Reviewer's report

Title: Associations between speech features and phenotypic variability in Treacher Collins syndrome

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Reviewer: Angela Morgan

Reviewer's report:

The title and abstract of the work accurately convey the study and its findings. This is a very well written manuscript that follows a logical order and clearly spells out the rationale of the study for the reader, leading to well formed research questions (although see minor point below). I found no significant formatting or grammatical errors. The authors have completed a thorough review of the literature and appropriately refer to relevant studies in the field throughout their work. A well crafted manuscript. A strength of the manuscript is in the speech methodology and interpretation of results. The paper will make a significant and meaningful clinical contribution within this specialized field.

Minor essential revisions

The research questions are well formed, yet it is important to alter the wording in the first question. The word variable implies one would be measuring speech at more than one time point. A better term could be the word similar…i.e., “How similar are the speech features in TCS …across ages? This is just a small change that will remove any ambiguity and is arguably a truer representation of what was examined. See also the first line of the discussion where the word variability is used again.

The methods are appropriate for addressing the research questions. The use of intra- and inter-rater reliability is appropriate and should be commended. Clearly a lot of rigorous work has gone into phenotyping this cohort of 19 participants. There is appropriate use of supplementary materials by inclusion of the rating scales used in the study to enable replication of the work.

Sample size and managing the sample: I had initial concerns about the division of the sample into paediatric and adult sub-groups when the sample was already small. Yet on reading the work, I can see that this was a clinically relevant approach. Indeed the findings indicate improvement in speech across the lifespan for individuals with TCS, including in the real-world outcome of speech intelligibility. Hence, I agree this was an appropriate approach for the authors to take. There should be mention of the limitation of the sample size here in the discussion however, as of course we cannot be sure that another sample of just 19 participants would lead to the same conclusions until this work has been replicated. We could be more confident about the findings with a sample of 50 or greater. I did not see any mention of this. Thankyou for including this in your revision.
My only other query regarding sample size was the number of statistical tests performed. Should there have been a correction for multiple comparisons?

Hearing impairment: It is surprising that hearing impairment was not reported to have more of an impact on speech outcome given the high rates of significant hearing impairment (i.e., 7 moderate, 6 severe and 1 profound – that is 14/19 participants in the study). Could the authors please discuss further why this may have been the case. Perhaps where you discuss the hearing impairment findings in the discussion – you could emphasize to the reviewer that the majority of participants had hearing aids fitted? Do you have any data on the success of hearing aid use/compliance for the participants in your study – even if you have just a note about how long the participants had been using hearing aids etc?

Something that was not clear to me – the methods read as though the individuals had the hearing tests on the 2 days of testing within this prospective speech study? Is that the case? I don’t think that would have been the case? But this is how it reads – so it sounds like hearing aids were fitted at that timepoint. But I imagine that many of these individuals (particularly the adults) may have had hearing aids for up to decades?

Introduction: It is difficult to get a feeling for the scale of past studies in relation to your sample of 19 participants. Please insert the sample N for the studies you mention. It is helpful to know the percentage of speech deficits in each group across these studies – but difficult to interpret more broadly in relation to the field without the N.

- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Minor typographical:

Characteristics of the study group, paragraph 3, last line – “All devices were appropriately fitted, but two individuals with an unilateral aid were assessed as requiring bilateral devices. – should be ‘a unilateral aid’.

Characteristics of the study group, under the Nordic orofacial screening test section - need to alter the following sentence to denote that there were issues with chewing and swallowing. As the sentence currently reads, it sounds like these basic skills were present rather than that individuals showed deficits in these skills.

Chewing and swallowing was equally as frequent, but present in 6/11 adults, 3/4 adolescents and all four children.

Discussion – line 4 – “Most of the adults had no or only one affected speech feature,” – suggest re-phrasing this sentence. A little awkward for the reader to read ‘no or only one’

Discretionary:

Speech composite score: Some statisticians or bioinformaticians would query the use of a composite score. It is challenging to say that 1 point means the same thing across all of the measures you have included. I understand the rationale for
this approach – to make comparisons more feasible. I feel this is probably acceptable given the authors have been so clear and specific about their intentions and methods. I felt I had to mention that I was a little unsure about this approach.

Do you have any basic information on the participants who declined to take part in your study? It would be helpful to determine whether you have a highly selected clinical sample, e.g., did only those individuals with more severe or less severe speech issues take part?

Ethics: Do you have a specific approval number/numbers for your ethical approval? Would be helpful to cite that specifically in the paper. I will leave this up to the discretion of the Editorial team to consider and follow-up.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.