Application of diffusion tensor imaging in detecting microstructural alteration of the trigeminal nerve root in patients with classical trigeminal neuralgia without neurovascular compression

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Research

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Abstract

Background

Diffusion tensor imaging (DTI) was used to detect microstructural alteration and influence of surgical intervention of the trigeminal nerve root (TR) in patients with classical trigeminal neuralgia (CTN) without neurovascular compression (woNVC) who had undergone internal neurolysis (IN).

Methods

Overall, 21 patients with CTN woNVC who underwent IN and 20 healthy controls were included prospectively. The differences in the means, kurtosis and skewness of each of the diffusivity metrics between the affected and unaffected nerves in patients and both nerves in controls, were then analyzed using the independent *t* test. Data from the affected side and the unaffected side before and 1 years after IN were compared.

Results

There were significantly different mean and kurtosis values for both FA and ADC of the affected side TR, compared to the unaffected side and control group respectively before IN. 1 year after surgery, most of these differences significantly reduced in comparison between the affected side and unaffected side, the affected side and control group, and these trends were also in accordance with the relief of pain. The Pearson correlation coefficient showed a strong negative correlation between decrease of ADC in the affected side compared to the surgical outcome in BNI total score.

Conclusions

The changes of diffusive property of TR could explain the efficiency of IN. The pretreatment DTI metrics could be an effective prognostic factor for providing potential noninvasive, brain-based biomarkers to support an optimal treatment selection for individual patients with CTN woNVC.

Background

Trigeminal neuralgia (TN) is a condition that can cause intense even unbearable orofacial pain localized to the sensory supply areas of the trigeminal nerve, which can dramatically interfere with the normal activities of daily living.[1] The pathological mechanism of classical TN has been recognized by the theory that it is a kind of disease results from neurovascular compression (NVC) of the trigeminal nerve root.[9] Microvascular decompression (MVD) was exactly designed based on this etiological explanation, and has been accepted as the most efficient treatment of classical TN currently.[22] However, strong evidence suggests that there are also a cohort patients of TN without NVC (woNVC) discovered by preoperative morphological magnetic resonance imaging (MRI) and proved by surgical finding.[8; 14; 24]

Traditional morphological MRI has been shown to be effective for depicting the fine trigeminal neurovascular anatomy, of paramount importance for determining NVC.[9; 23; 28] However, in several previous researches, investigators have found that there were some cases underwent MVD in absence of NVC yet showed positive NVC in preoperative image.[11; 14] In contrast, some clinical articles described that a significant number of TN patients have no NVC at all, and internal neurolysis (IN) has been reported as an emerging efficient surgical method for TN woNVC. [12; 31]

Recently, several studies have revealed the existence of microstructural changes in TN patients with NVCS (wNVC) using diffusion tensor imaging (DTI), which showed various alteration of the values diffusivity metrics: fractional anisotropy (FA), apparent diffusion coeffcient (ADC), radial diffusivity (RD), or/and axial diffusivity (AD).[10; 18; 21] These previous results indicated a water diffusion change in the microenvironment in the affected trigeminal nerves with NVCS, and the diffusivity metrics of DTI may be potential tools in evaluating the trigeminal nerves and in estimating the prognosis of TN. Additionally, one study used DTI and its diffusivity metrics to investigate pain relief in patients with TN 4 year after MVD, and suggested that FA and ADC can provide prognostic information.[13] Another study revealed that the preoperative diffusivity metrics of DTI have high predictive value for the prognosis of patients who underwent radiofrequency lesioning (RFL).[16] Also recent study reported that increased trigeminal nerves volume and FA, and a decreased ADC, AD, and RD represent the pathophysiology of TN, and decreased trigeminal nerves volume, FA, and AD compared with the normal side after a one-year follow-up of partial rhizotomy (PR) of sensory root of trigeminal nerve.[3] These studies provided us information and concepts that DTI and its diffusivity metrics may have clinical significance for microstructural change and prognosis evaluation.

We systematically evaluated FA and ADC values in a patient cohort that underwent IN for TN woNVC and looked for possible interactions with the clinical and anatomical parameters. We hypothesized that the microstructural status of the trigeminal nerve of the affected side is significantly different compared to the unaffected side in patients and controls, and these microstructural abnormality could be improved in the diffusion of the trigeminal root after IN.

