Author's response to reviews

Title: Trigeminal Electrophysiology: A 2x2 matrix model for differential diagnosis between Temporomandibular Disorders and Orofacial Pain

Authors:

Gianni Frisardi (frisardi@tin.it)
Giacomo Chessa (gchessa@uniss.it)
Gianfranco Sau (gfs@tiscali.it)
Flavio Frisardi (frisardi.flavio@tiscali.it)

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Trigeminal Electrophysiology: A 2x2 matrix model for differential diagnosis between Temporomandibular Disorders and Orofacial Pain (MS: 4517918732514052)

Point-by-point reply to the Reviewers

REVIEWER: GREGORY CRAMER

TITLE
DISCRETIONARY - The title is specific and concise. Mentioning the proposed diagnostic model may better describe the purpose of the paper.
R.: Done. Thank you.

SUMMARY/ABSTRACT
MAJOR - The conclusions stated in the summary are not fully expressed in the discussion section of the paper. The author promises a diagnostic model using electrophysiological models to help distinguish between facial pain, temporomandibular disorders (TMDs), and neurological damage; however, facial pain and TMD dysfunction are likely co-morbid conditions, and can confound exam results as the associated pain can be ipsilateral, contralateral, or both. There is no model developed in the paper to differentiate the facial pain from the TMD. In addition, electrodiagnostics to determine the extent of neurological damage to the trigeminal nerve seems to be a previously established procedure.

R.: Following this pertinent suggestion, three clinical cases were included in the discussion section (see Clinical Considerations, page 15-19) in order to better illustrate the proposed model for differential diagnosis. Indeed, the 2x2 matrix functions as a “notch” for TMDs and has good predictive validity for facial pain caused by organic damage to the trigeminal nervous system. It has reasonable predictive validity for identifying patients with facial pain not caused by TMDs while it loses a percentage of its predictive validity in cases of concomitant presence of TMDs and orofacial pain with no electrophysiologically documentable organic damage to the trigeminal system.

MATERIALS AND METHODS
MINOR - There was a brief discussion on recruitment (existing TMD or non-existing TMD), but very little detail on demographic information and other criteria that might exclude study participants, e.g., existing neurological damage due to disease or trauma, co-morbid conditions like diabetes mellitus, etc.
R.: Done. Thank you. Data for Clinical Criteria of exclusion have now been provided. See page 5

MINOR - Where was this study conducted, meaning, what was the clinical setting?
R.: Done. Page 5

DISCRETIONARY - Would the equipment used to conduct this study be readily available to clinicians managing similar conditions?
R.: Yes, of course.
DISCRETIONARY - P7 – change “no-normal” to “abnormal”
R.: Done. Page 8

DISCUSSION
MINOR - P9 – change “simmetry” to “symmetry” and capitalize the word Figure when contained in parentheses.
R.: Done.

MINOR - P10 – change “scheletal” to “skeletal”
R.: Done.

DISCRETIONARY - P12 – ensure the unit of measure is clear on “5-15”
R.: Done. Page 12

REFERENCES
MAJOR - Most references are before 1998, one in 2000, one in 2004, with the author relying heavily on early work from one of his co-authors. There is a wealth of more current information available on the subject matter.
R.: Done.

REVIEWER: JAMES DEVOCHT

Minor Essential Revisions

1. The Conclusions section in the Abstract does not really contain any
Conclusions
R.: Done.

2. In MATERIALS AND METHODS, first paragraph, it was not stated just exactly what criteria were used to determine whether or not a specific participant had TMD.
R.: Done.

3. When describing the technical nature of the jaw jerk reflex procedure, the EMG sampling rate should be given as well as the window width used for determining the peak-to-peak amplitude. How was it determined exactly where that window began for each data set.
R.: Done. Page 6

4. In the first line of the second paragraph of DISCUSSION, symmetry is misspelled.
A.: The mandibular reflex was also tested with the mandible in rest position. This condition excludes conditioning induced by occlusion and the mandibular reflex was also found to be symmetrical in TMD patients.
5. Toward the middle of the 3rd paragraph on page 10, skeletal (in connection with references 20 and 21) is misspelled as scheletal.  
**R.: Done.**

6. OP and TMD do not need to be defined again in Method of the Abstract when they were just defined in the paragraph immediately preceding that one.  
**R.: Done.**

7. At least in my mind, the term electrophysiologic tests is more general than just EMG (electromyography) and therefore it would be appropriate to specify that the voltages etc., mentioned to in the Method section of the Abstract, refer to EMG measurements.  
**R.: Done.**

8. In MATERIALS AND METHODS, the first paragraph ends with “electrophysical tests” but it would seem that “electrophysiological tests” would be more consistent with the Abstract as well as more accurate.  
**R.: Done**

9. In the Jaw jerk reflex section of MATERIALS AND METHODS, just to make it clear that EMG recordings are being made, it would seem better to end the first sentence with something like “triggered recording of the EMG activity levels.” instead of “triggered a sweep of the recording traces.”  
**R.: Done. Page 6**

