

Peer Review File

Article information: <http://dx.doi.org/10.21037/tau-20-1072>.

Reviewer A

Regrettably, I think that there are countless typographical errors in the manuscripts. I strongly recommend that the manuscript should be thoroughly reviewed by all the members of the research group.

Comment 1: Examples of typographical errors:

p1, l25: NB + imMSC (BDNF) group (n=8) (P 2, L 11)

p1, l26: Three NB groups (P 2, L 12)

p2, l2: treatment improves lower urinary tract function (P 2, L 17)

p2, l3: treatment accelerates recovery of injured nerve tissue (P 2, L 18)

p2, l21, peripheral ? nerve (P 4, L 2)

p6, l9: NB + imMSC (BDNF) group (n=8) (P 7, L 15)

p6, l10: Three NB groups (P 7, L 16)

p6, l14: In groups of NB with imMSC and with imMSC (BDNF) (P 8, L 2)

p7, l16: pelvic nerve ? (PN) (P 8, L 4)

Reply 1: We have modified our text as advised

Introduction

Comment 2: The introduction needs to be more specifically explained for readers, especially in p3, 14-19.

Reply 2: We added more explanations in introduction.

Changes in the text: (P 5, L 1-7)

Comment 3: Moreover, you should explain why you select MPG injured model for this study.

What does “neurotrophic muscles” mean? (P 3, L 116)

Reply 3: We reinterpreted it in the article

Changes in the text: (P 5, L 1)

Methods

Comment 4: The detailed procedures to injure MPG should be described. And urinary management after MPG injury should be also described, which might be associated with the histopathological findings of the bladder.

Reply 4: We described how to injure MPG in detail in our previous study, so we cited it as a reference. As to urinary management, we did not operate it, in case of impacting the results of cystometry.

Changes in the text: (P 8, L 10)

Comment 5: How did you decide the dose of imMSCs (1 x 10⁶ MSCs) and the timing (1 week) of injection?

Reply 5: Our lab did the preliminary experiment and referred to the literature of the previous experiment.

Changes in the text: (P 8, L 5)

Comment 6: Did the “muscle tissue of both sides of the bladder” in p6, 115 mean lateral wall of detrusor (smooth muscle) or skeletal muscles around the bladder??

Reply 6: We reinterpreted it in the article

Changes in the text: (P 8, L 4)

Comment 7: How did you decide the timing of CMG and histological examinations (only 4 d)?

Reply 7: We had not enough rat models and time to explore which is the optimal time, so we just follow earlier studied (References 16).

Comment 8: Why did you not evaluate these rats at different periods?

Reply 8: Indeed, we'd better evaluate rats in a long time. As time passed, the effect of stem cells treatment would be changed. Unfortunately, we had not enough rat models and time to explore which is the optimal time which was a shortcoming of this experiment (P 21, L 3).

Comment 9: You should describe how to calculate positive rate of nerve, RARP, etc.

Reply 9: We used image J to separate IF image into red, blue and green figure. Use what we wanted to calculate to divide the summation (P 15, L 3).

Results

Comment 10: The findings of CMG should be shown in Table with measured data such as baseline pressure, threshold pressure, maximum voiding pressure, maximum capacity, voided volume, post-void residual, inter-contraction interval, etc.

Reply 10: Truly, we considered using a table to display the CMG results. But when we finished the table, we found it hard to directly show the changes in different group. So, we finally chose figure 2 (P 12, L 10).

Comment 11: Why did the CMG lines of NB and NB + imMSCs rat significantly fluctuate? Please replace them with more representative ones. The horizontal axis needs a label, such as sec, mL, etc.

Reply 11: We revised CMG figure to make it clearer and add unit of x-axis.

Changes in the text: Figure 2 (P 12, L 10).

Comment 12: p12, l 13 to p13, l7; How did you define “recovery” or “recovery rate” ?

Reply 12: As we described in manuscript, positive rate of nerve in injured nerve meant nerve recovery (P 12, L 1-9).

Comment 13: P14, 120; How did you define “faster”?

Reply 13: During the same time, more muscle protein expression means faster in this manuscript (P 16, L 13-17).

Comment 14: Data on thickness of detrusor may be required. Therefore, HE findings of each group should be appeared in the Results.

Reply 14: Reviewer’s advice is meaningful, we would add a HE staining in the further experiment to detect the changes of detrusor.

Discussion

Comment 15: You mention clinical application of this therapy to NLUTD due to peripheral nerve injury resulting from radical pelvic surgery. In this situation, it may be convenient that stem cells are injected to the bladder at surgery. Why did you delay the injection by 1 week in this experiment?

Reply 15: During this 1 week, we made sure that NB bladder was established. And in this 1 week, denervated atrophy came out in bladder in nerve injured group. So, we need this one week.

Comment 16: Some parts of the Discussion would be based findings that are not presented in the Results. also, some parts of the text are not understandable.

Reply 16: We revised the discussion according to our results and corrected some parts to make it earlier to understand.

Reviewer B

Authors have presented data on the effects of bladder wall injection of MSC in neurogenic bladder. Following concerns were noted

Comment 17: Cystometry x-axis trace is missing the units and authors need to show trace with bladder contraction in the NB group

Reply 17: The units of x-axis were added. We thought because of bladder injury in NB group so that bladder contraction in NB group was not clear.

Changes in the text: Figure 2(P 12, L 10)

Comment 18: Cystometry of sham and NB+imMSCs (BDNF) groups appear to show detrusor overactivity.

Reply 18: Because unit of time was minute, so it looked like a detrusor overactivity. Actually, if we turned minute to second as the unit of x-axis, the cystometry results would be easier to understand, which could not be adapted in figures.

Changes in the text: Figure 2 (P 12, L 10).

Comment 19: Did the authors allow the cystometry to stabilize for 2-3 hours after catheter implant before making the experimental readings.

Reply 19: Truly, we did not allow the cystometry to stabilize for 2-3 hours after catheter implant, which is the shortcoming in our experiment. Because we detected cystometry under anesthesia, so we could not wait 2-3 hours which would make rats dead.