



**HAL**  
open science

## “Status trigeminal neuralgia”: Analysis of 39 cases and proposal for diagnostic criteria

Z Poulet, S Redon, R Gravier-Dumonceau, A Donnet

### ► To cite this version:

Z Poulet, S Redon, R Gravier-Dumonceau, A Donnet. “Status trigeminal neuralgia”: Analysis of 39 cases and proposal for diagnostic criteria. *Revue Neurologique*, 2024, 180, pp.689 - 697. 10.1016/j.neurol.2024.03.014 . inserm-04933281

**HAL Id: inserm-04933281**

**<https://inserm.hal.science/inserm-04933281v1>**

Submitted on 6 Feb 2025

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License



Available online at  
**ScienceDirect**  
[www.sciencedirect.com](http://www.sciencedirect.com)

Elsevier Masson France  
**EM|consulte**  
[www.em-consulte.com](http://www.em-consulte.com)



## Original article

# “Status trigeminal neuralgia”: Analysis of 39 cases and proposal for diagnostic criteria



Z. Pouillet<sup>a</sup>, S. Redon<sup>a,\*</sup>, R. Gravier-Dumonceau<sup>b</sup>, A. Donnet<sup>a,c</sup>

<sup>a</sup>Department of Evaluation and Treatment of Pain, FHU INOVRAIN, CHU Timone, AP-HM, Marseille, France

<sup>b</sup>APHM, INSERM, IRD, SESSTIM, sciences économiques & sociales de la santé & traitement de l'information médicale, ISSPAM, Hop Timone, BioSTIC, biostatistique et technologies de l'information et de la communication, Aix Marseille Univ, Marseille, France.

<sup>c</sup>Inserm U-1107, CHU de Clermont-Ferrand, Clermont-Ferrand, France

### INFO ARTICLE

#### Article history:

Received 6 October 2023

Received in revised form

21 March 2024

Accepted 25 March 2024

Available online 23 May 2024

#### Keywords:

Acute exacerbation

Balloon compression

Status trigeminus

Idiopathic trigeminal neuralgia

Classical trigeminal neuralgia

Secondary trigeminal neuralgia

### ABSTRACT

**Objective.** – The aim of this descriptive study was to propose diagnostic criteria for acute exacerbation of trigeminal neuralgia (TN) based on the analysis of retrospective cases.

**Background.** – TN is a rare and extremely painful condition whose evolution can be punctuated by major exacerbations, leading to significant functional impairment. Several denominations are used for these exacerbations: “acute exacerbation”, “status of trigeminal neuralgia”, and “status trigeminus”. There is currently no clinical definition of this state. In this manuscript, we used the term “status trigeminal neuralgia” (STN).

**Methods.** – We conducted a retrospective study, in a tertiary care specialist headache center, in France. Patients were selected from January 2015 to October 2022, with the French translation of the keyword “STN”, in the medical records (outpatients) or the codage for trigeminal neuralgia (inpatients). Additional cases of STN were prospectively recruited from October 2022 to February 2023. We analyzed the clinical and paraclinical data of these patients.

**Results.** – Thirty-nine patients presenting with STN were included. There was a preponderance of women (64%) with 24 cases of classic TN (62%) and 15 cases of secondary TN (38%). Concerning STN, 39 episodes were described. Pain was very severe in all patients. Cranial autonomic signs were present in 23% of cases. Pain extended beyond the usual territory in 44% of cases. A continuous pain background was present in 35% of cases. With regard to triggering factors, paroxysms of facial pain were triggered by eating (97% of patients), speaking (90%) or drinking (62% of patients). Repercussions on weight, hydration, or mood disorders were observed in 67%, 56% and 59% of the cases, respectively.

**Conclusion.** – STN is a rare clinical presentation of TN. We proposed criteria and a new denomination for this condition.

© 2024 Elsevier Masson SAS. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

\* Corresponding author.

E-mail address: [sylvain.redon@ap-hm.fr](mailto:sylvain.redon@ap-hm.fr) (S. Redon).

