Author's response to reviews

Title: Changes in the expression of aromatase, estrogen receptor alpha and beta in mandibular condylar cartilage of rats induced by disordered occlusion

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Version: 2 Date: 27 March 2012

Author's response to reviews: see over
Dear editors of BMC Musculoskeletal Disorders,

Please find attached revised manuscript entitled “Changes in the expression of aromatase, estrogen receptor α and β in mandibular condylar cartilage of rats induced by disordered occlusion” (MS: 6799771886418927).

We have made the revision according to the comments from reviewers. All the changes have been highlighted in blue.

We thank you and reviewers for your careful reading of our manuscript. We hope it is now acceptable for publication in your journal.

Yours sincerely,

(on behalf of all authors)
Response to referee 1’s comment

[Point 1]: The written English is not all points clear. Background, p. 3. line 8:

“estrogen...attracted", better to say “has attracted”.

[Response]: According to your suggestion, the “has” has been added. Please see the revised manuscript Page 3 Line 9.

[Point 2]: P. 12 “estrogen played an important role…”, better as: “estrogen plays…”.

[Response]: Thank you for your suggestion, the “played” has been changed into “plays”. Please see the revised manuscript Page 3 Line 13.

[Point 3]: P.4”. line 3 “TMJ is a load-bearing articulation with its load” better as “structure” or “unit”.

[Response]: According to your suggestion, the “articulation” has been changed into “structure”. Please see the revised manuscript Page 4 Line 3.

[Point 4]: P.4 Line 12, “The hypothesis of the present study was”, better as: “hypothesis is…”.

[Response]: Thank you for your suggestion, the “was” has been changed into “is”. Please see the revised manuscript Page 4 Line 12.
[Response]: According to your suggestion, the “was” has been changed into “is”. Please see the revised manuscript Page 4 Line 12.

[Point 5]: In the Results now much of the data is given as descriptive data, without statistics. P. 8, last line: “degenerative changes, characterized by interrupted continuity of hypertrophic layer, pyknotic, homogeneous and eosinophilic lesion with few nuclei, and areas filled with eosinophilic nuclei near subchondral bone (Fig 1b and 1c), were observed in 2 and 4 joints of 8 joints from the female 2-wk and 4-wk experimental subgroups, and in 0 and 2 joints of 8 joints from the male 2-wk and 4-wk experimental ones. However, thickening changes in condylar cartilage, especially in hypertrophic layer, were found in 1 and 3 joints of 2-wk and 4-wk male experimental subgroups”. The number of the animals with distinct pathological changes should be tested statistically in each group and either there were statistically more clear pathological changes in the experimental groups or not, this should be described.

[Response]: According to your suggestion, we have calculated and ranked the percentage of degenerative regions, which has been tested statistically. The result showed that the percentage areas of OA-like degenerative regions in 4-wk female experimental groups were higher than other control and experimental groups (P<0.05). Please see the revised manuscript Page 6 Line 15-Page 7 Line 3, Page 9 Line 1-3 and Page 23.

[Point 6]: On page 13 it is stated “Although there were degenerative areas without immunoreactivity in these condyles with thickening changes, they were small and had only an insufficient influence on the expression of extracellular matrix in the whole condylar cartilage.
This is not in accordance with the Abstract: "Degenerative changes, characterized by interrupted continuity of hypertrophic layer, pyknotic and eosinophilic lesion with few nuclei, areas filled with eosinophilic nuclei, were observed in more joints from female experimental groups than male ones." So if the statistical testing is done concerning the existence of clear pathological changes in each group, it would clarify the interpretation of the results.

[Response]: Thank you for your good suggestion! The sentence “Although there were degenerative areas without immunoreactivity in these condyles with thickening changes, they were small and had only an insufficient influence on the expression of extracellular matrix in the whole condylar cartilage” has been deleted.

Similar to our response to [Point 5], the statistical testing has been done concerning the existence of clear pathological changes in each group. Please see the revised manuscript Page 6 Line 15-Page 7 Line 3, Page 9 Line 1-3 and Page 23.

Response to referee 2 (Prof. Sunil Wadhwa)’s comment

[Point 1]: It is difficult to make any conclusions of sex differences in hypertrophic layer without immunohistochemistry and/or gene expression for Collagen type 10.

[Response]: Thank you for your suggestion! The immunohistochemical staining and real-time PCR for Col X have been performed, and the results have been added. Please see the revised manuscript Page 2 Line 4 and Line 14, Page 7 Line 6-7, Page 8 Line 10, Page 9 Line 19-Page 10 Line 9, Page 12 Line 9 and Line 12, Page 22 Line 9-10.

[Point 2]: The result section needs to be re-written. Cannot follow the treatment, time and sex
[Response]: According to your suggestion, the result section has been re-written. Please see the revised manuscript Page 10 Line 2-Page 11 Line 14.

[Point 3]: First paragraph of the discussion is not needed because it is just a repetition of the results section.

[Response]: According to your suggestion, the first paragraph of the discussion was deleted. Please see the revised manuscript Page 11.

[Point 4]: Is this really a model of degeneration particularly the degeneration that is seen during osteoarthritis?

[Response]: In the present study, obvious OA-like degenerative changes in mandibular condylar cartilage, characterized by interrupted continuity of hypertrophic layer, pyknotic, homogeneous and eosinophilic lesion with few nuclei, areas filled with eosinophilic nuclei near subchondral bone, and chondrocyte island, have been found. Similar changes have been also indentified in several published articles including ours, listing as following.


What we have to say is that these OA-like degenerative changes were found in rats or rabbits, and our conclusion should be moderated to rats, not as a common statement. One paragraph “When interpreting the present results, one should keep in mind that the present OA-like lesions, as well as the expression of cytokines, cannot be equated with OA in human being because of the obvious differences in occlusion, as well as TMJ, between rats and human” has been added at the end of the discussion. Please see the revised manuscript Page 13 Line 22-Page 14 Line 2.