10. At the end of the Jaw jerk reflex section, it is mentioned that latency was not measured. If it is going to be mentioned, it should be defined. However, I see no point in mentioning it just to say that it was not measured. If there was some substantive reason why it was not measured, it would seem appropriate to tell what that reason is. If there is no really significant reason, just don’t mention it at all.  
**R.: Done.**

11. In the next to the last paragraph before RESULTS, it is stated that “The percentage differences between the ipJJ amplitude and the ipsilateral R-MEPs amplitude for each side were calculated but not reported in the tables.” That raises the question of why were they not reported? Again, if that is all that is going to be said, it would seem more appropriate not to mention that at all.  
**R: Done**

12. In the second paragraph of RESULTS, a degree of asymmetry in the TMD groups was declared to have a “statistically significant difference” when compared to the control group. I assume that is be taken to mean that the P-value is less than 0.05. That is the commonly held notion, but there is nothing magic or even universal about that value of 0.05. Therefore, it seems appropriate to explicitly state what is meant by a “statistically significant difference”.  
**R: Done. Page 8**
13. When giving a P-value (as in Table 1), why not give the actual value rather than state that it is greater or less than some round number?

R: Done.

14. In the last paragraph of RESULTS, it seems to me that a reference, or some other basis should be given for determining what values were considered for the intervals given. Along that line, I didn’t really understand Table 3, but that could be more due to my unfamiliarity with that subject.

A: To make this clinical concept clearer, we have described three clinical cases in the discussion section including the relevant calculations.

**REVIEWER: JOHN H KALBFLEISCH**

(1) Signed informed consent procedures need to be stated in the Methods section.

R.: Done.

(2) The Mann-Whitney significance level is directed at the comparison of group medians (appropriate). The authors can consider showing significance levels of the t-test for comparing group mean levels (significance level = P-value). This can be added to Table 1.

R.: Done.

(3) page 7, line 8, change “parameters” to “statistics”.

R.: Done.

(4) page 7, line 11, insert “in medians” following “intergroup differences” (at the end of the sentence).

R.: Done.

(5) page 7, line 14, consider changing “no-normal” to “non-normal”.

R.: Done.

(6) Table 2. This is acceptable, but I feel that it can be replaced with a Figure that gives readers more insight into the results. The authors can consider a figure that is a (horizontal) dotplot of individual %values for each of the two study groups. This is displayed in two major sections, one on top of the other. The two sections are the two measurement scales (R-MEP% and JJ%). Therefore, each section has two dotplots (of 33 and 36 points). Superimposed on the dotplot distribution the group statistics (mean, median, percentiles) can be identified, but the measurement scale cut-point needs to be shown (a vertical line). If the dot-plot distribution is very skewed, the measurement scale can be shown on a log-basis (or some similar transform). This figure allows the reader to additionally see the diagnostic-test characteristics of sensitivity and specificity for the authors-selected cutpoints.
From Table 2: JJ% has sensitivity=0.75 and specificity=0.95. R-MEP has sensitivity=0.10 and specificity=0.95. If one uses means and sd’s from Table-1, and assumes normality, JJ% has approx sensitivity=0.71 and specificity=0.93; R-MEP% has approx sensitivity=0.25 and specificity=0.92. A similar presentation of sensitivity-specificity could be performed for JJ% for case values where R-MEP > 75% (as in Table 3).

A: We can only agree with this suggestion. However, the work necessary to create this type of figure would be extremely complex for lacking of statistical expert in our group. We hope that the Referee can accept it.

(7) Tables can be revised to the standard format for biomedical journals. One horizontal line below the column headings, and one horizontal line at the bottom of the columns (above any footnotes). Remove vertical all lines.

R.: Done.

(8) Anticipating that some readers will implement the suggested evaluations, I would suggest the authors can take a set of raw measurements for one subject and show how the Table 1 derived measures are calculated. This can be placed in an appendix.

R.: Done. We thought to include three clinical cases in the discussion section (Clinical discussion).

ASSOCIATE EDITOR:

(1) Can you provide criteria for determining the presence of TMD?

R.: Done.

(2) Can you provide the sampling rate and window width for the jaw jerk reflex?

R.: Done.

(3) Can you better clarify the statistically significant difference for degree of asymmetry?

A: Regarding this pertinent suggestion, by degree of asymmetry we mean the difference in ratio of EMG absolute value between side.

(3) Quoting the reviewer: ?The conclusions stated in the summary are not fully expressed in the discussion section of the paper. The author promises a diagnostic model using electrophysiological models to help distinguish between facial pain, temporomandibular disorders (TMDs), and neurological damage; however, facial pain and TMD dysfunction are likely co-morbid conditions, and can confound exam results as the associated pain can be ipsilateral, contralateral, or both. There is no model developed in the paper to differentiate the facial pain from the TMD. In addition, electrodiagnostics to determine the extent of neurological damage to the trigeminal nerve seems to be a previously established procedure?

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has good predictive validity for facial pain caused by organic damage to the trigeminal nervous system. It has reasonable predictive validity for identifying patients with facial pain not caused by TMDs while it loses a percentage of its predictive validity in cases of concomitant presence of TMDs and orofacial pain with no electrophysiologically documentable organic damage to the trigeminal system. This clinical eventuality was included in the conclusions.