Acta Neurochirurgica (2019) 161:1403–1405
https://doi.org/10.1007/s00701-019-03852-1

EDITORIAL (BY INVITATION) - FUNCTIONAL NEUROSURGERY - PAIN

Fraction of anisotropy and apparent diffusion coefficient as diagnostic tools in trigeminal neuralgia

Paulo Roberto Lacerda Leal[1]

Received: 11 February 2019 / Accepted: 13 February 2019 / Published online: 21 February 2019

Strong evidence suggests that classical trigeminal neuralgia (TN) is caused by a focal insult on the trigeminal root, usually due to neurovascular compression (NVC), justifying microvascular decompression (MVD) as the first neurosurgical option [29].

High-resolution magnetic resonance imaging (MRI) sequences (three-dimensional [3D] T2-weighted, 3D time-of-flight magnetic resonance angiography, and 3D T1-weighted-gadolinium, in association) revealed effective for depicting the fine trigeminal neurovascular anatomy, of paramount importance for planning MVD [18]. Also, structural abnormalities—such as nerve deviation, groove formation, or atrophy—can be seen in a large number of cases with TN [12]. Volume and cross-sectional area measurements obtained by MRI were significantly smaller on the affected nerves than on the unaffected nerves [19]. Pathological examination of specimens collected during surgery showed axonal loss and demyelination [11], but these morphological changes can be difficult to interpret.

As diffusion tensor imaging (DTI) is able to assess tissue integrity, this method has been applied to the study of abnormalities in white matter tracts, independent of their cause. DTI quantifies the amount of non-random water diffusion within tissues and provides unique in vivo information about the pathological processes that affect water diffusion as a result of microstructural damage [2]. Fraction of anisotropy (FA) and apparent diffusion coefficient (ADC) represent the two main DTI indices that are most widely used. FA describes how much molecular displacements vary in space and is related to the presence of oriented structures [28]. ADC, expressed as square millimeter per second, characterizes the overall mean-squared displacement of molecules and the overall presence of obstacles to diffusion [2, 28].

These evidences motivated several studies to examine structural abnormalities in the trigeminal nerve (TGN) of patients with TN using FA [5–7, 9, 10, 13–15, 17, 22–25, 30] and ADC [7, 13, 17, 23–25]. Most of the studies examining FA by comparing the affected and unaffected sides of patients and controls revealed a significant decrease in FA values [5–7, 9, 10, 14, 15, 17, 22–25]. Chen et al., Leal et al., and Lummel et al. reported a significant elevation in ADC values in the affected sides of patients [7, 17, 23]. Other three studies did not find differences in ADC values between affected and unaffected sides of patients and controls [13, 24, 25]. Concerning only DTI studies about TN caused by NVC, six articles found a significant decrease in FA values [14, 17, 22–25] and two a significant increase in ADC values [17, 23] in the affected nerves.

The measurement of FA and ADC provides robust values for quantifying the degree of microstructural abnormalities of TGN. Degeneration or damage of white matter tracts is expected to result in reduced FA, owing to the loss of directionality of diffusion and increase in ADC, that is due to diffusivity being averaged in all spatial directions as a result of the loss of myelin and axonal membranes [1]. However, studies had some limitations. Measurements were extracted using resolutions that may not be sufficient to reveal all abnormalities. With DTI, multiple images are collected so that the signal can be sensitized to diffusion in different directions, building up multiple measurements for each voxel in the brain [16]. Only six of the abovementioned studies were performed with 30 or more diffusion gradient-directions [5, 7, 9, 10, 17, 30]. Other limits are the potential partial volume effects caused by the small size of the root bathed in cerebrospinal fluid and the artifactual images caused by involuntary patient motion.

Two studies compared diffusion abnormalities in patients with TN before and after surgery [10, 15]. DeSouza et al. studied patients who underwent gamma knife radiosurgery (GKRS, 15 patients) or MVD (10 patients) and 14 controls

This article is part of the Topical Collection on *Functional Neurosurgery - Pain*

✉ Paulo Roberto Lacerda Leal
prlleal@hotmail.com

[1] Department of Neurosurgery, Faculty of Medicine, Federal University of Ceará, 100, Avenida Comandante Maurocelio Rocha Pontes, Sobral 62042-280, Brazil

