Dear Editor,

We appreciate the effort of Santos and colleagues for writing the letter entitled “Diffuse axonal injury: diffusion tensor imaging and cognitive outcome”1, about the published article by Grassi et al.2 We thank them for all their comments on our paper and we acknowledge the opportunity to reply to their considerations.

Traumatic brain injury remains a major public health concern, directly affecting millions of otherwise healthy individuals, as well as, indirectly, their household members, who usually have to deal with long-term sequelae, including psychiatric symptoms and cognitive deficits. During the last years, advanced magnetic resonance (MR) techniques have played an important role in detecting abnormalities that were once under-recognized when using conventional MR technology. In particular, diffusion tensor imaging represents an important advanced MR tool in the context of traumatic brain injury and diffuse axonal injury3. There are already extensive compendiums concerning the physics of diffusion tensor imaging, however, instead, in our work we aimed to briefly review its basic principles and main analytical methods (region-of-interest, tractography and voxelwise analyses), along with the main relevant findings in the context of traumatic brain injury and diffuse axonal injury3.

Taking into account the advantages of diffusion tensor imaging in the noninvasive exploration of brain microstructure and networks, one should not be surprised by the striking number of recent publications using this technique in the evaluation of patients at different stages after a traumatic episode, ranging from mild to moderate and severe injuries2,3. However, there is still an urge to associate diffusion tensor imaging findings with clinical aspects and to correlate the scores with cognitive outcomes, making it valuable and accessible as a prognostic tool in a daily clinical practice.

Fortunately, new scientific studies are evolving steadily and, soon after our recently-published paper2, new evidences have strengthened the relationship between diffusion tensor imaging abnormalities and diffuse axonal injury outcomes. As pointed out by Santos et al., the work conducted by Hellstrøm and colleagues4 indicated robust associations between self-reported cognitive, somatic and emotional symptoms, 12 months after mild traumatic brain injury with white matter diffusion tensor imaging parameters, extracted with a voxelwise analysis, dubbed as tract-based spatial statistics. This work also reinforced physiologic effects of aging on brain white matter structures, leaving the older brain more vulnerable to subtle injury-related processes5. This also emphasizes the need to control age as a potential confounding variable in case-control diffusion tensor imaging studies.

A work by Leon et al.6 assessed 217 victims with moderate to severe traumatic brain injury 19 days after the traumatic episode. Twenty-eight white matter fiber bundles were chosen because of their susceptibility to trauma and were evaluated by region-of-interest analysis. Diffusion tensor imaging metrics were highly associated with unfavorable clinical outcomes after six months to one year after the trauma.

Furthermore, a recent meta-analysis of 20 studies investigated correlations between diffusion tensor imaging measures and seven cognitive domains in mild to severe traumatic brain injury victims. All studies pointed to a concordance between diffusion tensor imaging parameters and cognition: increased fractional anisotropy values were associated with higher cognitive performance, especially regarding memory and attention functions6.

It is expected that diffusion tensor imaging evaluation will potentially have clinical application in head injury survivors in the near future. Nevertheless, most findings hereafter were based on single works and hence upcoming studies are awaited to highlight the prognostic value of diffusion tensor imaging. There is still much work to be done. Larger scale, longitudinal analyses with homogeneous traumatic brain injury groups may play a decisive role in how this technique will prove helpful in predicting a patient’s prognosis and also aiding in selection of patients who might benefit from targeted therapies.

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Conflict of interest: There is no conflict of interest to declare.
Received 13 August 2018; Accepted 20 August 2018.
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