Author's response to reviews

Title: Comparative clinical characteristics of neuromyelitis optica spectrum disorders with and without spinal cord atrophy

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Response

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Title: Comparative clinical characteristics of neuromyelitis optica spectrum disorders with and without spinal cord atrophy
Authors: Yanqiang Wang, Aimin Wu, Xiaoyu Chen, Lei Zhang, Yinyao Lin, Shaoyang Sun, Wei Cai, Bingjun Zhang, Zhuang Kang, Wei Qiu, Xueqiang Hu, Zhengqi Lu

Dear Prof. Mr Jhonell De Los Santos

Thank you very much for your letter and advice. Thank you very much for your work concerning my paper. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and the amendments are highlighted in red in the revised manuscript. Point by point responses to the reviewers’ comments (Mickael Bonnan, Philippe Cabre) are listed below this letter.

Thank you for the reviewers’ comments concerning our manuscript (Mickael Bonnan, Philippe Cabre)

We hope that the revised version of the manuscript is now acceptable for publication in your journal (BMC Neurology).

I look forward to hearing from you soon.

With best wishes,

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We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Replies to Reviewer 1 (Mickael Bonnan)

Reviewer's report:
This article deals with spinal cord atrophy (SCA) in neuromyelitis optica (NMO). Two large groups of patients are compared with and without SCA. Progression index did not differ between the two groups, but the SCA group have mainly higher EDSS at onset and longer disease duration. Biological differences in two groups are commented and authors suggest that the higher general inflammation is predominant in the SCA group and may be targeted to halt neurodegenerative processes leading to SCA. SCA is a major problem in NMO, since spinal cord atrophy drives impairment. Predictive factors of SCA are welcome and this article gives insight in this problem. Authors emphasized the eventual role of microinflammation which a new but personal and putative hypothesis. However, plasma exchange and early steroids are recognized to change the prognostic of severe relapses. Data about these major parameters are omitted and should be added. Title is sound but English should be revised.

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: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests

Answer: Yes, Thank you very much. This is a good suggestion. We thank the reviewer for raising this critical question. Current treatment strategies include the use of corticosteroids and plasmapheresis for acute attacks and general or humoral immunosuppression for attack prevention. Treatment in the acute phase includes intravenous steroids and plasma exchange therapy. Immunosuppressive agents are recommended for the prophylaxis of relapses. We agree with the reviewer’s viewpoint. We review the literature about these.


[2] Lim YM, et al. had reported. A minimal pre-existing disability is the primary determinant of the effectiveness of plasma exchange.

[3] Merle H, et al. had reported. In optic neuritis associated with NMO, sequential treatment with pulsed intravenous corticosteroids and PE is more effective than standard monotherapy with corticosteroids on visual acuity outcome.
Morrow MJ, et al had reported Acute NMO relapses are generally treated with high-dose intravenous steroids, with plasma exchange often used as a rescue therapy for those who do not respond.

Khatri BO, et al had reported. Maintenance plasma exchange appeared safe and may bring about improvement in disability and sustained stabilization of the clinical course in patients with steroid-refractory relapsing forms of NMO.

Bonnan M, et al had reported. Plasma exchange (PLEX) is an appropriate technique in severe NMO attacks. And is a safe and efficient add-on therapy in NMO, in synergy with steroids.

Our references are as follows:


Although, plasma exchange is expected to improve long-term prognosis of NMO. In fact, At present, parenteral corticosteroids are widely employed as first-line treatment of optic neuritis and myelitis attacks, whereas therapeutic plasmapheresis is applied in the case of corticosteroids failure. In our study, the 185 NMOSD patients, including 23 patients with SCA and 162 patients without SCA. All of the patients received high-dose corticosteroids pulses [(methylprednisolone 1g, IV/d for 5d) for 2–3 courses, each treatment interval was three days] during the relapse period. And in remission period, all the patients are treated with oral small doses of prednisone (8-20 mg/d, oral) combined with azathioprine (50-100 mg/d). These had shown the good clinical efficacy. None of the NMOSD patients had underwent therapeutic plasmapheresis. plasma exchange and early steroids are recognized to change the prognostic of severe relapses. To explore the relationship between plasma exchange and early steroids and spinal cord atrophy (SCA) of NMOSD patients. a prospective, randomized, double blind, placebo-controlled, Multi-centre study design will be used.
We retrospectively analyzed 185 patients with NMOSDs, including 23 patients with SCA and 162 patients without SCA, again. According to the time of admission (<7 days of onset or > 7 days of onset) and management (standard corticosteroid therapy) in hospital, analyses were performed separately in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>NMOSDs with SCA (n = 23)</th>
<th>NMOSDs without SCA (n = 162)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 days of onset</td>
<td>9 (39.1%)</td>
<td>128 (70.01%)</td>
<td>0.0539</td>
</tr>
<tr>
<td>&gt;7 days of onset</td>
<td>14 (60.9%)</td>
<td>34 (20.99%)</td>
<td></td>
</tr>
</tbody>
</table>

NMOSDs = neuromyelitis optica spectrum disorders; SCA = spinal cord atrophy; *: P<0.05; **: P<0.01; P values also reflect comparison of percentages in clinical features.

“The ratio of admission time of onset (<7 days of onset or > 7 days of onset) and management in the NMOSD patients without SCA was significantly higher than that in the patients with MO SCA (p = 0.0539). However, no significant difference existed between the two groups. Our results showed a higher percent rate of admission time of onset (<7 days of onset) and management in patients without SCA but did not reach statistical significance. Although early steroids is recognized to change the prognostic of severe relapses, and delay the progression of SCA. This is likely attributed to the small sample size. However, any suggestion of a positive link between these parameters and SCA must be prompt further investigation with larger, prospective studies.”

“None of the NMOSD patients had underwent therapeutic plasmapheresis.”

Answer: Thanks very much for your comments, we have tried our best to revise the English of the whole MS carefully, and we hope the revised paper will be more clear and accurate on expressions.
Replies to Reviewer 2 (Philippe cabre)

Reviewer’s report:
Wang and Coll report in a very large series of NMOSD frequency of spinal cord atrophy (12.5%). The authors show that spinal cord atrophy is linked to disease duration and that NMOSD patients with spinal cord atrophy exhibit a more severe disability.

The topic is of interest since very few papers focussed on this important neuro-radiological parameter along the course of NMOSD.

However, there is an important methodological weakness in this study since the authors poorly determined spinal cord atrophy in their study. In addition, reproducible tool ie cord area at C2 level has been already published to measure spinal cord atrophy on MRI (Loussef and Coll, Brain 1998). Most importantly, the authors did not discuss this limitation.

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that i have no competing interests' below

Answer: This is a constructive question and suggestion. We are very appreciated with these important consideration and comments by the reviewer and agree with this.

Sorry, no comprehensive reviews on the subject have previously been published.

As the reviewer said, “However, there is an important methodological weakness in this study since the authors poorly determined spinal cord atrophy in their study. In addition, reproducible tool ie cord area at C2 level has been already published to measure spinal cord atrophy on MRI (Loussef and Coll, Brain 1998). Most importantly, the authors did not discuss this limitation.”

Although, In our study, “Spinal cord atrophy were evaluated according to previous reports of neuromyelitis optica (NMO)“.

Our references are as follows:

However, Based on the reviewers' suggest. We review the literature about these.

We’ve recognized that this description in the previous copy was not accurate. This is an important methodological weakness in our study. During the month of October, We retrospectively analyzed 23 patients with SCA, again. And all of the MRI scans were analyzed by one experienced neuroradiologist [Zhuang Kang] and one neurologist [Wei Qiu] again. “Five contiguous 3-mm axial slices from the caudal landmark of the C2/3 intervertebral disc were reformatted from the volume data set
and a coil radiofrequency uniformity correction was applied. Cord area was measured using a semi-automated method previously described by Losseff NA, Leary S M, Kearney H, et al.” In accordance with the reviewer’s suggestion, we have confirmed these preliminary findings again.

Our reference is as follows:

