Author's response to reviews

Title: Physiological responses to low-force work and psychosocial stress in women with chronic trapezius myalgia.

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Author's response to reviews: see over
Response to reviewers’ comments:

Reviewer 1: César Fernández-de-las-Peñas

1. Authors should provide a description of the clinical features of the patients with trapezius myalgia, for instance, pain history (months), duration of pain, frequency (all day?), body diagram with pain area. A good description of the sample would improve the manuscript and extrapolation of the data. Did authors see if their data would depend of pain area of the patients?

Point taken. Table 1 has been extended to include details regarding pain history and pain intensity. We have not analyzed possible dependence of pain area. The pain drawings/pain areas were mainly used as a diagnostic tool to ensure that the patients’ pain was localized to the neck/shoulder area. The drawings were, unfortunately, not standardized enough for areas to be determined in a valid way.

2. Were the controls matched for age to the patients? This should be controlled.

The controls were matched for age. We have now clarified this in the subjects section.

3. On page 6 (methods), authors comment that they assessed pain intensity at rest in both groups. If they included controls, controls by definition can not have pain before the experiment. Authors should clarify this.

Both groups followed the exact same experimental protocol to keep the procedures as standardized as possible. This meant that all pain intensity ratings that were obtained for the patient group were also obtained for the control group, even if the control group was expected to rate zero pain intensity. Since we do not present the results of this particular pain rating in the results section we have now removed the sentence.

4. In addition and related to comment 3, authors should revise the methods section for checking the description of the experimental, since both groups can received the same experimental protocol, but outcomes may be different because controls have not pain before the study. In the table 1, I can see that controls have 4/100 points in pain, and this is not pain, it is discomfort. Readers would not understand how a healthy control subject have pain.

We used the International Association for the Study of Pain (IASP) definition of pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage". This means that a slight unpleasant feeling in the muscle could be interpreted as low pain intensity according to the definition. Hence, the subjects rated pain intensity – not intensity of discomfort. Since one of our procedures was insertion of a small catheter in the muscle (we will
provide details and results in a forthcoming article), it is possible that the control subjects felt some slight pain in the muscle at baseline.

The control group’s pain ratings were also used to assure that the exercises were not intense enough to induce moderate or high pain intensity in healthy subjects.

Reviewer: Kristian Bernhard Nilsen

Major Compulsory Revisions:

Background:
General comments:

1. The authors do not explain explicitly why the present study was performed. Why should another study on muscular activity and musculoskeletal pain be published? This should be clearly stated in the background together with a more detailed hypothesis.

Point taken. We have explained more in detail why the study was performed and clarified our hypotheses in the Background.

More specific comments

2. Paragraph 4 must be rewritten. It does not make sense.
Point taken. The paragraph has been rewritten.

3. Paragraph 7 and first part of paragraph 8 does not contribute essentially.

We agree. The paragraph is now deleted from the manuscript.

4. The authors argue for the use of TSST. A similar argumentation for the other tests would be appropriate.

Point taken. The paragraph concerning TSST has been removed in the re-writing.

Methods:
1. Information on the number of invitations, number of responders, number of eligible patients, number of excluded subjects (specifically for each step in the inclusion and experimental process) should be given.

Details regarding the number of invitations and eligible patients are now given in the manuscript. None of the subjects were excluded in the experimental process.
2. Information regarding the reference values should either be removed or a better explanation for why it is obtained (and why it is not reported in the results..).

We are not sure whether the referee is referring to the EMG reference recordings or something else. The EMG reference recordings are important because thickness of skin and subcutaneous fat, muscle size, electrode placement etc can influence the signal strength. These recordings provide the possibility to control for such differences and also provide an opportunity to compare the ability to relax the trapezius muscle when instructed to do so. The results are presented in paragraph 2 in the results section, in figure 3 and applied as covariates in the mixed model analyses of EMG data. We have now provided further explanation of why the recordings were made in the manuscript.

3. Statistics:
   a. Differential responses are described here, but not reported in the Results section?

   Error in the statistics section has been corrected. Absolute measurements are tested and not differential response variables. The tests are reported under the heading ‘TSST’ of the results section.

   b. A differential response variable on the effect of psychosocial stress on muscle activity is described relative to a reference relaxation, and not to the baseline value. Why?

   See above (point 2).

   c. A large number of correlations are performed. A discussion of the possibility of type I statistical error is justified.

