Neurology Asia 2025; 30(3) : 845 – 851

The prevalence and clinical significance of trigeminal neuralgia in patients with multiple sclerosis

İpek Güngör Doğan, Ebru Kaya, Sude Kendirli Aslan, Damla Çetinkaya Tezer, Serkan Demir

University of Health Sciences, Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital, Department of Neurology, Istanbul, Turkey

Abstract

Background & Objective: Trigeminal neuralgia (TN) is a debilitating neuropathic pain disorder characterized by sudden and intense episodes of facial pain, significantly impairing patients' quality of life. Diagnosing TN is particularly challenging in multiple sclerosis (MS), a chronic autoimmune, demyelinating, and neurodegenerative disease affecting the central nervous system. TN in MS is predominantly caused by demyelination, axonal loss, inflammation, and brainstem lesions. However, the overlapping symptoms of TN and other craniofacial pain disorders often lead to underdiagnosis and treatment delays. This study aimed to determine the prevalence and clinical characteristics of TN in MS patients, in a cohort of Turkish patients, with a focus on diagnostic challenges and treatment patterns. *Methods:* A single-center, cross-sectional survey was conducted, systematically assessing headache and facial pain symptoms among MS patients treated at the Sancaktepe Neuroimmunology Clinic, Istanbul, Turkey. *Results:* The findings revealed a significant prevalence of TN (39.8%) in MS patients, with a female predominance and a mean diagnostic delay of 14 months. Despite the availability of effective treatments, a substantial proportion of patients remained undiagnosed and untreated. *Conclusion:* There is urgent need to integrate routine TN screening into MS patient care to improve timely diagnosis and effective management. The study underscores the importance of a multidisciplinary approach in addressing this overlooked comorbidity, ultimately enhancing the quality of life for MS patients.

Keywords: multiple sclerosis, trigeminal neuralgia, pain, management

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disease characterized by demyelination, axonal damage, and neurodegeneration within the central nervous system, leading to a broad spectrum of neurological symptoms. Among these symptoms, neuropathic pain, including facial pain, is a particularly debilitating feature that severely affects patients' quality of life. Studies report that neuropathic pain occurs in up to 50% of MS patients, with trigeminal neuralgia (TN) representing one of the most severe and disabling forms of pain in this population.[1,2]

Trigeminal neuralgia is a neuropathic pain disorder presenting with sudden, excruciating episodes of facial pain. It is broadly classified into two types: classical TN, often associated with neurovascular compression, and secondary TN, which frequently arises due to underlying conditions such as MS. In the context of MS, TN is predominantly attributed to central demyelination of the trigeminal nerve, brainstem lesions, and chronic inflammation.[3,4] Epidemiological studies suggest that TN affects approximately 2-4% of MS patients, and in 1-5% of cases, TN may even be the presenting symptom of MS. Furthermore, MS patients are more likely to experience atypical or bilateral pain compared to individuals with idiopathic TN.[5,6]

Despite these findings, TN remains underdiagnosed in MS patients. The overlapping clinical features of TN and other craniofacial pain disorders, coupled with the complexities of managing a multi-symptom condition like MS, often lead to diagnostic delays and suboptimal treatment.[7] Addressing this gap is essential, as

Address correspondence to: Dr Serkan Demir, University of Health Sciences, Sancaktepe Sehit Prof. Dr. Ilhan Varank Training and Research Hospital, Department of Neurology, Emek, Namık Kemal Cd. No:54, 34785 Sancaktepe/Istanbul, Turkey. Tel: +905055960467, email: drsrkndemir@gmail.com

Date of Submission: 19 March 2025; Date of Acceptance: 2 May 2025

https://doi.org/10.54029/2025tjf

early diagnosis and targeted interventions can significantly improve patient outcomes.

We hypothesize that the prevalence of TN in MS patients is underestimated due to diagnostic challenges and a lack of routine screening protocols. This study aims to determine the prevalence and clinical characteristics of TN in MS patients at the Sancaktepe Neuroimmunology Clinic. By systematically evaluating the symptoms and treatment patterns, we seek to provide a foundation for integrating TN screening into routine MS management and improving clinical care for these patients.

