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TECHNIQUE EVALUATION

The MRI volumetry of the posterior fossa and its substructures in trigeminal neuralgia: a validated study

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Abstract
Purpose Our aim was to determine whether the anatomical configuration of the posterior fossa and its substructures might represent a predisposition factor for the occurrence of clinical neurovascular conflict in trigeminal neuralgia (TN).
Methods We used MRI volumetry in 18 patients with TN and 15 controls. The volume of the pontomesencephalic cistern, Meckel's cave and the trigeminal nerve on the clinical and non-affected sides was compared. The reliability has been assessed in all measurements.
Results The posterior fossa volume was not different in the clinical and control groups; there was no difference between the affected and non-affected sides when measuring the pontomesencephalic cistern and Meckel's cave volume either. The volume of the clinically affected trigeminal nerve was significantly reduced, but with a higher error of measurement.
Conclusions We did not find any association between the clinical neurovascular conflict (NVC) and the size of the posterior fossa and its substructures. MRI volumetry may show the atrophy of the affected trigeminal nerve in clinical NVC.

Keywords Trigeminal neuralgia · Neurovascular conflict · Posterior fossa · MRI volumetry · Validation

Introduction

Trigeminal neuralgia (TN) is a surgically treatable condition, the pathogenesis of which still remains unclear. There is good evidence of the presence of the neurovascular conflict (NVC) between the trigeminal nerve entry zone and one of the adherent vessels in TN [15]. Histological studies in TN patients revealed axonopathy, axonal loss and demyelination [9, 12]. NVC may represent a continued source of irritation to a trigeminal nerve that has already been previously affected by another pathological process. Regardless of

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how the NVC is associated with TN, microvascular decompression, developed by Janetta in 1967, leads to the elimination of NVC and successful pain relief [8]. NVC can be visualised by high-resolution MRI and may therefore strengthen the grounds for surgery. However, NVC has been demonstrated in healthy subjects too and the indication remains based on clinical findings [1, 14].

The aetiology of NVC has been attributed to the asymmetry of the pontomesencephalic cistern, and to a small posterior fossa size [13, 16, 20]. The trigeminal nerve volume has been reported to be decreased on the affected side [11]. Nonetheless, the role of anatomical configuration in the pathogenesis of TN remains unclear and is still a matter of debate. For this reason, we conducted an MRI volumetric study to assess whether the volumes of the posterior fossa, pontomesencephalic cistern or trigeminal nerve are associated with clinical NVC.

Materials and methods

Eighteen patients with TN were enrolled into the study. The diagnosis of TN was made based on the International Classification of Headaches criteria [7].The mean age of the patients was 56.3±14.4 (mean±SD) years, ranging from 30 to 71 years. TN was symptomatic in 11 cases on the right side and in 7 cases on the left side. The control group consisted of 15 subjects with a similar distribution of age and sex. The control subjects had signs neither of neurological nor of psychiatric deficit. The participants in the study were informed about the MRI volumetric acquisition and gave written informed consent. The design of the study was approved by the institutional ethical committee.

All patients with TN and controls were imaged using a 1.5-T MRI unit (Signa Excite, General Electric Medical Systems, Milwaukee, WI, USA) with a conventional head coil. The protocol included axial T2W FRFSE (fast relaxation fast spin echo) sequence, axial T2W FLAIR (fluid attenuated inversion recovery), and coronal 3D T1W images of the whole brain. In several cases, post-contrast coronal T1W images (gadolinium, at 0.1 mmol/kg body weight) were acquired. The volumetric acquisition of posterior fossa comprised an axial 3D FIESTA sequence (fast imaging employing steady-state acquisition). The parameters for the FIESTA sequence were TR 4.6 ms, TE 1.5 ms, flip angle 45°, FOV 25.00×20.00 cm, matrix 320×256, NEX 4, 0.391×0.391 mm^2 pixel size; 88 slices 0.8 mm thick with a 0.4-mm gap. The total scan time was about 12 min. Patients were instructed to keep their head straight during the MRI examination. There was no pathological enhancement of the affected trigeminal nerve in a T1-weighted post-contrast sequence.