Methods

Study Population

A total of 21 patients with classical TN (CTN) and 20 healthy controls were retrospectively included in our study. All patients were clinically examined by an experienced neurosurgeon (Dr. X.-F.J.) and met the criteria of the International Headache Society for TN.[1] CTN is defined as idiopathic, episodic, lancinating pain that lasted seconds, with pain-free episodes between attacks.[6] Only patients without previous surgical treatment for TN were included in this study. Patients with secondary factors may resulting in

TN, such as cranial tumors, or vertebrobasilar dolichoectasia resulting in brainstem compression, were excluded from this study. Patients with a diagnosis of multiple sclerosis (MS) or having signs or symptoms of MS were also excluded. Patients with bilateral facial pain were also excluded. Ipsilateral and contralateral nerves in these controls were based on the laterality of TN in matched patients. For example, controls matched to right TN patients will have ipsilateral nerve on the right.

MRI Examination And Analysis

MRI was performed on a 3.0-T MRI scanner (Signa HDx; 3T GE Healthcare) using a standardized protocol.[21] Images were obtained using an 8-channel head coil with sensitivity encoding parallel processing capability, with the application of 64 non-collinear directions of diffusion gradients. The sequences and their parameters are summarized in Table 1.

Table 1
Sequence parameters for anatomical imaging

Parameter	3D T1-BRAVO	3D-FIESTA	3D-TOF-MRA	DTI
TR (msec)	8.2	19	38	10.5
TE (msec)	3.2	3.4	2.3	6.5
FOV (mm)	240	180	200	220
Matrix (mm × mm)	256 × 256	360 × 360	320 × 224	256 × 256
Slice thickness (mm)	1.2	1.0	0.8	2.0
NEX (n)	1	2	1	4
Resolution	0.4 × 0.4 × 0.6	0.5 × 0.5 × 0.5	0.5 × 0.5 × 0.5	2 × 2 × 2
Duration	6 : 50	4 : 05	4 : 25	9 : 34

Morphological MRI Data Analysis

Three-dimensional brain volume T1-weighted postcontrast sequence (3D-T1 BRAVO), three-dimensional fast imaging employing steady-state acquisition (3D-FIESTA) and three-dimensional Time-of-Flight magnetic resonance angiography (3D-TOF MRA) images were analyzed collaboratively by 1 experienced neuroradiologists (Dr. J.Q.) and 1 experienced neurosurgeon (Dr. M.W.), who were blinded to the clinical data including the side of nerve affection. Multiplanar reconstructions were used to assess the trigeminal nerves on both sides separately using a step-by-step approach to determine the presence or absence of the NVC. Contact was declared if no layer of the CSF was discernible between the nerve and the respective vessel on the high-resolution 3D-FIESTA sequences.

Analysis Of The DTI Data Sets

Postprocessing and analysis of the DTI data sets were performed in a blind fashion (for clinical data and intra-operative findings) using the GE Healthcare AW VolumeShare™ 5 software on a commercially available workstation (AW 4.6; GE Healthcare). Accurate measurement was confirmed by the same two physicians with profound experience using this protocol. In order to limit potential partial volume effects due to the small size of the whole segment of trigeminal nerve root (TR) in posterior fossa, special attention was paid to the region of interest (ROI)-placement procedure: two physicians reviewed the ROIs on the FA and ADC colormaps and verified the DTI with the 3D-FIESTA anatomical images in the axial plane for a cross-reference, and reconfirm the ROIs by viewing the fusion imaging of FA and ADC colormaps emerged to corresponding 3D-BRAVO slice. An example of ROI placement is illustrated in Fig. 1a-d. For statistical analysis, we used the mean, kurtosis and skewness values of the two observers. The kurtosis of a normal distribution is equal to 3, and a normal distribution will have a skewness of 0, these two factors could provide insights into the shape of the distribution. The intraclass correlation coefficient of inter-observer reliability for the average FA and ADC were less than 5%.

Internal Neurolysis

All patients were placed in the park bench position and underwent suboccipital retrosigmoid craniotomy under general anesthesia. After complete exploration of the trigeminal root from the brainstem to the porus trigeminus of Meckel's cave, and verifying the situation of no NVC of whole segment of TR in posterior fossa, Drs. X.-F.J. and M.W. decided and performed IN together, which had been published previously.[31] Both intraoperative findings and postoperative review of operative video were used to confirm the diagnosis of woNVC TN retrospectively.

