

# Reply

## Resposta

Daphine Centola Grassi<sup>1</sup>, Grasiela Rocha Barros da Silva<sup>1</sup>, Celi Santos Andrade<sup>1</sup>

Dear Editor,

We appreciate the effort of Santos and colleagues for writing the letter entitled “Diffuse axonal injury: diffusion tensor imaging and cognitive outcome”<sup>1</sup>, about the published article by Grassi et al.<sup>2</sup>. 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 injury<sup>3</sup>. 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 injury<sup>2</sup>.

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 injuries<sup>2,3</sup>. 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 paper<sup>2</sup>, 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 Hellström and colleagues<sup>4</sup> 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 processes<sup>3</sup>. 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.<sup>5</sup> 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 functions<sup>6</sup>.

It is expected that diffusion tensor imaging evaluation will potentially have clinical application in head injury survivors in the near future. Nevertheless, most findings heretofore 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.

<sup>1</sup>Universidade de São Paulo, Faculdade de Medicina, Departamento de Radiologia, São Paulo SP, Brasil.

**Correspondence:** Daphine C. Grassi; Departamento de Radiologia do HC-FMUSP; Av. Dr. Enéas de Carvalho Aguiar, 255; 05403-900 São Paulo SP, Brasil; E-mail: daphinegrassi@gmail.com

**Conflict of interest:** There is no conflict of interest to declare.

**Support:** Grants 2015/18136-1, 2016/05547-6, 2017/17065-9 and 2018/03563-2 from Sao Paulo Research Foundation – FAPESP.

Received 13 August 2018; Accepted 20 August 2018.

## References

---

1. Santos JGRP, Casto JPS, Teixeira MJ, Andrade AF, Paiva WA. Diffuse axonal injury: diffusion tensor imaging and cognitive outcome. *Arq Neuropsiquiatr*. 2018;76(10):724. <https://doi.org/10.1590/0004-282X20180113>
2. Grassi DC, Conceição DD, Leite CC, Andrade CS. Current contribution of diffusion tensor imaging in the evaluation of diffuse axonal injury. *Arq Neuropsiquiatr*. 2018 Mar;76(3):189-199. <https://doi.org/10.1590/0004-282x20180007>
3. Shenton ME, Hamoda HM, Schneiderman JS, Bouix S, Pasternak O, Rathi Y et al. A review of magnetic resonance imaging and diffusion tensor imaging findings in mild traumatic brain injury. *Brain Imaging Behav*. 2012 Jun;6(2):137-192. <https://doi.org/10.1007/s11682-012-9156-5>
4. Hellstrom T, Westlye LT, Kaufmann T, Doan NT, Soberg HL, Sigurdardottir S et al. White matter microstructure is associated with functional, cognitive and emotional symptoms 12 months after mild traumatic brain injury. *Sci Rep*. 2017 Oct;7(1):1-14. <https://doi.org/10.1038/s41598-017-13628-1>
5. Leon ANC, Cicuendez M, Navarro B, Munarriz PM, Cepeda S, Paredes I et al. What can be learned from diffusion tensor imaging from a large traumatic brain injury cohort?: white matter integrity and its relationship with outcome. *J Neurotrauma*. Published Online: Jul 6, 2018. Available at: <https://doi.org/10.1089/neu.2018.5691>
6. Wallace EJ, Mathias JL, Ward L. The relationship between diffusion tensor imaging findings and cognitive outcomes following adult traumatic brain injury: a meta-analysis. *Neurosci Biobehav Rev*. 2018 Sep;92:93-103. <https://doi.org/10.1016/j.neubiorev.2018.05.023>