METHODS

Study design and setting

This study was designed as a single-center, cross-sectional survey conducted at the Sancaktepe Neuroimmunology Clinic. The primary objective was to evaluate the prevalence and clinical characteristics of TN in patients with a confirmed diagnosis of MS. The study is approved by the local ethical committee of our hospital with the number E-46059653-050.04-262337566. The patient included in the study signed an informed consent form.

Patient selection

Participants were recruited from the clinic's MS patient registry. Inclusion criteria were as follows: 1. Age ≥18 years; 2. Clinically or radiologically confirmed diagnosis of MS according to the 2017 McDonald criteria; 3. No history of other neurological disorders that could confound the diagnosis of TN. Patients were excluded if they had: 1. Severe cognitive impairment preventing accurate symptom reporting; 2. A history of craniofacial trauma or invasive surgical procedures unrelated to MS.

Eligible patients underwent a detailed clinical assessment, including a structured interview and neurological examination, to identify symptoms consistent with TN. Symptoms were defined using the International Classification of Headache Disorders-3 (ICHD-3) criteria.

Data collection

Participants completed a symptom-focused questionnaire, designed to systematically capture data on: Demographic information (age, gender, smoking history, family history of TN or MS); MS subtype and disease duration; Expanded Disability Status Scale (EDSS) scores; Presence, laterality, and characteristics of facial pain; Previous TN diagnosis and treatment history. Medical records were reviewed to cross-check reported symptoms and treatments.

Statistical analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR), depending on data distribution. Categorical variables were expressed as frequencies and percentages. Comparisons between groups (diagnosed and undiagnosed TN) were made using the Mann-Whitney U tests. Mann-Whitney U tests were used to look for statistical significance between groups in the study. All statistical analyses were conducted using [SPSS], with a significance threshold set at $p < 0.05$.

RESULTS

Out of 221 participants, 133 patients reported no headache or facial pain complaints. Remaining 88 patients had pain related complains that are compatible with TN. Among these, 31 patients (35.2%) received a definitive diagnosis of TN, while 57 patients (64.8%) exhibited symptoms consistent with TN but had not been formally diagnosed (Figure 1).

Gender and age distribution

Among the 31 diagnosed TN cases, 54.8% were female (n=17) and 45.2% were male (n=14) *($p > 0.05$).* On the other hand, 80.7% of undiagnosed patients with TN symptoms were female (n=46) and 19.3% were male (n=11) *($p > 0.05$)* (Figure 2). This notable female predominance suggests potential gender-related biological or social factors influencing symptom presentation and diagnosis.

Age analysis revealed that the majority of patients in both groups were between 25-40 years old, comprising 45.16% of diagnosed TN cases and 56.17% of undiagnosed cases *($p > 0.05$)* (Figure 3). The concentration of cases within this age range aligns with the typical age of peak MS activity, further emphasizing the need for TN screening in younger MS populations.

Symptom characteristics and treatment

Symptoms were bilateral in 41.9% of diagnosed cases, while 41.9% reported left-sided and 16.2%

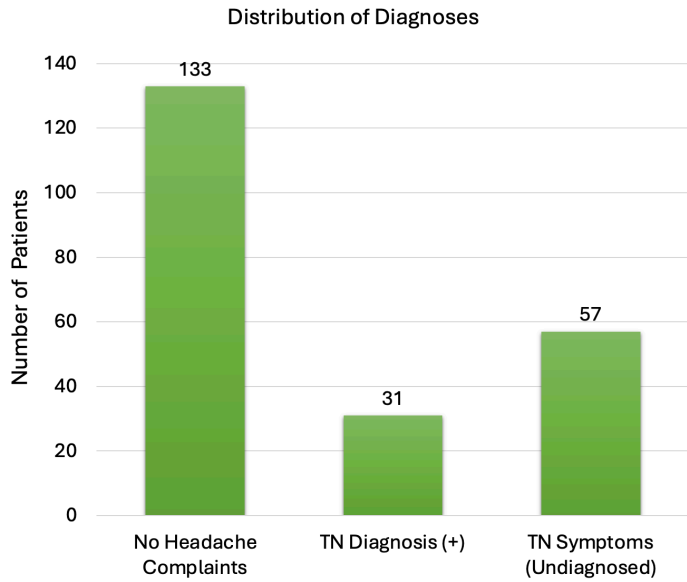


Figure 1. Distribution of diagnoses

right-sided pain. Bilateral presentation was more common in MS-associated TN, consistent with its central nervous system etiology.