Evaluation Of The Effect Of In On Pain

Two neurosurgeons (Drs. Q.-S.D. and S.-D.W.) assessed all 21 patients in person at discharge (generally on postoperative day 7), at the first outpatient visit (usually around postoperative day 50), and at 1 year after surgery by the Barrow Neurological Institute (BNI) pain intensity score and the BNI facial numbness score, which were considered comprehensively by adding the total of both scores (Table 2). The results of follow-up at 1 years after surgery were considered as the final outcome in this study.

Table 2
Barrow Neurological Institute Pain Intensity Score, Facial Numbness Score, and Total Evaluation of Results

(P) Evaluation of pain relief by BNI pain intensity score
1 No pain, no medication
2 Occasional pain, not requiring medication
3 Some pain, adequately controlled with medication
4 Some pain, not adequately controlled with medication
5 Severe pain/no pain relief
(N) Evaluation of numbness by BNI facial numbness score
1 No facial numbness
2 Mild facial numbness, not bothersome
3 Facial numbness, somewhat bothersome
4 Facial numbness, very bothersome
(T) Total evaluation of results = (P) + (N)
2 Excellent
3 Good
4 Fair
≧ 5 Poor

Statistical Analysis

The differences in mean values, as well as the kurtosis and skewness values of each of the diffusivity metrics (FA and ADC) was compared in the affected and unaffected sides of patients 1 years after surgery. These results were also compared with those of the affected and unaffected sides of patients preoperative and compared with controls using a paired-sample two-tailed *t* test. Correlations between increase of FA, decrease of ADC in affected sides and surgical outcome in BNI total scores were analyzed respectively. Data was presented as mean ± standard error of the mean (SEM) or standard deviation (SD). The Pearson correlation coefficient was calculated, and a linear regression curve was plotted using GraphPad Prism® statistical analysis software. A *p*-value of < 0.05 was considered significant.

Results

Clinical Patient Characteristics

A total of 21 patients were enrolled (10 men and 11 women) (Table 3). The mean duration of TN symptoms was 63.6 ± 8.2 months (range 18–138 months). All patients had TN despite being on medication (carbamazepine or oxcarbazepine) for at least 6 months before surgery was scheduled. Among these, the left side was affected in 8 patients (38.1%), and the right side was affected in 13 patients (61.9%). 15 patients presented with an isolated affection in a single branch of the trigeminal nerve, which included the second branch (V2) in 9 patients (42.9%) and the third branch (V3) in 6 patients (28.6%). No patient exhibited involvement of the first trigeminal branch (V1) alone. 5 patients (23.8%) presented with a combined affection of V2 plus V3, and 1 patient (4.8%) presented with a combination of V1 and V2. No patients, all 3 branches (V1–V3) were involved.

Table 3
Demographics and disease features of 21 patients with TN

Factor	Value*
Total	21
Sex (male/female)	10/11
Age (year)	56.63 ± 7.98
Symptom duration (month)	63.6 ± 8.2
Side affected (L/R)	8 / 13
Nerve branch	
V1	0
V2	9
V3	6
V1 + V2	1
V2 + V3	5
V1–3	0

* Values are presented as the number of patients unless otherwise stated.

Preoperative Morphological MRI Findings

The absence of NVC in 17 cases (81.0%) and the suspicious NVC in other 4 cases (19.0%) on the affected side were determined based on conventional morphological MRI. Structural abnormalities such as nerve deviation or atrophy of affected side compared by unaffected side can be seen in 9 cases (42.9%). The morphological MRI also verified that no cases showed the manifestations of MS.

Intraoperative Finding

The absence of NVC was found in all patients after complete exploration of the trigeminal root from the porus of the trigeminal Meckel's cave to the trigeminal root entry zone (TREZ) at the pons. Four cases in whom suspicious NVCs were identified in preoperative imaging did not have actual compression during surgical exploration.

Surgical Results

At discharge, on the 7th postoperative day on average, all patients reported neuralgia relief. At the outpatient visit on postoperative day 50, 19 patients (90.5%) were pain-free and 2 still had some background pain which was not bothersome. At the 1 year postoperative visits, there was an excellent (T = 2) outcome for 11 (52.4%) patients, a good (T = 3) outcome for 5 (23.8%) patients, a fair (T = 4) outcome for 3 (14.3%) patients, and a poor (T = 5) outcome for 2 (1.0%) patients.

