Author's response to reviews

Title: Upper limb position control in fibromyalgia

Authors:

Ellen Marie Bardal (ellen.bardal@svt.ntnu.no)
Karin Roeleveld (karin.roeleveld@svt.ntnu.no)
Tonje Okkenhaug Johansen (tonje.okkenhaug.johansen@stolav.no)
Paul J Mork (paul.mork@svt.ntnu.no)

Version: 2 Date: 13 June 2012

Author's response to reviews: see over
Responses to editor and reviewers comments:

We thank the editor and the reviewers for the positive evaluation of the paper and the efforts in further improving the manuscript. The manuscript has been revised in accordance with the reviewers’ comments and suggestions.

Reviewer #1 (page reference follows revised manuscript):

Version: 1 Date: 6 February 2012
Reviewer: Christian Duval
Reviewer's report:

The authors wanted to verify whether the ability to maintain limb position with and without loading was different in patients with fibromyalgia. Their hypothesis is that there is a deficit in proprioceptive feedback that may modify this capacity. They used a protocol where subjects were asked to maintain limb position by using visual feedback. They used variability in limb position during the task, as well as power distribution to examine the proposed deficits. They found that variability in limb position was different, but it did not reach statistical significance. However, there was a clear increase of power distribution in lower frequencies in fibromyalgic patients compared to controls. They attribute this fact to disruption of sensory feedback mechanisms.

In general, the paper is well written, and deserves attention. However, there are numerous issues that need to be addressed before the paper is considered for publication.

Major comments

1. **Reviewers comment:** In the Background section, you hypothesized “that the patient group will show higher amplitude oscillations than HCs”. However, this hypothesis is not addressed any more in the Discussion section. In fact, the results presented in this study tend to refute this hypothesis. What does this mean clinically? Moreover, literature mentioned in “Time domain” section of the Discussion indicated that patients in pain condition should not present difference in steadiness compare to control subjects. Then, on which literature your hypothesis is based on?

   **Response to comment:** Unfortunately, after submitting the manuscript we realized that the legends indicating group belonging in figure 3 were switched for the FM patients and HCs. We apologize for making this mistake, and the figure has now been corrected. Accordingly, the reviewer was misled in that figure 3 indicated a lower amplitude oscillation in patients than HCs. A sentence has been added in the first paragraph of the discussion to indicate that our results neither support nor refute the hypothesis of increased amplitude oscillations in FM. As mentioned in the last paragraph of the introduction, our hypothesis is based on the reported motor problems and altered sensory feedback processing in FM and not in chronic pain in general.

2. **Reviewers comment:** In the entire document, the terms “vertical acceleration of the limb” and “position of the limb” were almost used as synonyms. However, they not mean the same. You must mention how the conversion from acceleration to position has been made. Some issues can rise from the conversion. Firstly, the double integration of acceleration to obtained displacement value is not very efficient (Norman, Edwards et al. 1999). Secondly, for instance, a slow drift of the arm would probably not be detected by the accelerometer. Here, I suggest using the term “displacement” instead of “position”. Finally, how the linear “displacement” has been transformed in angular “displacement”? Is the length of different segments of the
upper limb have been measured? You must provide more information about the feedback presented to participants. What were they seeing on the screen (e.g. acceleration of the limb)? Is it an enhanced feedback? There is ample literature on the effect of enhanced feedback, and its influence on limb oscillations (see Loncharich & Newell (2011)).

Response to comment: We agree that the use of the accelerometer signal needed more explanation. Therefore we added the following text on page 6: The acceleration signal is determined by two components; the gravitational force and changes in the velocity of the accelerometer. The effect of the gravitational force is dependent on the orientation of the accelerometer in space which forms a robust signal which we have calibrated to arm position (degrees). Since we used an isometric task, the main component of the acceleration signal was determined by this arm position and was therefore used for feedback. The small variations around this main gravitational component are caused by the actual acceleration of the limb.

The feedback on the screen was slightly enlarged, but the screen was placed at a larger distance from the eyes than the arm, therefore, feedback was not enhanced to avoid overcorrection. More information about screen size and display range is added in the document on page 7.

We agree that a difference in segment length could affect limb acceleration. Unfortunately, the length of the segments has not been recorded. However, subject height was measured, which is related to limb segment length, and no relation between subject height and fluctuations or fluctuation frequencies have been found.

The term position of the limb is used when we refer to the task itself and the presentation of time domain variables, since these are given in degrees.

3. Reviewers comment: In the discussion section (page 13), you mentioned that muscles co-activation should explained difference between FM patients and HC participants. However, muscle co-contraction is known to increase oscillations amplitude (Carignan, Daneault et al. 2009; Daneault, Carignan et al. 2010) (tremor). This is not the case since amplitude were similar between groups and variance of limbs is similar between groups (even lower in the FM group).

