Author's response to reviews

Title: Recovery of an injured corticoreticular pathway via transcallosal fibers in a patient with intracerebral hemorrhage

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Version: 3
Date: 17 April 2014

Author's response to reviews: see over
Reviewer 1

In this case report, the authors insisted that DT tractography demonstrated the recovery of an injured CRP via transcallosal fibers. Although the paper is quite interesting, there are serious concerns in this paper and the conclusion led by the authors does not sound convincing.

[Major points]

1) There is a possibility that the depicted lines of the left CRP at 16 weeks were artifacts, since fiber crossing, a major artifact in tractography1, is occasionally observed at the corpus callosum. The authors should set other combinations of ROIs for depicting the CRP and validate the lines (for example, (1) seed ROI: reticular formation of the medulla, target ROI: contralateral premotor cortex, (2) seed ROI: midbrain tegmentum, target ROI: contralateral premotor cortex). They also should show other tractography data of different timings such as follow-up after 16 weeks.

Answer: We agree with the reviewer’s comments. To rule out the possibility of artifact and for the more clear interpretation of result, we added 10-week DTT result. On the result of 6-week DTT, the reconstructed CRP fibers in affected hemisphere did not show the transcallosal fiber. On the other hand, discontinued CRP was weakly connected to the transcallosal fiber via corpus callosum on 10-week DTT, and it became thicker and was connected to the contralateral cerebral cortex via transcallosal fibers on 16-week DTT. In addition, the reconstructed CRPs in unaffected hemisphere also did not show the trancallosal fiber at the level of corona radiata. On the other hand, some studies have reported on motor recovery by transcallosal fibers of the corticospinal tract in stroke patients [1-3]. Consequently, we think that this result can be closely related with compensation of the injured CRP for the motor recovery.
Reference


NeuroRehabilitation 2009, 24(2):159-164.

2) Moreover, since the validation of the depicted lines of tractography is quite difficult, it is necessary to present the supporting data using other modalities such as electrophysiological examinations or functional MRI that show the increased activation of the contralateral premotor cortex.

Answer: Electrophysiological examinations such as transcranial magnetic stimulation can be used for the evaluation of the corticospinal tract status. However, as far as we are aware, there is no electrophysiological examination method for evaluation of the corticoreticular pathway. Regarding the functional MRI, it can be used for evaluation of distal joints which are related with the corticospinal tract. However, the proximal joints which are related with the function of the corticoreticular pathway can not easily be evaluated using function MRI due to motion artifact. As a result, for evaluation of the corticoreticular pathway, DTT is a almost unique method.

3) Since the conclusion is extraordinary novel, the authors should present the similar results in case series if possible. The authors already have reported stroke and head trauma cases involved the CRP. I wonder if there were other cases in them showing the recovery like this case.

Answer: Actually, it is first case which showed recovery of CRP via transcallosal fiber. So, we cannot present the other patients which showed similar recovery mechanism. However, regarding the corticospinal tract, there have been a few studies which have reported on motor recovery by transcallosal fibers in stroke patients. So, we already described in the discussion as follows (underline).
Discussion

This finding suggests that recovery via transcallosal fibers might accompany poorer motor outcome than recovery via the normally existing neural pathway of the CRP. On the other hand, with regard to the CST, a few studies have reported on motor recovery by transcallosal fibers in stroke patients [14-16]. Consequently, to the best of our knowledge, our study is the first study to demonstrate motor recovery by transcallosal fibers of the CRP in a stroke patient.


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.
Reviewer 2

Minor Essential Revisions

1. Corticoreticular pathway injury exists in what kind of patients? Why is author interested in the mechanism of it?
   
   Answer: It is well known that the CRP is originated from the premotor cortex and descended through the corona radiata, the anterior part of posterior limb of the internal capsule, midbrain tegmentum and terminated at the pontomedullary reticular formation. Therefore, any patients with the lesion in such CRP pathways including stroke and traumatic brain injury can show injury of the CRP. In addition, CRP is known as an important neural tract for proximal muscle and leg muscles. So, it is closely concerned with gait ability and trunk control. Therefore, we think that the investigation on the recovery mechanism of an injured CRP is important in the research fields of stroke rehabilitation.

2. The sequence number in the Case Presentation part is wrong.
   
   Answer: We cannot understand what mean the sequence number in the case presentation part. Could you please let us more detail information about the sequence number?.

3. What’s the cause of the spontaneous ICH?
   
   Answer: The patients had a history of hypertension and diabetes mellitus for past several years. So, we think those were the risk factors of the spontaneous ICH.

4. What kind of medicine has been used during the six-month post onset?
   
   Answer: We already described as follows (underline).

Case Presentation
He presented with severe weakness of the right upper and lower extremities with more severe weakness of proximal joint muscles than distal joint muscles (MRC: right shoulder abductor; 2−, finger extensors; 3+, hip flexor; 2+, ankle dorsiflexor; 3) (Table 1). He was administered comprehensive rehabilitative therapy, which included neurotropic drugs (dopaminergic drug [pramipexole, amantadine, and levodopa] and antidepressant [venlafaxine]), movement therapy, and neuromuscular electrical stimulation of the affected shoulder abductor, finger extensor, and ankle dorsiflexor[9,10].

5. What’s the function of TMS in this study, needs to be clarified.

Answer: We employed to demonstrate the recovery process of the corticospinal tract. So, we revised as follows.

**Transcranial Magnetic Stimulation**

Transcranial magnetic stimulation (TMS) was performed to demonstrate the recovery process of the corticospinal tract using a Magstim Novametrix 200 magnetic stimulator with a 9-cm mean diameter circular coil (Novametrix Inc).

6. How to get the conclusion that “recovery via transcallosal fibers might be associated with poorer motor outcome than recovery via the normally existing neural pathway of the CRP”? As authors did not compare two outcomes in the current study, it seemed to a comparison with a previous study.

Answer: To make clear the ambiguity, we revised the manuscript as follows.
Conclusion
We demonstrated recovery of an injured CRP via transcallosal fibers in a patient with ICH.
We believe that this might be one of the mechanisms for recovery of an injured CRP. In addition, when comparing motor outcome with that of previous study [8], our results suggest that recovery via transcallosal fibers appeared to be associated with poorer motor outcome than recovery via the normally existing neural pathway of the CRP.

Level of interest: An article of importance in its field

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: No.