A total of 18 patients had brainstem lesions on cranial imaging. Of these, 8 patients were in the group previously diagnosed with TN *($p < 0.05$)*.

Diagnosed patients experienced a mean delay of 14 months from symptom onset to diagnosis. This highlights systemic gaps in timely recognition and intervention.

Treatment patterns

Among patients with a TN diagnosis, pharmacological treatments included carbamazepine (38.5%), gabapentin (6.5%), pregabalin (6.5%), and lamotrigine (3%). Approximately 25% of patients received polytherapy, while 6.5% underwent surgical intervention (microvascular decompression), with partial symptom relief reported in all surgical

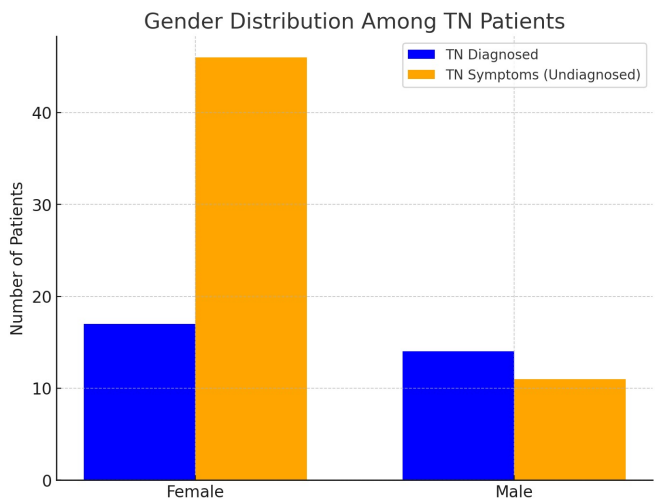


Figure 2. Gender distribution among TN patients

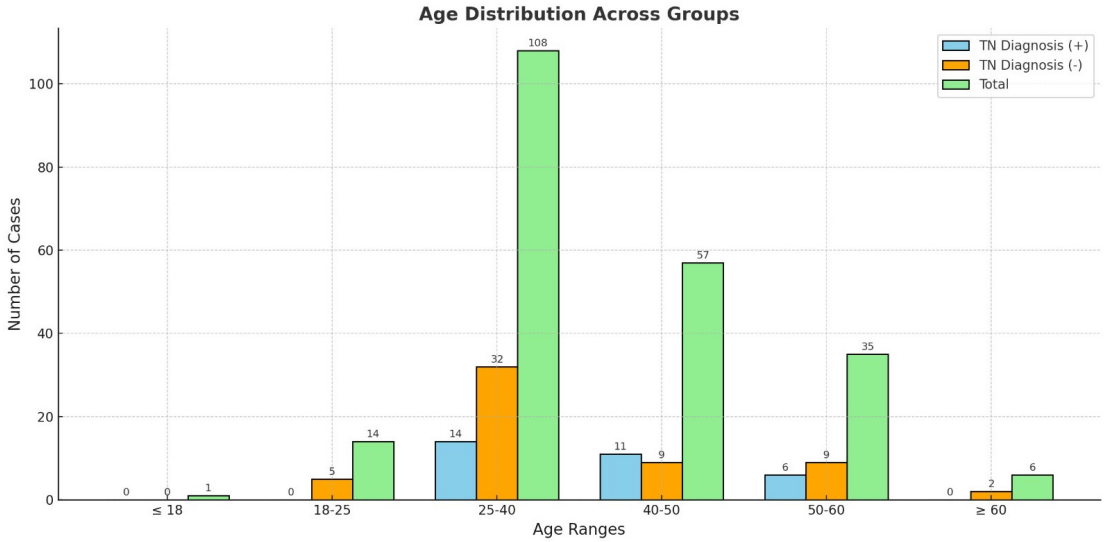


Figure 3. Age distribution across groups

cases.

Full benefit from medical treatment: Younger patients (25-40 years) experienced the highest success rates (60%), with success rates declining with age (50% for 41-60 years and 40% for >60 years) (Figure 4).