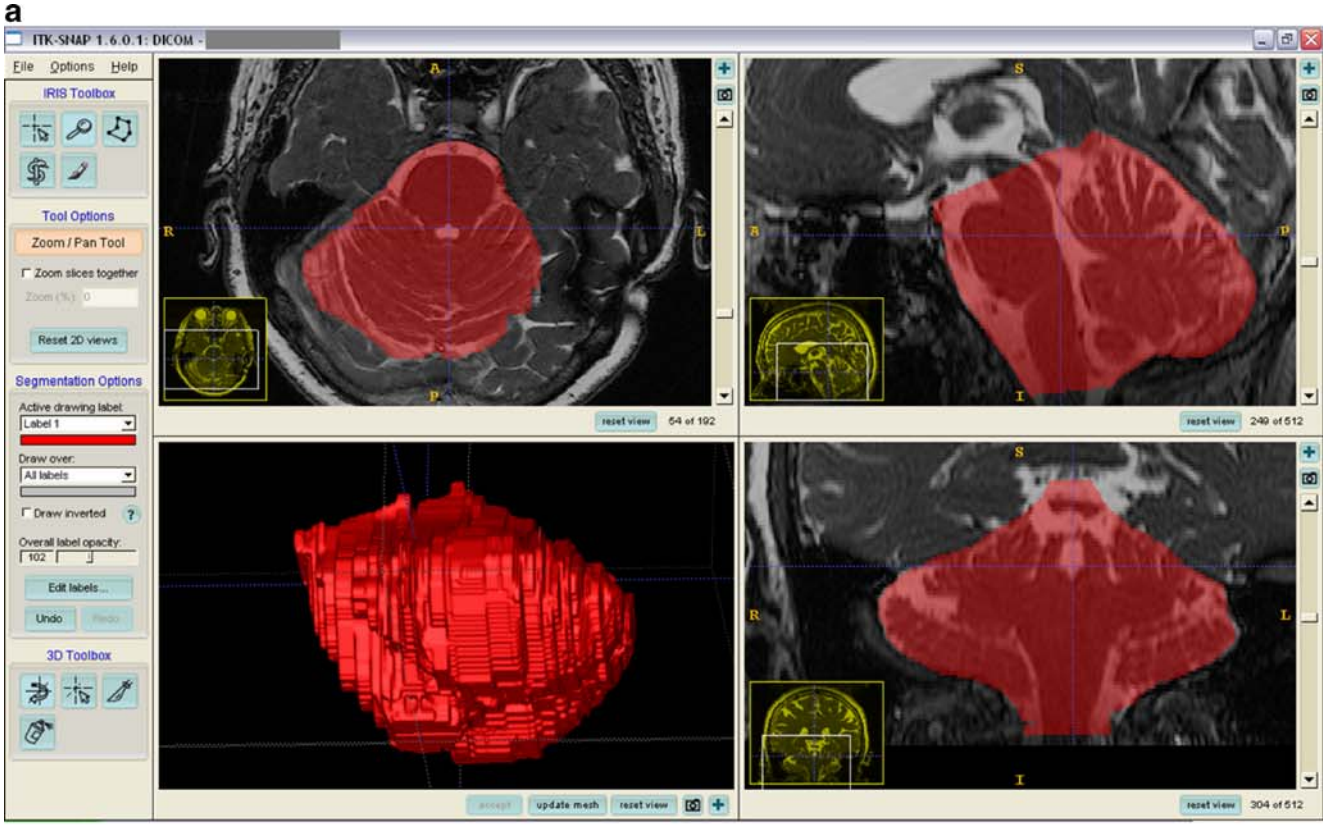
The MRI images were transferred to a Tomocon workstation (Tomocon, Unis Computers, Brno, Czech Republic). 3D multiplanar reconstruction was used to visualise nerves and vessels in the proximity of the pons and within the pontomesencephalic cistern. Two neuroradiologists evaluated the images blindly to the laterality of the patients' symptoms. The NVC on MRI was confirmed if no cerebrospinal fluid could be detected between the vessel and the nerve in two of the three orthogonal planes in the 3D view. As a next step, ITK SNAP software was used for the segmentation of MRI images. ITK SNAP is a piece of software that allows simultaneous 3D image viewing and outlining of the selected region of interest (ROI) in three orthogonal planes [23].

The posterior fossa volume was defined as the region bordered by the tentorium of the cerebellum, the clivus and the occipital and pyramidal bones. The inferior border was set by a plane through the posterior rim of the foramen magnum (Fig. 1a). To compensate for intersubject variability in the head size, the volume of the posterior fossa was normalised to the intracranial volume.

