

Format for ANSWERING REVIEWERS

August 29, 2014

Dear Editor,



Enclosed please find the edited manuscript in Word format (file name: 11634-review.doc).

Title: Functional topography of the corpus callosum investigated by DTI and fMRI.

Authors: Mara Fabri, Chiara Pierpaoli, Paolo Barbaresi, Gabriele Polonara

Name of Journal: *World Journal of Radiology*

ESPS Manuscript NO: 11634

The manuscript has been improved according to the reviewers' suggestions:

1 The format has been changed

2 The text has been revised as suggested by the reviewers

Reviewer 00685045

In this review the authors discuss the organization of the corpus callosum focusing on primary functions such as vision, audition and somatosensation. The manuscript was well written. I have the following comments. My major concern is that it was not obvious to me what is the unique contribution of this work to the literature. Specifically, how is the current report different from previous work by the authors (e.g., as cited in Fig. 3)?

The paper is an invited review of the functional organization of the corpus callosum; as such it is not expected to provide new data. As customary, our previous work has been compared, discussed and integrated with findings by other authors.

I would like to know how was the literature searched for the review? How were articles selected?

We selected papers reporting a clear activation of the corpus callosum evoked by a clear task or by sensory stimulation.

Perhaps a table summarizing these studies (e.g., function and corpus callosum location) will be helpful for the reader.

A Table (Table 1) summarizing the studies reporting activation in the CC has been added, as suggested. The following reference has been added in the legend and to the reference list:

Gawryluk JR, Mazerolle EL, D'Arcy RCN. 2014. Does functional MRI detect activation in white matter? A review of emerging evidence, issues, and future directions. Frontiers in Neuroscience, doi: 10.3389/fnins.2014.00239.

The manuscript was also lacking theoretical reference. Is there a theoretical framework these findings support? For example, does the organization of anterior/posterior regions of the corpus callosum present an expected organization signature?

The theoretical framework underlying the findings discussed in the paper is that the CC has a topographical organization, still not completely elucidated, that however can be explored in humans with the newer imaging techniques. The emerging hypothesis, which is however still far from being confirmed, is that the anterior and posterior regions CC, whose demarcation has not yet been clearly identified by anatomical criteria, may have different roles.

To highlight this notion, the following sentence and reference have been added in the paragraph "Final remarks", just before the "Conclusions":

"Another important issue to be resolved with the newer techniques, like diffusion fMRI (LeBihan, 2012), is whether the anterior and posterior portions of the CC have different roles".

LeBihan D. 2012. Diffusion, confusion and functional MRI. NeuroImage 62: 1131-1136.

Minor comments: 1. Page 4 "Myelination is believed to proceed..." Please provide a reference.

The following references have been added in the text and to the reference list:

Deoni SCL, Mercure E, Blasi A, Gasston D, Thomson A, Johnson M, Williams SCR, Murphy DGM. 2011. Mapping infant brain myelination with magnetic resonance imaging. J Neurosci 31: 784-791.

Provenzale JM, Isaacson J, Chen S. 2012. Progression of corpus callosum diffusion-tensor values during a period of signal changes consistent with myelination. AJR Am J Roentgenol 198: 1403-1408.

2. Page 11 Typo: "Final remarques" should be remarks.

The word has been edited.

3. Fig. 1: Please identify in the caption what number 1-7 refer to. Could you provide an image with a higher resolution?

Both changes have been made.

4. Fig. 2: Please refer to the source of these data.

They are the authors' original data, the source has now been added.

Reviewer 00012499

Well written review. The DTI part, however, is not up to date. Please discuss the impact of the

chosen b values on DTI of corpus callosum. ADC increases with the use of longer b values, also in corpus callosum [Papinutto et al. MRI 2013;31;827-39] and 3-compartment models may be needed to explain diffusion in cc [Ferizi et al., MRM 2013; in press].

The question raised by the reviewer is important; however, we feel it is outside the scope of this review, because the DTI data we have collected and discussed are not the basis of our study. Actually, the b-value we have used in our investigations is 1000 s/mm², and pixel size is 2 x 2 mm. With these intermediate values, FA recording in a 1.5 T magnet is scarcely affected (Papinutto et al., 2013). The data by Papinutto et al. do not undermine our choice of parameters, since the different values found in different CC regions may be due to structural differences between areas rather than to technical limitations. The paper by Ferizi et al. regards a single subject. However, a sentence has been added at the end of page 7 to take the notion into account, as follows: "It has recently been suggested that acquisition factors such as b-value and voxel size can affect the quantification of DTI parameters (i.e., FA and mean diffusivity, MD; Papinutto et al., 2013). For this reason extreme caution is required when comparing data obtained using different acquisition factors.", and the paper by Papinutto et al. has been added to the reference list.

Specific comments; p6, 2nd par: replace "..techniques ...PET, ...MRI, fMRI..." with: "MRI techniques including fMRI..."

The suggestion has been accepted.

Fig.1: replace this image by one with a better spatial resolution.

As also suggested by the other Reviewer, the image has been replace with one having better spatial resolution.

3 References and typesetting have been corrected

1 In the crosscheck report, which colored is similar with other articles, you need to revise these sentences to minimize the overlap.

The text has been revised to minimize the overlap.

2 For all references, please add PubMed citation numbers and DOI citation to the reference list and list all authors.

PMID (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>)

DOI (<http://www.crossref.org/SimpleTextQuery/>)

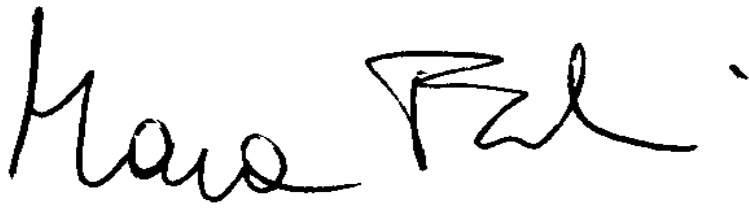
Such as: 1 **Nayak S**, Rath S, Kar BR. Mucous membrane graft for cicatricial ectropion in lamellar ichthyosis: an approach revisited. *Ophthal Plast Reconstr Surg* 2011; e155-e156 [PMID: 21346670 DOI: 10.1097/IOP.0b013e3182082f4e]

For all references, when present, the PubMed citation numbers and DOI citation to the reference list have been added. All authors are listed.

3 Please mark the location of table 1 in the text. Thank you!

The location of Table 1 has been marked in bold in the text on page 9.

Thank you again for publishing our manuscript in the *World Journal of Radiology*.

A handwritten signature in black ink, appearing to read 'Mara Fabri'.

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