Diffusion Parameters From DTI

Diffusion metric data (FA and ADC) extracted before IN and 1 year after surgery is summarized in Table 4. Before IN, the mean FA in the affected side (0.26 ± 0.09, confidence interval [CI] 0.23–0.30) was significantly lower ($p < 0.05$) than the mean FA in the unaffected side of patients (0.39 ± 0.10, CI 0.35–0.44) and the mean FA in both sides of the controls (0.54 ± 0.06, CI 0.51–0.57) (Fig. 2a). The mean ADC in the affected side (4.75 ± 1.05 mm^2/s, CI 4.27–5.23) was significantly higher ($p < 0.05$) than the mean ADC in the unaffected side of patients (2.38 ± 0.37 mm^2/s, CI 2.21–2.55) and the mean ADC in both sides of controls (3.24 ± 0.43 mm^2/s, CI 3.04–3.45) (Fig. 3a). Both of the kurtosis values of FA and ADC in the affected side were significantly higher ($p < 0.05$) than that of the unaffected side of patients and mean of both sides of the controls preoperatively.

Table 4
Baseline characteristics of patients in each group FA and ADC of the TGN in the affected side before and after IN of patients (n = 21), in the unaffected side before and after MVD of patients (n = 21), and in normal control subjects (n = 20).

Groups	Controls	Unaffected side before IN	Affected side before IN	Unaffected side 1 year after IN	Affected side 1 year after IN
FA					
Mean ± SD	0.54 ± 0.06	0.39 ± 0.10	0.26 ± 0.09*	0.40 ± 0.11	0.36 ± 0.07
Median	0.54	0.42	0.26	0.42	0.38
95% CI	0.51–0.57	0.35–0.44	0.23–0.30	0.35–0.45	0.33–0.40
Kurtosis	-0.70	-0.45	1.13*	-0.67	-1.2*
Skewness	0.43	-0.58	0.46	0.15	-0.17
ADC (mm^2/s)					
Mean ± SD/s	3.24 ± 0.43	2.38 ± 0.37	4.75 ± 1.05*	2.67 ± 0.62	3.49 ± 0.65*
Median	3.27	2.38	4.87	2.43	3.41
95% CI	3.04–3.45	2.21–2.55	4.27–5.23	2.38–2.95	3.19–3.78
Kurtosis	-0.20	1.57	0.29*	1.54	-1.03*
Skewness	-0.34	1.30	-0.78	1.40	-0.14

FA fraction of anisotropy, ADC apparent diffusion coefficient, IN internal neurolysis, SD standard deviation, CI confidence interval, * = statistical significance

One year after IN, the mean FA in the affected side (0.36 ± 0.07, CI 0.33–0.40) was similar ($p > 0.05$) to the mean FA in the unaffected side of patients (0.40 ± 0.11, CI 0.35–0.45) and the mean FA in both sides of the controls (0.54 ± 0.06, CI 0.51–0.57) (Fig. 2a). The mean FA in the affected side was significantly higher ($p < 0.05$) than the mean FA in the affected side of patients before surgery (Fig. 2b). One year after IN, The mean ADC in the affected side (3.49 ± 0.65 mm^2/s, CI 3.19–3.78) was significantly higher ($p < 0.05$) than the mean ADC in the unaffected side of patients (2.67 ± 0.62 mm^2/s, CI 2.38–2.95), but had become similar ($p > 0.05$) to the mean ADC in both sides of the controls (Fig. 3a). The mean ADC in the affected side was significantly lower ($p < 0.05$) than the mean ADC in the affected side of patients before surgery (Fig. 3b). The analysis of kurtosis and skewness of FA and ADC comparing affected side before

IN and Affected side 1 year after IN respectively showed that, the kurtosis of both metrics became notably lower ($p < 0.05$) postoperatively.

After IN, the Pearson correlation coefficient did not show a strong correlation ($r = 0.3928$, $p = 0.0202$) between increase of FA in the affected side compared to the surgical outcome in BNI total score (Fig. 4a). However, the Pearson correlation coefficient showed a strong negative correlation ($r = -0.5237$, $p = 0.0148$) between decrease of ADC in the affected side compared to the surgical outcome in BNI total score (Fig. 4b).