The true anatomical borders of the pontomesencephalic cistern cannot be reliably inferred from the MR image. Therefore, to achieve the highest possible reproducibility of measurement, we set arbitrary borders for the ROI delineation. The segmentation included only a part of the pontomesencephalic cistern extending from the fifth to the seventh and eighth cranial nerves. The superior border of the measurement included the slice above the level where the trigeminal nerve could be identified on either side. The first slice where the seventh/eighth cranial nerve on either side could be identified in its full length defined the inferior boundary. The lateral boundaries were set at the medial side of the trigeminal nerve exit from the pons (Fig. 1b). Performing manual presegmentation by defining the above stated borders, an area for further analysis was then obtained. Next, the automated extraction of CSF volume by method of volume growing was performed. Manual correction of the ROI was implemented wherever the area of the growing algorithm did not correspond to the predefined boundaries (e.g. in the case of the separation of the Meckel's cave, see Fig. 1b). The acquired ROI was then "cut in half" by simple volume subtraction with a separation line leading through the infundibulum and aqueduct and the volumes for the affected and non-affected sides were then acquired. Meckel's cave was segmented by using a semiautomated technique with manual presegmentation and correction as described above (Fig. 2a). The segmentation of the trigeminal nerve started at

Fig. 1 **a** Segmentation of the posterior fossa in three orthogonal views and a 3D reconstruction of the segmented ROI. **b** Manual correction of automated volume growing was implemented to delineate the ROI in predefined borders. The lateral boundaries of the pontomesencephalic cistern were arbitrarily set at the medial edge of the exit of the trigeminal nerve (*arrow*)