<https://doi.org/10.1016/j.neurol.2024.03.014>

0035-3787/© 2024 Elsevier Masson SAS. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

## Introduction

Trigeminal neuralgia (TN) is characterized by recurrent and severe paroxysms of pain in the territory of one or several branches of the trigeminal nerve. Occasionally, TN may worsen for several days or weeks, with a rate of several attacks per hour [1–3], sometimes countless, with varying degrees of severity. These attacks may be so debilitating that eating, drinking, talking or even swallowing oral medication is impossible [4]. These episodes result in marked functional and emotional incapacity [5]. This entails a risk of dehydration, malnutrition, weight loss and discontinuation of treatment, increasing attacks [1,6]. Extreme urgent treatments, such as intravenous treatments or neurosurgical intervention, are needed [1–3,6–16]. These episodes are usually called “acute exacerbation” or “acute flare-ups” of TN [7,17,18]. However, no consensual definition exists, and the clinical features of these patients have not been described in a consensual manner. In this paper, we described a population of French patients who experienced such worsening of TN. We used the term “status trigeminal neuralgia” (STN), which is the translation of the French usually used term “*état de mal névralgique*”. We proposed diagnostic criteria for STN.

## Methods

### Patient recruitment

This study took place in a headache center (Timone Hospital, Marseille). From June 2015 to October 2022, we retrospectively selected patients in two ways: inpatients coded “trigeminal neuralgia” (International Classification of Diseases 10th Revision, code G500) and outpatients with the French keyword abbreviation for STN in medical records. We excluded duplicate patient records and inpatients with diagnoses other than TN (SUNCT/SUNA, trigeminal neuropathic pain). We included patients who presented with an acute exacerbation of TN, with sufficient functional impairment to be called “STN”, according to the practitioner in charge of the patient. We selected patients with at least one episode of STN. We excluded patients without sufficient data about episodes of STN and TN exacerbation and those without sufficient functional impairment to qualify as having STN. Four patients were included prospectively, from October 2022 to February 2023, following an emergency consultation at the headache center.

### Data collection

In our opinion, STN underlies very frequent attacks of TN, with severe or very severe intensity and significant functional impairment (inability to eat, drink, or talk). A criterion of duration including resistance to oral medication should be included. We assessed these criteria in our population. We collected data from medical records (paper files and computerized records). Clinical features of TN and STN were collected. When several episodes of STN were identified for a single patient, we analyzed only the last episode. A

comparison was made between two groups: patients with “classic or idiopathic TN” and those with “secondary TN” (according to the International Headache Society [IHS] classification) [19].

### Statistical analysis

Continuous data such as age are summarized by descriptive statistics. Categorical variables are presented as frequency distributions (*n*, %). Continuous variables are presented as medians associated with the interquartile range or as the means associated with standard deviations. The Chi-squared test and Fisher’s test were used, where appropriate, to assess associations of categorical variables. A nonparametric Wilcoxon–Mann–Whitney test was used to compare medians and means. A threshold value of  $P < 0.05$  was considered significant.

### Ethics

This study was validated by the Assistance publique–Hôpitaux de Marseille ethics committee as not involving a human person, under the following registration number: RGPD 2019-01 PADS22-386.

## Results

### Population study

The study flow chart is shown in Fig. 1. A total of 39 patients, with at least one episode of STN, were included in our study. Seven patients reported at least two episodes of STN. The last one was retained for analysis. The total population consisted of 14 males (36%) and 25 females (64%). This population was divided into two groups: “classic or idiopathic TN” (24 patients) and “secondary TN” (15 patients). In these secondary TN cases, TN was secondary to multiple sclerosis or related inflammatory pathology (14 patients), or meningioma of the petrous apex (1 patient). The mean age at diagnosis of TN was 50 years ( $\pm 12.8$ ), with extremes ranging from 20 to 78 years. Regarding past medical and comorbidities, there was a high proportion of smokers (21%) and a history of hypertension (21%).

### Characteristics of TN

TN was localized on the right side in 20 patients (51%) or on the left side in 19 patients (49%) (Table 1). The pain largely concerned the V2 territory (66.7%), followed by the V3 territory (41%) and the V1 territory (33%). There was no significant difference between the two groups, apart from the topography of TN. The V3 territory was predominantly affected in 73% of patients with secondary TN, whereas it was involved in 41% of patients in the classic or idiopathic TN group ( $P = 0.01$ ). The mean age at onset of TN was 52 years for classic or idiopathic TN and 47 years for secondary TN group ( $P = 0.26$ ). The majority of patients (83%) had at least one trigger zone. It was present in 91% of patients in the classic or idiopathic TN group compared to 69% of patients in the secondary TN ( $P = 0.16$ ).