Partial benefit from surgical treatment: Surgical outcomes showed higher consistency across age groups, with partial relief reported in 90% of patients aged 25-40, decreasing slightly to 85% (41-60 years) and 75% (>60 years) (Figure 4).

In contrast, none of the undiagnosed patients (n:57) were receiving medical treatment for their symptoms, underscoring the critical need for routine TN screening to initiate effective interventions.

Among those diagnosed with TN, 30 patients had relapsing-remitting MS (RRMS) and 1 patient had primary progressive MS (PPMS). In the undiagnosed group, 50 patients had RRMS, 6 patients had PPMS and 1 patient had radiologically isolated syndrome (RIS). The expanded disability status scale (EDSS) is detailed in Figure 5.

In this study evaluating 88 patients, approximately 41% of patients reported smoking history of 4 cigarettes per day for an average of

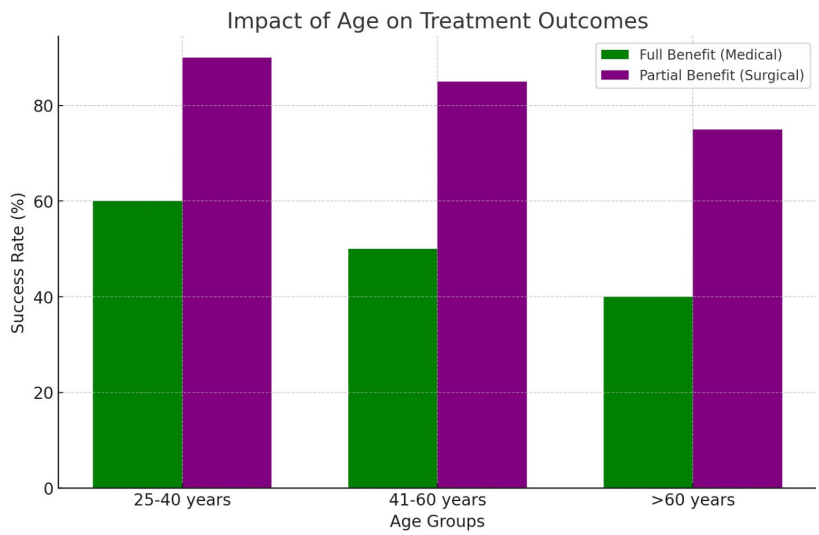
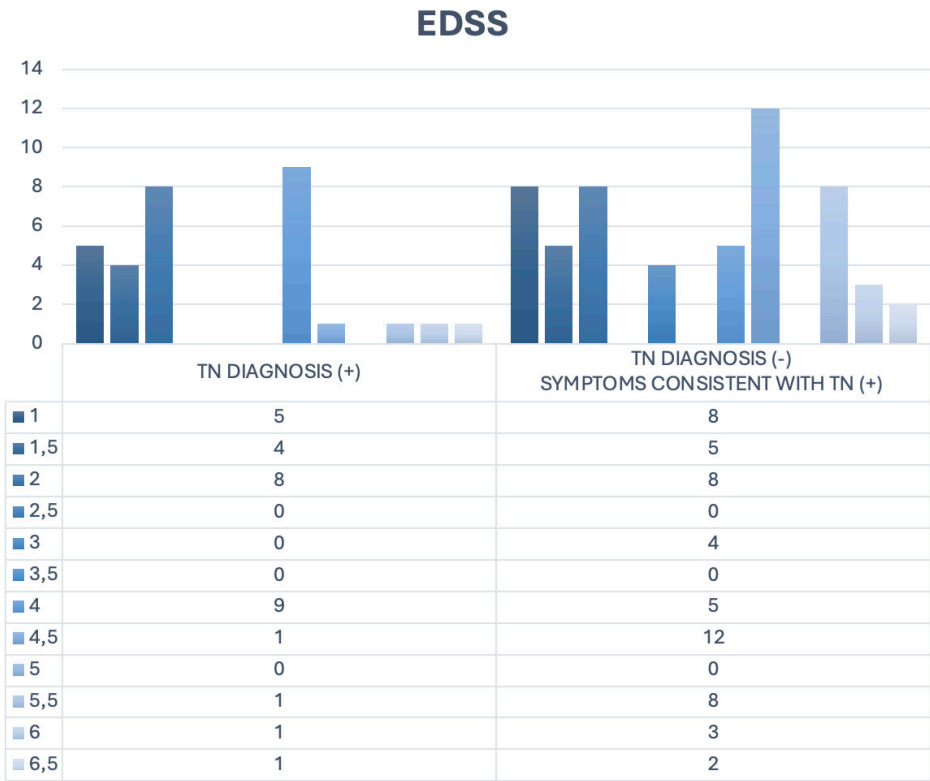