a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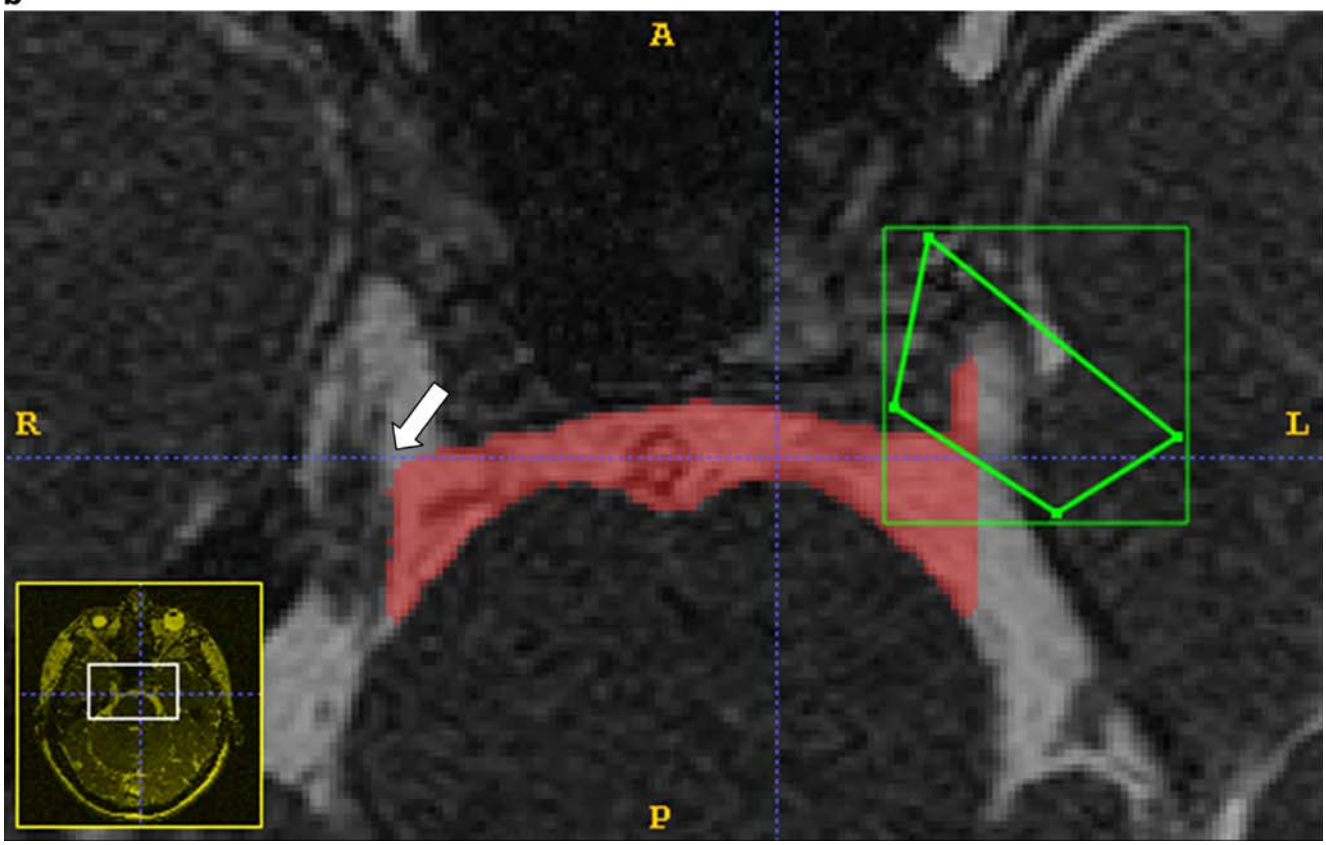
b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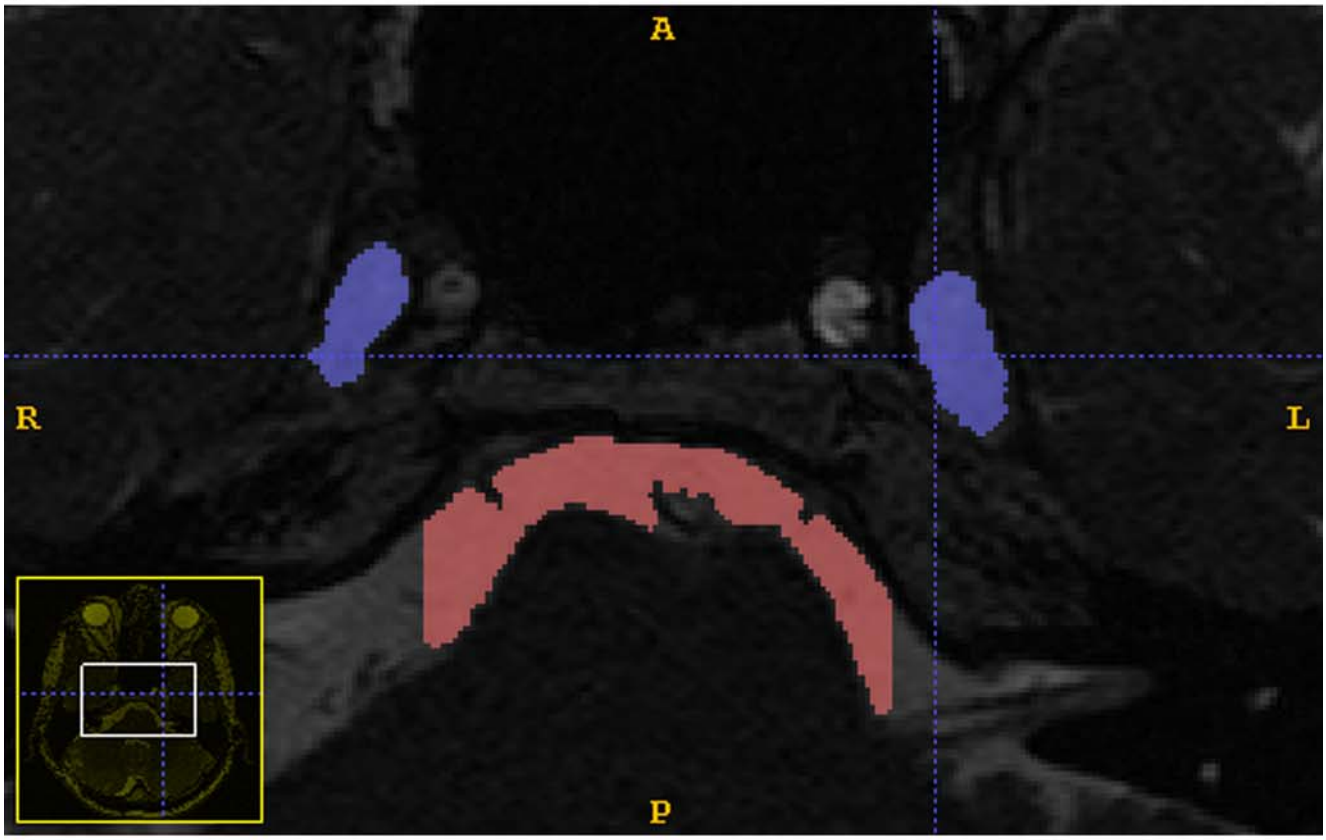
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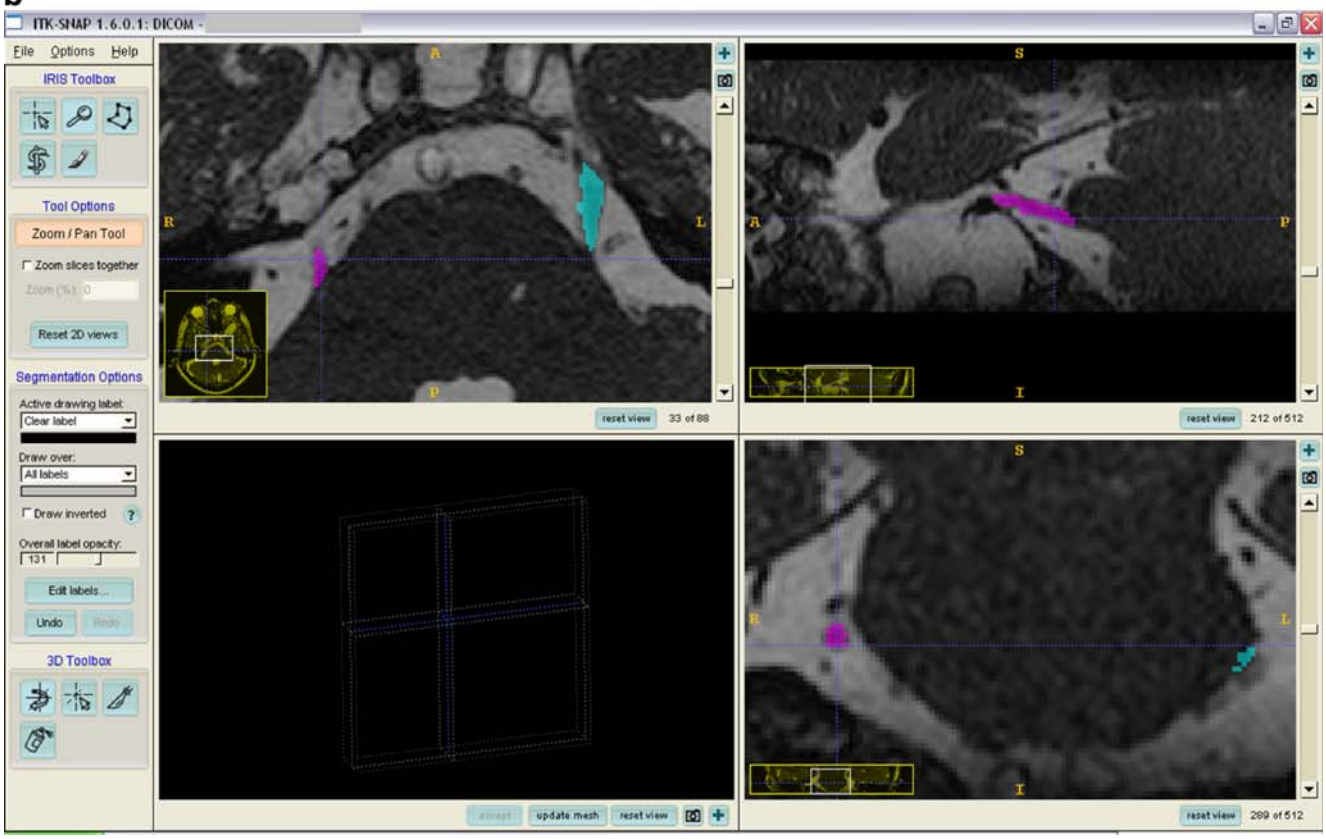
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◀ **Fig. 2** **a** The delineation of both the pontomesencephalic cistern and Meckel's cave. **b** The segmentation of the trigeminal nerve in a 3D view from Meckel's cave to the exit point from the pons