Response to comment: As described above (see comment 1 above), the legend in figure 3 was switched between groups in the original manuscript. We have now rephrased the reporting of results for the time domain data to indicate the tendency of more variance in limb oscillatory amplitude among FM patients compared to HCs (see also comment 8 below).

4. Reviewers comment: There are missing results in the Result section. For instance, shoulder/neck pain was compare before and after the testing, but only the before value was mentioned in the manuscript (table 1). Also, SDs average of the two groups were compared, but never showed. This is only a few examples; there are more missing results in the manuscript.

Response to comment: We have now included the VAS score of shoulder/neck pain after testing in table 1. Regarding the average SDs we have now made a change to the reporting of time domain variance in the results section (see also comment 8 below). We have now added a column in figure 5 to include the results for the middle frequency band.

5. Reviewers comment: In the Muscle strength section of the Discussion, it is suggested that lower strength of the shoulder abductors of the FM group should be explained by
presence of pain in that region. Then, this interpretation is used to suggest the role of pain in the oscillation power spectrum distribution. This is too speculative.

Response to comment: We agree. The following text has been removed from the discussion section (p. 15): “Moreover, the similar finding in limb oscillation distribution for the elbow and shoulder joint might indicate that the changed power spectrum distribution is not directly affected by pain. This is in line with the weak correlations between pain-variables and power distribution found in the present study.”

6. Reviewers comment: Results addressing confounding factors should be added to the paper. Also, the gender of the healthy controls should be mentioned.
Response to comment: New within-group correlation analyses have been added in the results section. Except for arm girth there was no correlation between the background variables and normalized power in any of the frequency bands. Arm girth was significantly correlated in 15 of 32 possible correlations (2 groups, 2 tasks, 4 load levels = 32 correlations), and may therefore be a possible confounding factor. However, since there is a significant group difference in arm girth, the variable cannot be used as a confounder in our statistical model (Miller, G A, and Chapman, J P (2001) Misunderstanding analysis of covariance. Journal of abnormal psychology, 110(1), 40-48). As mentioned in the discussion (p.16, 2. para), if arm girth is a significant confounder in our analyses the relative effect should be highest in the unloaded tasks; however, this was not the case.
Gender of the HCs is now mentioned in the methods section (p. 4, 3. para).

Minor comments
7. Reviewers comment: Why results of the middle frequency band are not presented in Fig. 5?
Response to comment: See comment 4 above.

8. Reviewers comment: Did you do post-hoc (t tests) for the time domain analysis? If yes, please mention these results. Have you performed any corrections for multiple statistical comparison (e.g. Bonferroni correction)?
Response to comment: We have now made a slight change for the reporting of the results of the time domain analysis (p. 9, 3 para), i.e., included the results for group comparisons within the different load conditions.
We have not performed any multiple statistical comparisons (i.e., Bonferroni correction not relevant).

9. Reviewers comment: Can you define the type of oscillations mentioned in the first sentence of the third paragraph? Do you mean tremor or variation in limb position due to un-sustained muscle contraction?
Response to comment: The term ‘tremor’ has now been added in a parenthesis in the first sentence of the third paragraph.

10. Reviewers comment: What are the “selected anthropometric measures”? And how were they measured? For instance, where was the upper arm girth measured? Did you intend to measure the amount of fat, muscle volume, or simply take into account the mass of the limb? Please be more specific.
Response to comment: The term “selected anthropometric measures” has now been replaced with a listing of the actual variables (p. 5, 2. para) and we have added a description of the anthropometric measurements. The intention was to record anthropometric measures that indicate limb mass and to check whether these measures represent confounders for the amplitude of oscillations (time domain) and the frequency distribution of oscillations (frequency domain).
11. **Reviewers comment**: Where, on the upper limb (e.g., distance from the elbow), were attached the force transducers in the MVC condition? Why use two force transducers? Is the MVCs were performed in both arm at the same time? A better description of the methodology is needed. 

**Response to comment**: The force transducers used during elbow flexion and shoulder abduction were attached at the same positions as the loads in the position tasks (see description in figure legend [Fig. 1] original manuscript and also response 12 below). Two force transducers were used to check whether shoulder abduction was performed symmetrically. However, since there was no difference between the dominant and non-dominant side we chose to report the results from the dominant side only. The description of the recording of the MVCs has been changed to clarify the procedure (p. 7, 2 para).

12. **Reviewers comment**: Why the elbow flexion condition was performed unilaterally while the shoulder abduction task was performed bilaterally? And why the latter task was performed bilaterally while the non-dominant side was not assessed? 

**Response to comment**: The shoulder abduction task was performed bilaterally in an attempt to minimize the (potential) contribution from other muscles (e.g., by the oblique abdominal muscles by lateral bending). These issues are of little concern during elbow flexion since the upper arm was supported both medially and laterally. We did not assess the non-dominant side since the main purpose of the MVC measurement was to check whether reduced strength represents a confounder, i.e., we report MVC for the same arm that was used in the position task.