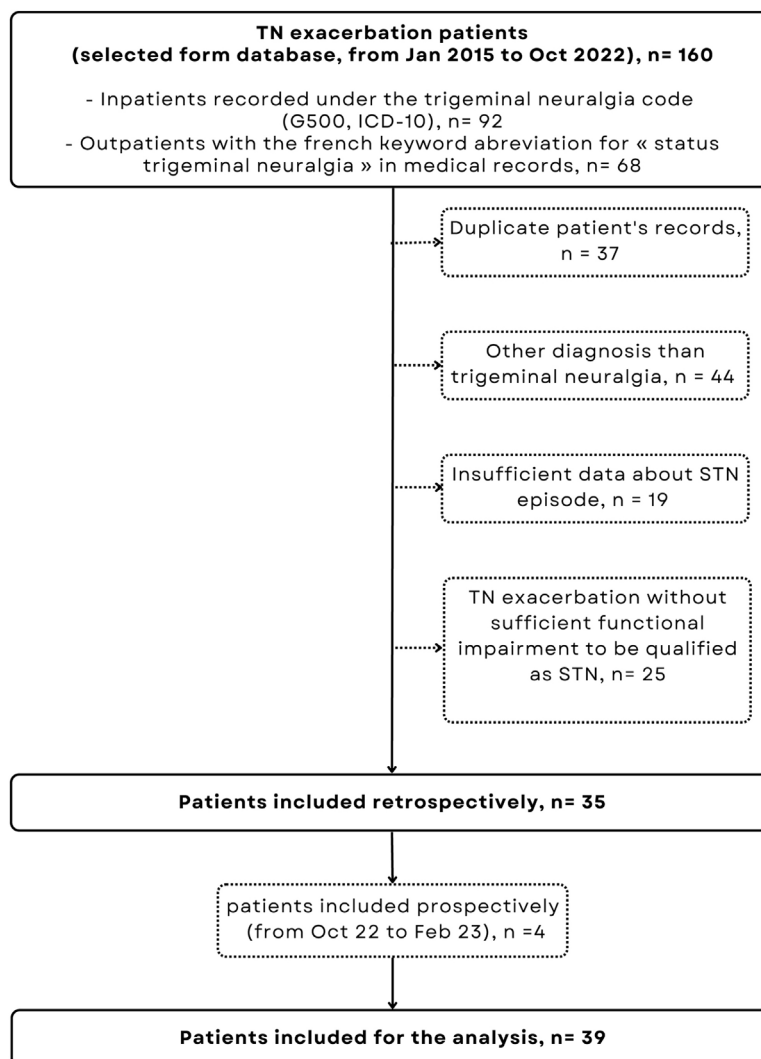


Fig. 1 – Flow chart.

Table 1 – General characteristics of the population study.

Variable	Total cases of TN (n = 39)	Classic or idiopathic neuralgia (n = 24)	Secondary neuralgia (n = 15)
Gender: male/female	14/25	9/15	5/10
Mean age at diagnosis (years) [± SD]	50.2 [± 12.8]	52.1 [± 13.7] (range: 20–78)	47.2 [± 11.0] (range: 29–65)
Pain distribution (in parentheses: patients with cranial autonomic symptoms)			
Pain side: right/left	20 (5)/19 (8)	11 (4)/13 (4)	9 (1)/19 (4)
V1	2 (0)	0	2 (0)
V2	11 (3)	9 (2)	2 (1)
V3	11 (3)	6 (1)	5 (2)
V1–V2	10 (6)	9 (5)	1 (1)
V2–V3	4 (1)	0	4 (1)
V1–V2–V3	1 (0)	0	1 (0)
Presence of a trigger zone	29	20	9
Number of trigger zones: 1/≥ 2	21/7	15/4	6/3
Median number of TN drugs the patient received (range)	4 (1–5)	4 (1–5)	4 (2–5)
Median number of surgical procedures the patient received for TN (range)	2 (0–9)	2 (0–9)	2 (0–7)

Cranial autonomic symptoms were present throughout the course of TN in 13 patients (33%) with classic or idiopathic NT and five patients (33%) with secondary TN. They were described from the beginning of the disease and mainly occurred in the most severe attacks. In these patients, the V1 territory was involved in the majority of cases (9 patients). The most frequent symptom was ipsilateral tearing. Pain was described as “electric shock-like”, sometimes in bursts. Five patients had a seasonal worsening of TN: autumn (3 patients), winter (1 patient), or biannual worsening (1 patient). During the course of TN disease, a median of four different TN treatments were administered (IQR 3–4). A median of two surgical treatments per patient were attempted (IQR 1–4, with extremes of up to 9 surgeries in the same patient).