   We have now added a short discussion of statistical error.

   d. The interaction between pain/stress, emg and group is not reported in the mixed model analysis. Why? Instead a correlation between pain and EMG with both groups merged (and not separately for each group) is reported. Why? The authors conclude later in the discussion that they have found a positive correlation between pain/stress and EMG. However, if this correlation is not stronger or specific for the patient group, the external validity of this finding is rather small. Furthermore, the correlation between pain and emg is not significant for the time periods which the patients have higher EMG compared to controls.

   The interaction effects were not significant and therefore not included in the models. Since separate mixed model analyses were made for each dependent variable, interactions between dependent variables could not be included in the model. The correlations presented are merely an attempt to describe the relation between variables.
4. Have the authors performed any sample size calculations? This should be clearly stated in the text.

Sample size calculations were performed based on a primary outcome variable not reported in this manuscript. We have, instead, included a short discussion about statistical power in the Discussion.

Results
1. Complete statistics should be reported.

Point taken. F-values are now provided.

Discussion:
General comments
1. Too much of the results are presented in the Discussion.

Point taken. We have removed some of the repeats.

2. Other papers are referred and discussed very superficially. The number of citations could be reduced (but not necessarily), and those citations used should be discussed and compared to the present results more in detail.

Point taken. Parts of the discussion have been re-written and the citations used are discussed and compared to the present results more in detail.

Specific comments
3. Autonomic responses, section 5: “Pain and stress are complex phenomena with systemic effects and dysfunctions .. should be reflected distant from the painful region” This statement is not necessarily correct [1, 2]. Please consider another formulation.

Point taken. The sentence has been removed.

Minor Essential Revisions
1. The first sentence in the in abstract is a bit too conclusive.

Point taken. We have reformulated the sentence.

2. Paragraph 6 in the Introduction should be reformulated

Point taken. The paragraph has been rewritten.
3. If a written informed consent was obtained this should be stated.

It is already stated in the subjects section that informed consent was obtained. We have clarified this with an ‘Ethics’ heading.

4. The statement “The Stress-Energe questionnaire has proven its usefulness..” should be removed or documented.

The statement has been reformulated and documented.

5. The ECG channel input range and accuracy is reported in mVRMS. Please check if this is correct.

The reported input range is what the manufacturer reports.

6. In the discussion the term “prime mover” is used. Please consider to use another term.

We believe that prime mover is the appropriate term. It is widely used in literature concerning anatomy, biomechanics and kinesiology.

7. The reference to Nilsen et al is so superficial that the meaning is lost.

Point taken. There is now a more detailed description of the reference.

**Reviewer:** Lars L. L Andersen  
**Reviewer’s report:**

General:
The present study investigated muscle activity and sympathetic activity in women with and with trapezius myalgia. The study has strong and well-described methods, and provides relevant new knowledge to the field. It is shown that increased sympathetic tone is not linked to trapezius myalgia (at least with the present methods). A particularly interesting result was that trapezius EMG was higher during uninstructed rest (but not when subjects we instructed to fully relax). Of course we don’t know whether this was also the case before pain developed, but it may explain that these women develop pain in the long run. Could the authors come up with some speculations in the discussion as to why trapezius activity was higher (since it appears that sympathetic tone was not the reason).

The discussion of instructed/uninstructed rest has been extended. We also have mentioned in the discussion now that there are different explanations for the often reported higher EMG activity in subjects with chronic pain.
We also have added a few sentences concerning myofeedback interventions as possible treatment strategies to counteract the phenomenon.

Specific comments:
p.2. Abstract: last paragraph: Please specify “increased muscle activity during uninstructed rest...” or something like that

Point taken, now corrected in the text.

Introduction:
P.3. paragraph 4: In relation to the pain-adaptation model you may want to cite a recent study on trapezius myalgia from the group of Gisela Sjøgaard, showing decreased activity specifically of the trapezius muscle during maximal voluntary isokinetic contraction (Andersen et al., 2008)

The study is now cited in the introduction.

P.3. paragraph 6: regarding reference 21: refer to the original article – if it exists – rather than the ph.d. thesis

The original article has not yet been published.

Methods:
P.5. paragraph 2: Could you further specify “several palpable tender spots” ... How many spots need to be tender to have the diagnosis?

We have re-written the description of the clinical examination to clarify how the diagnosis was set.

P.5. paragraph 3: Were exclusion criteria assessed by questionnaire, interview, or examination?

The exclusion criteria were assessed by interview and examination. We have clarified this in the subjects section.

P.7. para 5: I am curious why the authors chose the NRS scale instead of VAS. Could you write 2-3 lines in the methods on the advantage compared with VAS?