Figure 4. Impact of age on treatment outcomes



	TN DIAGNOSIS (+)	TN DIAGNOSIS (-) SYMPTOMS CONSISTENT WITH TN (+)
1	5	8
1,5	4	5
2	8	8
2,5	0	0
3	0	4
3,5	0	0
4	9	5
4,5	1	12
5	0	0
5,5	1	8
6	1	3
6,5	1	2

Figure 5. The expanded disability status scale (EDSS)

7.5 years. Additionally, 69% of patients reported no other chronic illnesses; while among those with comorbidities, 10% had hypothyroidism, 9% had hypertension, 8% had hypercholesterolemia and 4% had diabetes.

In total, 6 of those 88 patients reported a family history of similar headache symptoms *($p < 0.05$)*.

Family history of TN diagnosis (p=0.034) and findings of brainstem involvement (p=0.047) emerged as key factors potentially differentiating between groups ($p < 0.05$). No statistically significant differences were observed between the groups for other variables such as gender, age, and smoking status ($p > 0.05$).

DISCUSSION

Comparison with existing literature

Our study identifies a prevalence of TN symptoms in 39.8% of MS patients, which does not align with previous findings that suggest a prevalence rate of 2-4% for TN in MS patients, with some reports extending to 14% in specific cohorts.[1,3] This highlights the heterogeneity in prevalence rates, potentially influenced by differences in diagnostic criteria, study designs, or population characteristics. Moreover, the higher prevalence of bilateral pain in our study (41.9% of diagnosed cases) aligns with the literature that indicates MS-associated TN often presents with atypical or bilateral features due to central nervous system demyelination.[4,6]

Notably, our study revealed an average diagnostic delay of 14 months, which is consistent with prior reports suggesting that TN is frequently underdiagnosed in complex neurological conditions like MS.[7] This diagnostic delay underscores the necessity of raising clinical awareness and improving diagnostic tools for TN, especially in patients with overlapping pain syndromes.

The significant association between familial history of trigeminal neuralgia (TN) and the presence of brainstem involvement in multiple sclerosis (MS) patients with TN symptoms underscores the potential role of genetic predisposition and central demyelinating processes in the pathophysiology of TN. This finding suggests that both inherited susceptibility and lesion localization within the brainstem may contribute to the manifestation and severity of TN in MS, warranting further investigation into

shared neurobiological mechanisms and potential therapeutic targets.

Clinical implications and recommendations

Our findings emphasize the critical need to integrate routine TN screening into the clinical management of MS patients. This is particularly important given the impact of delayed diagnosis on patients' quality of life and functional status. Based on our results and existing evidence:

Pharmacological management

First-Line Therapy: Carbamazepine remains the cornerstone of treatment for TN in MS due to its efficacy in controlling neuropathic pain in up to 90% of cases.[8] However, clinicians should monitor for potential side effects, such as dizziness and hyponatremia, which may be exacerbated in MS patients.

Second-Line Options: For patients intolerant to carbamazepine, alternatives such as gabapentin, pregabalin, and lamotrigine can be considered, although their efficacy in MS-related TN is less well-established.[8,9]

Surgical Interventions:

Refractory cases may benefit from surgical options such as microvascular decompression or gamma knife radiosurgery. Our findings showed partial symptom relief in all patients who underwent microvascular decompression, consistent with prior studies reporting a high success rate in refractory TN.[10,11]

Patients with MS-associated TN may require tailored surgical approaches due to the central nature of the disease pathology.

Comprehensive pain management:

Multidisciplinary teams involving neurologists, pain specialists, and psychologists are essential to address the multifaceted nature of TN in MS patients. This approach can improve adherence to treatment and overall patient outcomes.