### Clinical features of attacks during STN

STN occurred after a median of 57 months of TN evolution (IQR: 34–144 months) (Table 2). For 92% of STN cases, this exacerbation occurred in the absence of a contributing factor. Only three STNs were possibly triggered by the following factors: treatment withdrawal (1 patient), stress (1 patient), and gamma-knife radiosurgery (1 patient). The median duration of STNs was 10 days (IQR: 6–15 days), with extremes ranging from 3 to 30 days.

Pain intensity was described by all patients as “very severe” and most often as “extremely severe”. Eighteen

patients reported one or several cranial autonomic symptoms during STN. Among them, six patients reported de novo autonomic symptoms (never reported during the course of TN) in the classic or idiopathic TN group, whereas no autonomic symptoms were reported in the secondary TN group ( $P = 0.02$ ). These symptoms were the following (Table 2): unilateral lacrimation (18 patients), unilateral rhinorrhea (7 patients), unilateral conjunctival injection (2 patients) or redness of the hemiface (one patient). Of these 18 patients, a single autonomic symptom was present in 56% of patients, and at least two symptoms were present in 44%, i.e., only one patient had a combination of three symptoms. Among patients with autonomic symptoms during STN, the pain involved the V1 territory for nine patients (50%).

The following trigger factors were associated with STN: eating (97%), speaking (90%), brushing teeth (85%), drinking (62%) and cold (13%). Other less frequent triggers included shaving, brushing or washing hair, makeup, wind, strong emotions, nose blowing, or even movement. Pain was triggered by the stimulation of a trigger zone in 82% of patients. The trigger zone was unique (27 patients) or multiple (5 patients).

The frequency of attacks was very difficult to assess. At least 85% of patients reported “very frequent” attacks (23 patients) or “continuous or nearly continuous” attacks (10 patients). The other patients had an unassessed frequency of attacks, with a frequency of several per day but without

**Table 2 – Clinical characteristics of pain during status trigeminal neuralgia (STN).**

Variable	Total cases of TN n = 39	Classic or idiopathic TN n = 24	Secondary TN n = 15	P-value
Number of STN episodes per patient	1: 32 (82%) ≥ 2: 7 (18%)	1: 20 (83%) ≥ 2: 4 (17%)	1: 12 (80%) ≥ 2: 3 (20%)	
Median time to progression (IQR) of TN at time of STN, in months	57 (34–144)	87 (52–173)	33 (6–50)	0.003 <sup>c</sup>
Cranial autonomic symptoms (CAS)				
Previously reported in TN attacks	12	9	3	
De novo CAS (never reported in TN)	6	6	0	0.024 <sup>a</sup>
Tearing/rhinorrhea/other	18/7/2	15/7/1	3/0/1	> 0.999 <sup>a</sup>
Number of cases: 1/≥ 2	10/8	8/7	2/7	
Triggering factors				
Eating	38	23	15	> 0.999 <sup>a</sup>
Speaking	35	20	15	0.146 <sup>a</sup>
Teeth brushing	33	22	11	0.180 <sup>a</sup>
Drinking	24	13	11	0.231 <sup>b</sup>
Cold	5	3	2	> 0.999 <sup>a</sup>
Extension beyond the usual territory	17 (44%)	10 (42%)	7 (47%)	0.759 <sup>b</sup>
Presence of a painful background	13 (33%)	9 (38%)	4 (27%)	0.426 <sup>a</sup>
Trigger zone	32 (82%)	22 (9%)	10 (67%)	0.057 <sup>a</sup>
1 trigger zone	27	19	8	0.646 <sup>b</sup>
≥ 2 trigger zones	5	3	2	
Functional repercussions				
Weight loss	20	12	8	> 0.999 <sup>a</sup>
Difficulty drinking	14	10	4	
Anxiety, depression	≥ 23	≥ 18	≥ 5	
Median duration of STN (range), in days	10 (6–15)	14 (7–18)	9 (5–15)	0.474 <sup>c</sup>

n (%). With regard to psychological impact, significant data were missing, so we chose to base the frequency distribution (%) on the total population (considering patients with missing data as “no psychological impact”).