We realize that we have used the term NRS incorrectly. The pain ratings were assessed using a VAS scale with numbers (0-10) below the line for guidance.

P.8 para 3: The SENIAM recommendations are now available online, it may be worthwhile to provide an internet link

Good point. We have provided the internet link.
P.8 para 4: please provide the name/brand/manufacturer etc. of the wireless EMG datalogger

The datalogger was custom made by the Department of Biomedical Engineering and Informatics, University Hospital, Umeå, Sweden. This information is now given in the manuscript.

p.8. para 6: Why was a 6th order butterworth filter chosen? compared to traditionally 4th order. If three 2nd order filters were applied to obtain a 6th order filer, this can cause a small shift in the time-domain of the EMG

What was the width of the RMS, i.e. how many msec?

Strictly, the data were filtered twice with 3rd order butterworth filters, once forward and once in reverse to eliminate phase distortion and minimize startup and ending transients (using Matlab function filtfilt). Small time shifts were not considered a problem for the 5 min segments taken during the experiment. For the reference recordings, however, the entire recording, rather than the small segments, was filtered and the segments for RMS calculations were cut out after filtering. The RMS calculations were made for the entire segments, i.e. 5min segments during the experiment and 5sec segments from the reference recordings. We have clarified this in the methods section.

p.9. para 1: How often did this occur?

In total, the percentage of “bad data” was 5.5% for the trapezius muscle and 5.8% for the deltoid muscle. This information is now given in the manuscript.

P.10 para 3: For the mixed model with autoregressive structure you used two different approaches, the AR(1) and the ARMA(1,1). I am curious, what was the reason for testing the model with ARMA(1,1)?

A series of covariance structures were tested and the Schwarz Bayesian Information Criterion was used to guide the final selection of covariance structure. The AR(1) and ARMA(1,1) were best suited for our data and we chose to present the results from the AR(1) analyses in the results section.

Did you perform adjustments of the p-values for multiple comparisons (e.g. Bonferroni, Tukey or the like?)

In the post-hoc analyses, the p-values were adjusted with Bonferroni correction but the tests presented in the tables were not. The reason for not adjusting these p-values was to reduce the risk of type II error, given the sample size. This information is now given in the manuscript.
Did you check with a statistician that it is valid to perform correlations using two contrast groups? Alternatively, did you try to make the correlations solely for MYA?

Point taken. We now have included only correlations for MYA in table 3.

Results:
Please provide F-values next to the p-values of the main effects throughout the results section

Point taken. F-values are now provided.

p.12 para 4: Group effect was 1.7 uV. By eye, the group effect looks much larger (Fig. 3), please re-check these results.
Also, please refer to fig.3 in the EMG section

The mean difference between groups was 19.7 µV. However, since the analyses were made using ln-transformed EMG measurements, the group effect derived from the mixed model analysis was much smaller. A reference to fig. 3 has now been added.

Discussion:
In general, there are some repeats from the results section, which is a bit redundant. The authors should consider looking through this again.

We have removed some of the repeats from the results section.

p.15 para 3: Trapezius EMG was higher during uninstructed rest, but not when subjects we instructed to fully relax. I find this highly interesting, and think you should do some speculations on to why this is so. Potentially, this could explain why these women develop pain (with the limitation that we did not know their EMG pattern before they got pain). And what can we do to counteract this phenomenon? E.g. should they be reminded several times a day to relax their muscles (since they can relax their muscles when told to)? Feel free to put in some speculations on this part in the manuscript.

See above (general comments).

p.16 para 6: I think you should consider calculating HRV. Even though it is not obtained during standardized conditions, it is obtained during similar conditions for CON and MYA. Thus, you can compare between the groups during the specified conditions. The time periods during the different tasks are sufficient to calculate HRV for each separate condition.

We have certainly considered calculating HRV. Since we have limited experience of HRV calculations at this point, we cannot guarantee valid HRV data from the
experimental conditions in this study. In forthcoming studies we are planning to include HRV measurements.

Figures:
Please provide the relevant information in terms of significant differences (*).

Indicating significant differences in the figures can be helpful for the reader. However, the number of time points is quite large and the figures become difficult to interpret if all the significant differences between time points in the post hoc analyses are indicated by asterisks.

Table 2: Spell out the abbreviations (e.g. below the table)

Point taken, Now corrected.

Table 3: Are P-values adjusted for multiple comparisons?

No they are not. See explanation above.