13. **Reviewers comment**: Since the acceleration of the upper arm was measured in a 45 degrees abduction of the shoulder position, how and why the vertical acceleration was calculated? Why don’t simply use the tangential acceleration? 

**Response to comment**: We simply used the vertical component of the accelerometer signal. Because of the orientation of the accelerometer on the segment, this component represents acceleration perpendicular to the longitudinal axis of the segment, which is vertical acceleration in the underarm, but not upper arm. We specified this in the text.

14. **Reviewers comment**: Please explain why you use loading. Just mentioning that you want to see the effect of loading is insufficient. You must explain the rationale behind it. 

**Response to comment**: First, different loading conditions were included to avoid confounding by limb mass. In other words, it can be assumed that a difference in frequency amplitude distribution between groups is independent of limb mass provided that different loads impose similar proportional changes in both groups. Second, two previous studies (Gerdle et al 2008; 2010) showed that differences between FM patients and HCs in firing rate, muscle fiber conduction velocity and differential activation of the trapezius muscle are load dependent. Thus, frequency distribution of limb oscillations may very well be affected by level of external loading. A reference to the studies by Gerdle et al has been added in the second paragraph in ‘Background’.

15. It would be wise to remove non-pertinent information, if it does not influence the protocol or the results. 

**Response to comment**: We are uncertain what information should be regarded as non-pertinent. The manuscript has been revised according to the reviewers’ recommendation and some information has been removed while some new information has been added.

**Level of interest**: An article of limited interest
Reviewer #2 (page reference follows revised manuscript):  
Version: 1 Date: 4 May 2012  
Reviewer: Kerstin Wentz  
Reviewer's report:

1. **Reviewers comment:** The concept of chronic pain is used in a very wide sense. Many different kinds of pain may be chronic and whether fibromyalgia is representative of chronic pain conditions that also affects a large subgroup of the population is not made clear.  
**Response to comment:** We agree and have now replaced the term ‘chronic pain’ with fibromyalgia (FM) where relevant. Our intention was not to generalize our findings to all chronic pain conditions.

2. **Reviewers comment:** In the background section fibromyalgia is described in terms of being a non-inflammatory disease and also associated with alterations in central processing in pain. Simultaneously from recent research the phenomenon of central inflammation in fibromyalgia is reported (e.g. Kadetoff et al., 2011). This makes the background section account appear as somewhat simplified or insufficient. This same principle seems also to apply to the question posed on neural processes that might induce alterations in neuromuscular control in chronic pain syndromes. There seem to be a kind of leap in coherence from muscular dynamics to the phenomenon of chronic pain meaning that sufficient argumentation regarding different dimensions of pain and links to muscular dynamics is not presented.  
**Response to comment:** We have now removed the term “non-inflammatory” from the first sentence in the introduction (whether FM is an inflammatory condition is not relevant for our study and no further changes have been made). We are uncertain what the reviewer asks for in the second part of the comment. Motor problems seem to be common in FM (see reference 5 and 6 in original manuscript) but are mainly self-reported. Thus, the purpose of our study was to investigate whether an association exists between FM and alterations in motor control, i.e., an attempt to bridge the gap between FM and the assumed association with motor problems by applying objective measures of motor performance. In other words, we attempt to bridge the gap that the reviewer describe as a “…leap in coherence from muscular dynamics to the phenomenon of chronic pain…”.

3. **Reviewers comment:** The participant’s characteristics are presented in table 1 and regarding tender point count and the FIQ score the control group is missing. Tender point count and FIQ scores are also not used in the calculations which makes the presence of these figures in table 1 not appearing as thoroughly planned. From table 1 can also be learned that the fibromyalgia group is physically significantly different from the healthy control group regarding body mass, upper arm girth and almost significantly physically different from the controls regarding height and epicondylar humerus width. The groups are thereby physically different (shorter, heavier with a wider girth). A relationship between these differences and a higher level of neck and shoulder pain (table 1) cannot be excluded. This same objection might apply to all the different measurements accounted for in the result section. Simultaneously this kind of investigations stands forth as important when trying to understand more regarding e.g. the dynamics of different defined conditions of pain and might thereby constitute a base for an article introducing a method?  
**Response to comment:** Unfortunately, we did not record number of tender points among the HCs but the scoring of shoulder/neck pain before and after testing indicates a sizeable difference in symptom level between the groups. It should be
noted that the descriptive variables reported in table 1 are mainly intended to serve as background information about the study sample and are not part of our main analysis/results.

Regarding the influence of physical characteristic: see comment 6, reviewer #1 above. The association between physical characteristics and pain *per se*, is beyond the scope of this paper (i.e., the main focus is on the association between pain/FM and motor control characteristics).

**Level of interest:** An article of limited interest  
**Quality of written English:** Acceptable  
**Statistical review:** No, the manuscript does not need to be seen by a statistician.