the point where the nerve emerges from the pons, and the other arbitrary cut was made at the entrance of the nerve to the Meckel's cave (Fig. 2b).

Two operators, who were blind to the clinical data during measurement, performed the segmentation. In 10 subjects all measurements were performed twice with a 6-week interval to assess the reproducibility of the measurement.

All patients were operated on using the retrosigmoid approach and microvascular decompression (MVD). The NVC was found in all cases. Most of the patients did well after the surgery with only 2 patients complaining of residual symptoms. No failure of treatment was found.

Statistical analysis

The intrarater variability of MRI volumetric measurement was assessed as the mean difference of the repeated measurements divided by their mean. The volume difference between the pontomesencephalic cistern and the trigeminal nerve volume on the affected versus non-affected side was analysed using the Wilcoxon paired test. For comparing the volumes of the posterior fossa in patients with TN and NVC and controls, the Mann–Whitney *U* test was used. Differences between the values were considered significant at a p value of <0.05.

Results

The NVC on MRI was present in 17 out of 18 cases on the clinical side (94%). On the contralateral side to the TN, NVC was present in 9 out of 18 subjects (50%). In the healthy control group NVC was found in 7 out of 15 subjects (46.7%), and in 4 cases NVC was identified bilaterally, meaning 37% (11/30) of the investigated trigeminal nerves in a control group (see Tables 1 and 2).

The posterior fossa volumes of the clinical and control groups showed no significant difference, both with regard to raw and normalised volumes (see Table 3). In men, the posterior fossa volume was significantly larger than in women (207.3±11.8 cm^3 versus 181.6±15.9 cm^3, $p<0.01$).

Table 1 Identification of the presence of neurovascular conflict in clinical individuals

	Affected	Non-affected side
TN patients	94.4% (17/18)	50% (9/18)

TN: trigeminal neuralgia; NVC: neurovascular conflict

Table 2 Identification of the presence of neurovascular conflict in control individuals

	NVC presence in subjects	NVC presence in trigeminal nerves
Controls	46.7% (7/15)	37% (11/30)

This difference was no more statistically significant after the normalisation of the raw data to intracranial volume. The intraindividual variability of measurement for posterior fossa volume was 1%.

No significant difference was found in the pontomesencephalic cistern volume when comparing the clinical and control groups (1.9±0.55 cm^3 versus 1.82±0.42 cm^3, $p=0.22$, see Table 3). Comparison of the volumes on the affected and non-affected sides did not reveal any asymmetry of the pontomesencephalic cistern in TN patients (0.936±0.265 cm^3 versus 0.972±0.325 cm^3, $p=0.19$, see Table 4). The variability of the measurement was 18%. After unblinding the data we saw that a relatively high error of measurement was caused by the variability of the setting of the inferior border. To establish whether this inaccuracy could have influenced the asymmetry, we compared the variability of the ratio for the affected versus the non-affected side volumes and this remained low with repeated measurements (3.3%).

In the instance of Meckel´s cave no significant asymmetry was found between the affected and the non-affected sides (0.491±0.277 cm^3 versus 0.466±0.286 cm^3, $p=0.41$). There was a high variance of the volumes of Meckel´s cave both in the study and the control groups (0.2–0.73 cm^3). The intrarater variability of the measurement was calculated as 12%. The mean volume of both Meckel's caves was not significantly different in TN patients and the control group (0.478±0.138 cm^3 versus 0.462±0.151 cm^3, $p=0.17$).

The volume of the affected nerve was significantly reduced in comparison to that of the healthy side (0.059±0.026 versus 0.068±0.018 cm^3, $p<0.05$; Table 4). The variability of this measurement was 22%. The mean volume difference between the affected and non-affected sides was 27%. Regarding the variability of the measurement in only 7 of the 18 patients. the volume difference between the affected and the non-affected nerve exceeded 22%. There was no difference in the mean volume of the trigeminal nerve between the TN patients and the control group (0.064±0.021 versus 0.061±0.011, $p=0.62$).

Discussion

It has been shown in the literature that high-resolution MRI can be highly sensitive in the demonstration of NVC [2, 17, 19]. However, NVC itself does not seem to be a specific marker

Table 3 Comparison of volumetric measurements of posterior fossa structures between the clinical and the control group

	TN patients (cm^3)	Controls (cm^3)	Variability of repeated measurement (%)
Posterior fossa volume raw	189.4±21.9	194±13.2	0.9
Posterior fossa volume normalized	134.2±7.2	138.3±11.9	0.5
Pontomesencephalic cistern volume	1.9 ±0.55	1.82±0.42	18
Meckel´s cave	0.478±0.138	0.462±0.151	12
Trigeminal nerve	0.064±0.021	0.061±0.011	22

of TN and it has also been demonstrated in healthy volunteers with an incidence of up to 56% [1, 14]. In our sample, we found a high incidence of NVC on MRI in controls (37%) and on the unaffected side (50%). The sensitivity of high-resolution MRI using a FIESTA sequence was high (94%), and the specificity was 100%. These findings are in accordance with numerous previous reports [2, 19]. MRI remains only a complementary tool for the indication of microvascular decompression (MVD), and a negative MRI finding does not represent a contraindication to surgery.

We did not find any difference in the size of the posterior fossa between the subjects and controls. Mueller and Levy described an abnormality in the configuration of the skull when performing craniometric measurements with plain cranial X-rays in 1963 [16]. An association between the pathological configuration of the posterior fossa and TN has been described in case reports of achondroplasty and Chiari malformation [5, 22]. An association among TN, asymmetry of petrous bone and unilateral impression has also been reported [18]. In 1966, Gardner and Dohn published a relationship between the incidence of hemifacial spasm and TN in patients with Paget's disease [4].

However, these reports were only sporadic over last four decades and have been limited to case reports or short series; studies based on X-ray planimetric measurement are obsolete today. They were based on the hypothesis that the malformation of the posterior fossa may lead to the disfiguration of the course of the vessels and the increased incidence of clinical NVC. If this were true, the incidence of TN in patients with basilar impression or Paget's disease would have been reported to be higher than in the normal population, but no such reports have so far been published. Our results represent precise posterior fossa volume assessment based on 3D data with high intrarater reliability. Considering our data, we believe that the presence of posterior fossa malformation and TN is only coincidental.

Similarly, we were not able to find any association between clinical NVC and asymmetry in the pontomesencephalic cistern volume. Recently Rasche et al. have reported the reduced volume of the pontomesencephalic cistern on the affected side in patients with TN [20]. Their finding is interesting, but in our study we were not able to reproduce their results. One of the reasons for this may be the difference in the MRI volumetric approach. The midline border of the pontomesencephalic cistern in Rasche et al.'s paper is not clearly defined and no data on intraindividual or interindividual error of measurements are given. In our experience, the variability of pontomesencephalic cistern volumetry was relatively high; this fact can be attributed to the variability of the caudal boundary setting. Nevertheless, this would not have changed the asymmetry of the pontomesencephalic cistern and influenced our results. The variability of the ratio between the affected and non-affected sides in repeated measurements remained low.

We found significant atrophy of the affected trigeminal nerve compared with the healthy side. On the other hand, in 7 controls (out of 15) in whom the NVC was present we did not observe any asymmetry between the nerve volumes. Considering the measurement variability in the clinical group, only 7 of the 18 patients would have been safely diagnosed with atrophy of the trigeminal nerve and benefited from MRI volumetry. Atrophy of the trigeminal nerve has been observed intraoperatively in a large series of cases [21]. The demonstration of trigeminal nerve volume asymmetry by means of MRI volumetry is interesting, but its low sensitivity prevents its use on a routine basis. In another study that was concerned with trigeminal nerve volumetry, the intrarater reliability was not given [11]. The lower variability of volumetric measurement might be achieved with a 3 T MRI unit.

For the data obtained by MRI volumetry, the validation of the measurement is crucial, especially in small and anatom-

Table 4 Comparison between the affected and non-affected sides in patients with TN and controls, (*$p<0.05$)

	Affected (cm^3)	Non-affected side (cm^3)
Pontomesencephalic cistern	0.936±0.265	0.972±0.325
Meckel's cave	0.491±0.277	0.466±0.286
Trigeminal nerve	0.059±0.026*	0.068±0.018*

ically complex structures [3, 6, 10]. If we want to assess for instance the influence of long-term Leksell gamma knife (LGN) or MVD on the atrophy of the trigeminal nerve, we must be sure of using a validated and reliable tool.

Based on our results, we conclude that in the search for the cause of TN, investigation of the size of the anatomical compartments of the posterior fossa does not represent a perspective direction. More attention and effort should be given to the MRI demonstration of processes that might affect the trigeminal nerve itself.

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