[10]. Authors established a cutoff of at least a 75% reduction in preoperative pain to distinguish effective from ineffective treatment [10]. After effective treatment (group of 6 patients who had GKRS and 9 patients who had MVD), the FA abnormality in the affected side resolved such that FA increased and was no longer significantly different from the unaffected side or controls [10]. However, FA remained significantly lower in the affected side compared with the unaffected side and controls in the ineffective treatment (group of 9 patients who had GKRS and 1 patient who had MVD) [10]. Authors suggested that surgical treatment can effectively resolve pain by normalizing trigeminal root abnormalities [10]. In Hodaie et al.'s study, radiosurgery resulted in 47% drop in FA values at the target with no significant change in FA outside the target, demonstrating highly focal changes after treatment, suggesting that radiosurgery primarily affects myelin [15].

The mechanisms underlying the analgesic effect of surgical treatment are not well understood. Previous studies performing ultrastructural and immunohistochemical analyses of the TGN in patients with TN have consistently shown abnormalities at the root entry zone including demyelination [26]. Cottee et al. performed a cat model of demyelination mediated by pressure on the optic nerve and found remyelination 6 weeks after pressure cessation and a possible recovery at 11 weeks after pressure cessation [8]. The reversible increase of FA could be explained with neural tissue recovery with remyelination after nerve decompression. On the other hand, the nerve damage caused by chronic pulsatile vascular compression can be definitive due to irreversible lesions in TGN myelin, even after removal of the compression, explaining the persistence of loss of anisotropy after surgery.

ADC increase quantifies the overall presence of obstacles to diffusion, being correlated with not only demyelination but also with neuroinflammatory processes and/or neuroedema [1]. The possible recovery of ADC values would suggest an improvement of conduction and reduction of edema of the trigeminal root after surgery.

MRI studies have shown that images of NVC on the TGN frequently occur in persons without facial pain and it is widely admitted that a contact between a vessel and the TGN is not necessarily pathological [3, 27]. Further, a certain number of patients with TN do not display NVC [4]. Certain authors did not find changes in DTI parameters in asymptomatic individuals with unilateral NVC [20, 21], suggesting that neither demyelination nor axonal injury exists when a vascular contact is not pathological.

In summary, DTI indices allow to better understand the pathophysiology of TN as well as treatment effects. DTI may become an essential diagnostic test for TN in the near future.

References

1. Basser PJ, Pierpaoli C (1996) Microstructural and physiological features of tissues elucidated by quantitative-diffusion-tensor MRI. J Magn Reson 213:560–570
2. Basser PJ, Mattiello J, Le Bihan D (1994) Estimation of the effective self-diffusion tensor from the NMR spin echo. J Magn Reson 103:247–254
3. Brînzeu A, Drogba L, Sindou M (2018) Reliability of MRI for predicting characteristics of neurovascular conflicts in trigeminal neuralgia: implications for surgical decision making. J Neurosurg 1:1–11
4. Burchiel KJ (2016) Trigeminal neuralgia: new evidence for origins and surgical treatment. Neurosurgery 63(Suppl 1):52–55
5. Chen DQ, DeSouza DD, Hayes DJ et al (2016) Diffusivity signatures characterize trigeminal neuralgia associated with multiple sclerosis. Mult Scler 22(1):51–63
6. Chen F, Chen L, Li W et al (2016) Pre-operative declining proportion of fractional anisotropy of trigeminal nerve is correlated with the outcome of micro-vascular decompression surgery. BMC Neurol 16:106
7. Chen ST, Yang JT, Yeh MY et al (2016) Using diffusion tensor imaging to evaluate microstructural changes and outcomes after radiofrequency rhizotomy of trigeminal nerves in patients with trigeminal neuralgia. PLoS One 11(12):e0167584
8. Cottee LJ, Daniel C, Loh WS et al (2003) Remyelination and recovery of conduction in cat optic nerve after demyelination by pressure. Exp Neurology 184:865–877
9. DeSouza DD, Hodaie M, Davis KD (2014) Abnormal trigeminal nerve microstructure and brain white matter in idiopathic trigeminal neuralgia. Pain 155:37–44
10. DeSouza DD, Davis KD, Hodaie M (2015) Reversal of insular and microstructural nerve abnormalities following effective surgical treatment for trigeminal neuralgia. Pain 156(6):1112–1123
11. Devor M, Govrin-Lippmann R, Rappaport H (2002) Mechanism of trigeminal neuralgia: an ultrastructural analysis of trigeminal root specimens obtained during microvascular decompression surgery. J Neurosurg 96:532–543
12. Erbay SH, Bhadelia RA, O'Callaghan M et al (2006) Nerve atrophy in severe trigeminal neuralgia: non-invasive confirmation at MR imaging – initial experience. Radiology 238:689–692
13. Fujiwara S, Sasaki M, Wada T et al (2011) High-resolution diffusion tensor imaging for the detection of diffusion abnormalities in the trigeminal nerves of patients with trigeminal neuralgia caused by neurovascular compression. J Neuroimaging 21:102–108
14. Herweh C, Kress B, Rasche D et al (2007) Loss of anisotropy in trigeminal neuralgia revealed by diffusion tensor imaging. Neurology 68:776–778
15. Hodaie M, Chen DQ, Quan J et al (2012) Tractography delineates microstructural changes in the trigeminal nerve after focal radiosurgery for trigeminal neuralgia. PLoS One 7:e32745
16. Johansen-Berg H, Rushworth MF (2009) Using diffusion imaging to study human connectional anatomy. Annu Rev Neurosci 32:75–94
17. Leal PR, Roch JA, Hermier M et al (2011) Structural abnormalities of the trigeminal root revealed by diffusion tensor imaging in patients with trigeminal neuralgia caused by neurovascular compression: a prospective, double-blind, controlled study. Pain 152:2357–2364
18. Leal PRL, Hermier M, Souza MA et al (2011) Visualization of vascular compression of the trigeminal nerve with high-resolution 3-T MRI: a prospective study comparing pre-operative imaging analysis to surgical findings in 40 consecutive patients who underwent micro-vascular decompression for trigeminal neuralgia. Neurosurgery 69(1):15–26