TN in MS subgroups

Our subgroup analysis revealed that the majority of TN cases occurred in females and patients aged 25-40 years, aligning with prior findings of female predominance in both MS and TN populations.[2,6] Hormonal and genetic factors may play a role in this gender disparity and warrant further investigation. Additionally, the high prevalence of TN in RRMS patients in our cohort suggests that routine screening in this subgroup could be particularly beneficial. For limitations and future directions, while our study provides valuable insights, it is limited by its single-center design and reliance on self-reported data for symptom assessment. Future multicenter studies with larger sample sizes and longitudinal designs are needed to validate these findings and establish standardized screening and treatment protocols for TN in MS patients.

In conclusion, this study highlights the significant prevalence of TN in MS patients, revealing diagnostic and therapeutic challenges. TN is often underdiagnosed in MS patients, leading to delayed treatment and reduced quality of life. Our study demonstrates that a positive familial history of TN and brainstem involvement are significant correlates of TN symptoms in MS patients, emphasizing the intricate interplay between genetic and neuroinflammatory factors. These results reinforce the necessity for a more comprehensive assessment of MS patients presenting with TN, as identifying these risk factors could facilitate earlier diagnosis, tailored treatment strategies, and improved patient outcomes. Further research and a multidisciplinary approach are crucial to improve the management of this condition and enhance the clinical outcomes and daily functionality of MS patients.

DISCLOSURE

Financial support: None

Conflict of interest: None

REFERENCES

1. Brownlee WJ, Hardy TA, Fazekas F, Miller DH. Diagnosis of multiple sclerosis: progress and challenges. *Lancet* 2017; 389:1336-46. doi: 10.1016/S0140-6736(16)30959-X.
2. McBenedict B, Goh KS, Yau RCC, *et al*. Neuropathic pain secondary to multiple sclerosis: A narrative review. *Cureus* 2024;16(6): e61587. doi: 10.7759/cureus.61587.
3. Joanna MZ. Diagnosis and differential diagnosis of trigeminal neuralgia. *Clin J Pain* 2002; 18(1):14-21. doi: 10.1097/00002508-200201000-00003.
4. Ali SMS, Shafique MA, Mustafa MS, *et al*. Effectiveness of gamma knife radiosurgery in the management of trigeminal neuralgia associated with multiple sclerosis: a systematic review and meta-analysis. *Neurosurg Rev* 2023;47(1):12. doi: 10.1007/s10143-023-02246-3.
5. Petrou C, Doxakis A, Barrera MAA, Konstantinidou P. Association of trigeminal neuralgia with multiple

sclerosis: A comprehensive review of neuropathic pain treatment. *J Mult Scler Res* 2023;3(1):1-8. DOI: 10.4274/jmsr.galenos.2023.2023-1-1

6. MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain* 2000; 123:665-76. doi: 10.1093/brain/123.4.665.
7. Maarbjerg S, Di Stefano G, Bendtsen L, Cruccu G. Trigeminal neuralgia - diagnosis and treatment. *Cephalalgia* 2017; 37(7):648-57. doi: 10.1177/0333102416687280.
8. Gronseth G, Cruccu G, Alksne J, *et al*. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. *Neurology* 2008;71(15):1183-90. doi: 10.1212/01.wnl.0000326598.83183.04.
9. Athanasiou TC, Patel NK, Renowden SA, Coakham HB. Some patients with multiple sclerosis have neurovascular compression causing their trigeminal neuralgia and can be treated effectively with MVD: report of five cases. *Br J Neurosurg* 2005; 19:463-68. doi: 10.1080/02688690500495067.
10. Yang XS, Li ST, Zhong J, *et al*. Microvascular decompression on patients with trigeminal neuralgia caused by ectatic vertebrobasilar artery complex: technique notes. *Acta Neurochir* (Wien) 2012; 154:793-7; discussion 797. doi: 10.1007/s00701-012-1320-6.
11. Broggi G, Ferroli P, Franzini A, *et al*. Operative findings and outcomes of microvascular decompression for trigeminal neuralgia in 35 patients affected by multiple sclerosis. *Neurosurgery* 2004; 55:830-8; discussion 838-839.