrate commonly used tinnitus measures into a comprehensive questionnaire; and (2) studying the effectiveness of a masking therapy based on multiple-frequency matching for tinnitus suffers. The first aim highlighted in this study is not appropriate for the purpose of measuring outcome of an intervention as it is not common to cherry pick the items from standardized outcome measures and to create a composite scale as this may result in biased and misleading results [3,4]. Also, the second aim does not have the appropriate study design. For instance, with a limited sample size and other issues highlighted in this letter, the study reported is a pilot or feasibility outcome of efficacy, not effectiveness. Please refer to a report by Singel et al. [5] to study the difference between efficacy and effectiveness trials. For these reasons, the study does not appear to address both the stated aims fully.

Study design: The authors report that they used a cross-over design, although it is not clear how this was conducted. There were 30 participants in this study. Without any power or sample size calculations provided, the validity of the statistical results is questioned. How randomization took place is also not clear. Authors state that the patients diagnosed with "nervous tinnitus" were accepted onto the study. An explanation of what nervous tinnitus is and how this diagnosis was reached is lacking. It was stated that the tinnitus was to be present for 12 months. However, Table 1 indicates that the disease age was 6 months for some participants. It thus appears as though there are some contradictions here. It was stated that patients underwent pure-tone and acoustic immittance audiometric examinations to characterize tinnitus. How these approaches were used to characterize tinnitus is unclear. The degree of hearing loss the participants had is not stated and how variations of degree of hearing loss were addressed during the sound presentation is not explained.

Treatment rationale and specific of the signal: No background information into existing research regarding sound therapy or results of systematic reviews is provided. There is no clear context or rational for this study or why a single sound was selected as the comparator. Moreover, it is not clear how 'multiple-frequency masking' was actually delivered i.e. via an ear-level device or via the soundfield. Matlab was mentioned in the introduction, but there was no further mention regarding how this was implemented. Was the treatment at a hospital or at home? The statement "tinnitus treatment will begin according to the result of scale" provides no clear explanation. It sounds like the tinnitus was masked, however, masking tinnitus completely is generally not advised. It would be helpful to have a rational as to why the tinnitus was masked and not partially masked. It is alarming that there were adverse reactions such as nausea, dizziness and hearing loss. It would be helpful to have reported how

many patients had each of these symptoms. A treatment requiring patients to attend a hospital appointment for 20 minutes twice a day does not seem feasible. The time gap between treatments was not explained. The population actually selected may have been skewed to those able to attend such appointments. As there is no information on the ratio of people invited and those actually participating, drawing conclusions is difficult.

Outcome measures and data analysis: As highlighted earlier, it is not recommended to create a composite by cherry picking some items from standardized outcome measures [3,4]. Moreover, there is great concern regarding the way the outcome measures were scored and used. The scoring of the Tinnitus Handicap Inventory is incorrect, which could invalidate all the findings in this study. Stating "never" was scored at four and "always" at zero, indicating that the scoring has been incorrectly reversed. For the Anxiety scale, two of the categories mentioned are the same "most of the time" for option 3 and 4, which is a further inaccuracy. Questions from different questionnaires were combined to make a new questionnaire. There appears to be some validity testing done on the questions extracted from the various outcome measures. As there is no mention of how this was done in the methods section, it brings the validity of this newly designed outcome measure into question. It would have been much more helpful having the statistical analysis plan in the methods section instead of a list of what SPPS is able to do.

Factual and grammatical errors: The manuscript has many grammatical and factual errors, although we highlight only a few. The introduction contains misleading statements such as "tinnitus is an auditory nerve disorder." There are many causes of tinnitus [6], of which this is only one. The statement "tinnitus sounds usually contain three to five dominant frequencies"; has no reference and would not be accurate in view of the heterogeneous nature of tinnitus. A

further statement "it is convenient to use Matlab platform to treat tinnitus" lacks clear rationale, and is of questionable clinical value as not many tinnitus management providers have access to Matlab (developed by MathWorks, Natick, United States). As such, the Matlab application is not regarded as a convenient nor conventional intervention.

Interpretation of results: In view of these limitations, stating multiple-frequency masking is superior should be made with caution, as a significant difference was only found in the third course of frequency. The size of this difference is unknown as effect sizes were not calculated.

Overall, the reported details about the methodology and results are inadequate and do not logically support the authors' conclusion regarding the efficacy of their approach. The challenges facing patients and researchers in the field of tinnitus intervention are substantial and most adequately served when best practices regarding study design, using validated outcome measures, and interpreting results are employed. The availability of documents outlining and supporting such practices, referenced herein, merit attention from all prospective researchers and authors.

References

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