19. Leal PR, Barbier C, Hermier M et al (2014) Atrophic changes in the trigeminal nerves of patients with trigeminal neuralgia due to neurovascular compression and their association with the severity of compression and clinical outcomes. J Neurosurg 120:1484–1495
20. Lin W, Chen YL, Zhang QW (2014) Vascular compression of the trigeminal nerve in asymptomatic individuals: a voxel-wise analysis of axial and radial diffusivity. Acta Neurochir 156:577–580
21. Lin W, Zhu WP, Chen YL et al (2016) Large-diameter compression arteries as a possible facilitating factor for trigeminal neuralgia: analysis of axial and radial diffusivity. Acta Neurochir 158:521–526
22. Liu Y, Li J, Butzkueven H et al (2013) Microstructural abnormalities in the trigeminal nerves of patients with trigeminal neuralgia revealed by multiple diffusion metrics. Eur J Radiol 82:783–786
23. Lummel N, Mehrkens JH, Linn J et al (2015) Diffusion tensor imaging of the trigeminal nerve in patients with trigeminal neuralgia due to multiple sclerosis. Neuroradiology 57:259–267
24. Lutz J, Linn J, Mehrkens et al (2011) Trigeminal neuralgia due neurovascular compression: high-spatial-resolution diffusion-tensor imaging reveals microstructural neural changes. Radiology 258:524–530
25. Lutz J, Thon N, Stahl R et al (2016) Microstructural alterations in trigeminal neuralgia determined by diffusion tensor imaging are independent of symptom duration, severity. and type of neurovascular conflict J Neurosurg 124(3):823–830
26. Marinković S, Cetković M, Gibo H et al (2010) Immunohistochemistry of displaced sensory neurons in the trigeminal nerve root. Cells Tissues Organs 191(4):326–335
27. Peker S, Dinçer A, Necmettin Pamir M (2009) Vascular compression of the trigeminal nerve is a frequent finding in asymptomatic individuals: 3-T MR imaging of 200 trigeminal nerves using 3D CISS sequences. Acta Neurochir 151:1081–1088
28. Pierpaoli C, Basser PJ (1996) Toward a quantitative assessment of diffusion anisotropy. Magn Reson Med 36:893–906
29. Sindou M, Howeidy T, Acevedo G (2002) Anatomical observations during microvascular decompression for idiopathic trigeminal neuralgia (with correlations between topography of pain and site of the neurovascular conflict). Prospective study in a series of 579 patients. Acta Neurochir 144(1):1–12 discussion 12-3
30. Wilcox SL, Gustin SM, Eykman EN et al (2013) Trigeminal nerve anatomy in neuropathic and non-neuropathic orofacial pain patients. J Pain 14(8):865–872