Discussion

DTI abnormalities in the trigeminal nerve root of TN

The findings of this study are based on a unique patient population with CTN woNVC. Various previous studies investigating TN wNVC by using diffusion MRI have provided detailed evidence of microstructure abnormalities related to NVC. The majority of these research applied DTI metrics comparing the affected and unaffected sides in patients with classical TN and controls, and expounded a significant decrease in FA mean value and a significant increase in ADC mean value [2–4; 19], and utilization of 7.0 T MRI tractography also supported these opinions by a recent paper [25]. While others argued different even opposite opinions of the changes of DTI metrics values between affected and unaffected sides in patients and controls.[7; 20; 21] From the perspective of microstructure alteration related to surgical intervention, Hung et al. analyzed diffusion abnormalities in 31 TN patients and 16 healthy controls, revealed three ipsilateral diffusivity thresholds of response-pontine AD, MD, cisternal FA-separating 85% of non-responders from responders.[10] Tohyama et al. found RD and mean diffusivity (MD) were also significantly higher in the affected nerve of long-term responders compared to their unaffected nerve at 6 months after gamma knife radiosurgery (GKRS).[29] Lee et al. investigated DTI parameters of trigeminal nerve in 21 cases of TN before and after stereotactic radiosurgery (SRS), and focused on the cisternal segment of trigeminal nerves on affected side, in symptoms of < 5 years cases were associated with decreased FA ,while in symptoms of ≧ 5 years cases were associated with increased FA post-SRS.[15] From the results of our study, not only the mean values of FA and ADC showed significant differences between affected and unaffected sides, affected and control's sides, but also the kurtosis of FA and ADC behaved significant higher differences between affected and unaffected sides, affected and control's sides. The former finding is consistent with the mainstream opinion of above studies, the latter may elucidate further understanding of TN1 woNVC. No matter the decrease of FA mean value or the increase of ADC mean value reflects the microstructural changes in the trigeminal nerve even with the absence of neurovascular compression. And the significantly higher kurtosis values in FA and ADC, which indicates great concentrated around the mean and had a little variance of microstructural texture of the involved nerves. The interesting results may inspire the discovery of mechanism of TN1 woNVC which is distinct from TN1 wNVC.

Postoperative DTI Changes Of TN And Underlying Mechanism

Few reports has been published on long-term investigation of DTI abnormalities after surgical treatment for TN. In Dr. Sindou's series of studies, all patients underwent MVD with a complete exploration of the TR and detection of direct neurovascular contact in all cases, after removal of the compression, the loss of FA remained, but ADC normalized in the affected nerves, suggesting improvement in the diffusion of the trigeminal root.[13] DeSouza et al. studied DTI parameters and brain gray matter (GM) analyses of TN patients who underwent GKRS (15 cases) or MVD (10 cases) and 14 controls, and found that the FA abnormality in the affected side resolved such that FA increased and was no longer significantly different from the unaffected side or controls in the effective treatment group, however, FA remained significantly lower in the affected side compared to the unaffected side and controls in the ineffective treatment group. Then the authors concluded that surgical treatment can effectively resolve pain by normalizing trigeminal root abnormalities.[5] There has been several research findings discussing the abnormalities of diffusion MR based on histopathological evidences. Wang et al. reported a case of isolated trigeminal nerve hypertrophic interstitial neuropathy (HIN), which was revealed by histopathological examination and can be consider as pathology of refractory TN.[30] Lin et al. established model of TN using adult male Sprague-Dawley rats, and found that the pathological alteration located at plasticity of the central nervous system (CNS) - peripheral nervous system (PNS) transitional zone and the level of histone acetylation in the TREZ.[17] Nomura et al. much longer spans of central myelin than those reported previously can contribute to TN, especially in cases where central myelin is extended to an unprecedented degree.[26] Zhang et al. proposed application of DTI-derived metrics, especially $\lambda_{||}$ (consistent with axonal membrane stabilization) and $\lambda_{\perp}$ (consistent with remyelination) for explanation for diffusion recovery following MVD in short term.[32] In our study, a strong negative correlation was found between decrease of ADC in the affected side compared to the surgical outcome in BNI total score. The ADC maps has been acknowledged to used to characterize myelination and to detect abnormalities in the developing brain.[27] We hypothesize that nerve pathological alteration revealed by ADC values could be related to irreversible lesions in TR myelin. Little information is available about the long-term completeness of remyelination in the cranial nerves. Pathological myelination seems to be the most likely explanation for TN woNVC, even that the nerve roots appear entirely normal. In our study, the kurtosis values of FA and ADC became significantly lower ($p < 0.05$) postoperatively also demonstrate that recovery of the ultra little variation may contribute to pain relief.

Correlation between changes of diffusion metric values of the trigeminal root and outcome of IN

Diffusive abnormalities after IN, especially the decrease of ADC, confirmed a strong negative correlation with the 1 year surgical outcome in BNI total score in our study. As far as we know, no prior studies have reported the relevance between the diffusivity metrics and the prognosis of TN after IN. Our results attempted to provide potential noninvasive, brain-based biomarkers to support an optimal treatment selection for individual patients with TN woNVC.

Technical Limitations

In regard to limitations of the study, firstly, the small sample size of our cases is also one of the limitations in this study. Secondly, the follow up period may not be long enough for investigate the full view of alteration of diffusive metrics.

Conclusions

The DTI technique was used to investigate TR microstructure in patients with TN1 woNVC. The changes of diffusive property of TR could explain the efficiency of IN. The pretreatment DTI metrics could be an effective prognostic factor for providing potential noninvasive, brain-based biomarkers to support an optimal treatment selection for individual patients with TN woNVC.

Abbreviations

ADC
Apparent diffusion coefficient
DTI
Diffusion tensor imaging
FA
Fraction of anisotropy
IN
Internal neurolysis
MRI
Magnetic resonance imaging
NVC
Neurovascular compression
TN
Trigeminal neuralgia

Declarations

Consent for Publication

The manuscript contains no individual person's data in any form.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study is approved by the Ethics Committee of Anhui Provincial Hospital.

Competing interest

The authors declare that they have no competing interests.

Availability of data and material

The data and material of this study will be shared with reviewers or editors if necessary.

Authors' contributions

Conception and design: Wu, Jiang. Acquisition of data: Wu, Qiu, Dong, Wang. Analysis and interpretation of data: Wu, Qiu. Drafting the article: Wu, Qiu. Critically revising the article: Wu. Reviewed submitted version of manuscript: Fu. Statistical analysis: Wu. Administrative/technical/material support: Wu, Li. Study supervision: Niu.

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Figures

Figure 1

a,b Diffusion tensor imaging (DTI) showing examples of green box-shaped regions of interest (ROI) used for quantitative analysis of DTI parameters in the whole segment of trigeminal nerve root (TR) in posterior fossa. c,d Reconfirm the ROIs by viewing the fusion imaging of FA and ADC colormaps emerged to corresponding 3D-BRAVO slice. e Operative view of internal neurolysis (IN) procedure with longitudinal division of the trigeminal nerve using a straight micro knife dissector.

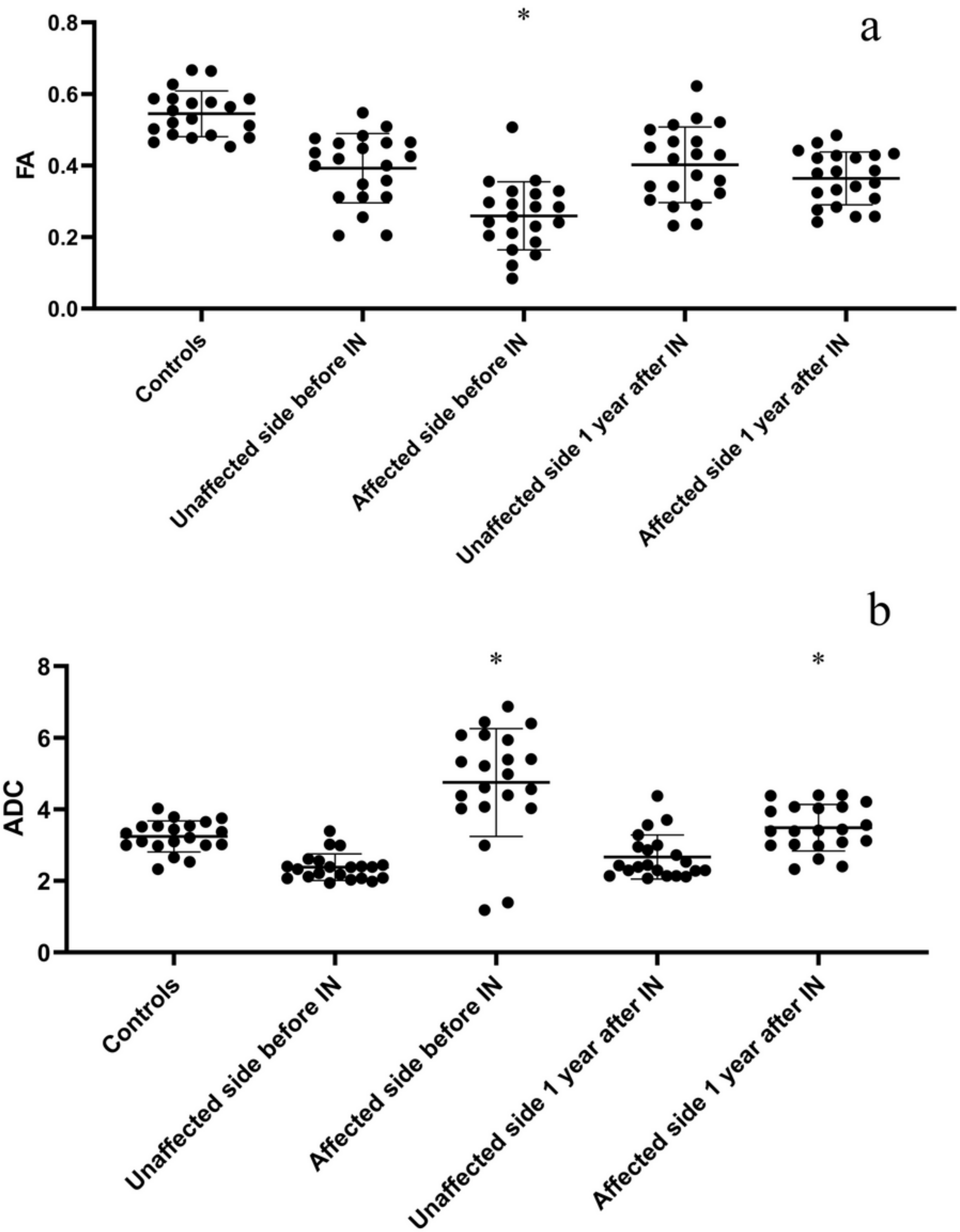

Figure 2

a Graph showing a fraction of anisotropy (FA) data before and after internal neurolysis (IN). Before IN, the mean FA in trigeminal nerve root (TR) in the affected side of patients was significantly lower ($p < 0.05$) than the mean FA in the TR in the unaffected side of patients and the mean FA of the TR in both sides of control subjects. 1 years after IN, the mean FA in the affected side of patients was similar to the mean FA in the unaffected side and the mean FA in both sides of control subjects. b Graph showing FA data connected by lines for each respective affected nerve of patients. The mean FA in the affected side was significantly higher ($p < 0.05$) than the mean FA in the affected side of patients before surgery. * statistical significance

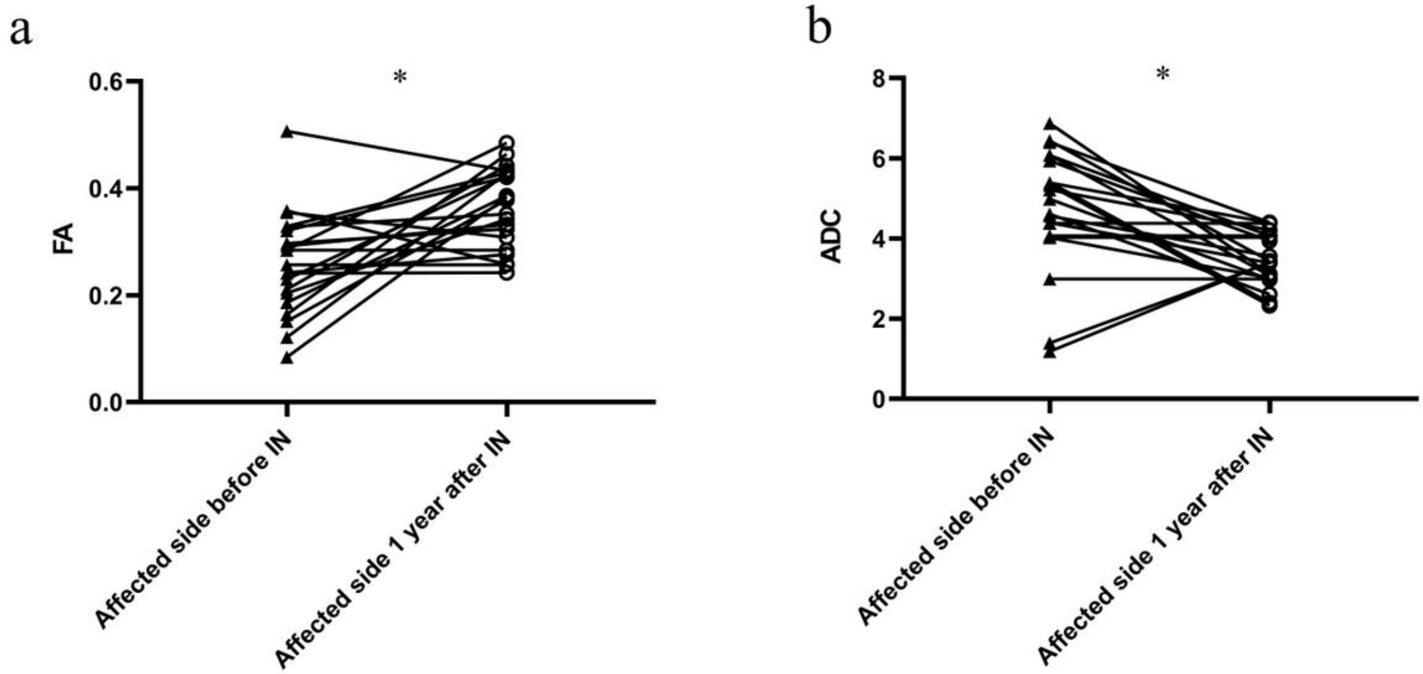

Figure 3

a Graph showing a apparent diffusion coeffcient (ADC) data before and after internal neurolysis (IN). The mean ADC in the affected side was significantly higher ($p < 0.05$) than the mean ADC in the unaffected side of patients and the mean ADC in both sides of controls. One year after IN, The mean ADC in the affected side was significantly higher ($p < 0.05$) than the mean ADC in the unaffected side of patients, but had become similar ($p > 0.05$) to the mean ADC in both sides of the controls. b Graph showing ADC data connected by lines for each respective affected nerve of patients. The mean ADC in the affected side was significantly lower ($p < 0.05$) than the mean ADC in the affected side of patients before surgery. * statistical significance

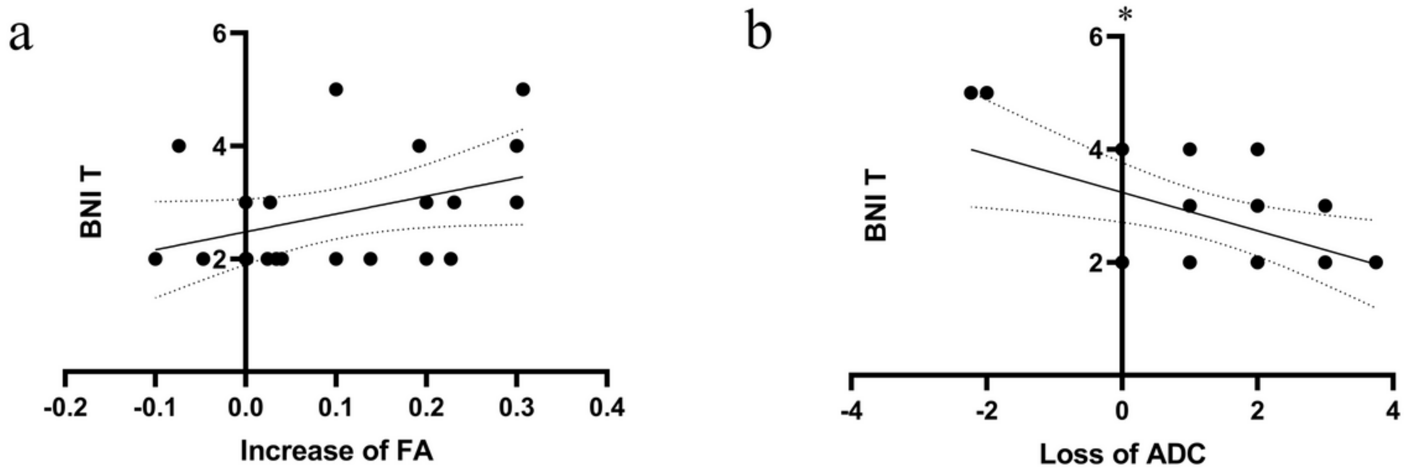

Figure 4

Linear regression plot derived from the relationship between the changes in the fraction of anisotropy (FA) and the apparent diffusion coefficient (ADC), in affected nerves vs surgical outcome in BNI total score respectively. a the Pearson correlation coefficient did not show strong correlation between increase of FA in the affected side compared to the surgical outcome in BNI total score. b the Pearson correlation coefficient showed a strong negative correlation between decrease of ADC in the affected side compared to the surgical outcome in BNI total score. * statistical significance