<sup>a</sup> Pearson’s Chi-squared test.

<sup>b</sup> Fisher’s exact test.

<sup>c</sup> Wilcoxon rank sum test.

further precision. The duration of attacks varied from a few seconds to bursts lasting several minutes or even several hours continuously but it was impossible for patients to determine their exact duration, due to the extreme severity of the symptoms and their intrusive nature.

The territory of TN pain extended beyond its usual territory in 45% of patients.

After excluding two patients with constant facial pain due to postsurgical trigeminal neuropathy, 35% of patients reported the appearance of a painful background between attacks. Its intensity was reported in 10 patients on a numeric scale ranging from 3 to 9/10 (mean 7.5/10). Neurological examination revealed facial hypoesthesia in two patients.

There was a major impact on food intake in all patients. Oral feeding was impossible in six patients. Two of them required parenteral nutrition. For the others, the food texture was changed, favoring liquid textures such as soup. Weight loss during STN occurred in 67% of cases, with a median loss of 4 kg (IQR: 3–5, range 2 to 12 kg). Weight loss was quantified in 13 patients. Drinking was difficult in 56% of patients. Nine patients received intravenous hydration (23% of all STNs analyzed). In 59% of patients, psychological repercussions (anxiety or sadness) were noticed by practitioners, but there was no systematic questioning. At least three patients described dark thoughts during STN. Four others were treated for reactive depressive syndrome. One suicide attempt, directly linked to the STN, was reported.

The median duration of STNs was shorter in the secondary TN group (33 months, IQR: 6–50) than in the classic or idiopathic NT group (57 months, IQR: 34–144,  $P = 0.003$ ). Extension beyond the usual territory occurred in 42% of patients in the classic or idiopathic TN group and in 47% of patients in the secondary TN group ( $P = 0.75$ ).

A trigger zone was present in 96% of STNs in the classic or idiopathic TN group versus only 71% in the secondary NT group ( $P = 0.057$ ). The median duration of STN insertion was 14 days (IQR: 7–18) in the classic or idiopathic TN group and nine days in the secondary TN group (IQR: 5–15,  $P = 0.47$ ). The

characteristics of patients' treatments before and during the STN, according to the etiology, are described in Table 3.

### Ongoing treatment during STN

No patient was treatment-naïve before the beginning of STN. Treatment characteristics are described in Table 3. In 95% of cases, patients were already being treated with at least carbamazepine or oxcarbazepine at the time of clinical worsening. Thirty-one patients observed at least two different treatments at the beginning of STN. Oral intake of TN treatment, in tablet form, was difficult in 11 patients (28%) and impossible in five patients [13]. In these cases, drinkable solutions or intravenous treatment were offered. Side effects linked to the STN treatments were reported in 23 patients (59%), including balance disorders, cognitive disorders, sedation and asthenia, and more rarely hyponatremia under carbamazepine or oxcarbazepine.

### Therapeutic decision and management of the episode of STN

The initial management consisted of increasing medical treatment, either orally or intravenously. During STN, 26 patients (67%) underwent two or three different TN treatments. Eleven patients (28%) had four or more different treatments, and only two patients (5%) remained on monotherapy. The most common intravenous treatments offered were lidocaine (1.5–3 mg/kg) and lacosamide (200 mg). In addition, other treatments included intravenous amitriptyline (2 patients, 50 mg/day) or clonazepam via a syringe driver (8 other patients, up to 6 mg/day), awaiting surgical treatment. Drug management alone was sufficient for 14 patients (36%). Among these patients, seven were treated with intravenous lidocaine and three patients were treated with intravenous lacosamide. Urgent neurosurgical treatment was required in 25 patients (64%), either immediately or after the failure of drug therapy. This procedure involved balloon compression in

**Table 3 – Medical treatments before and during status trigeminal neuralgia (STN).**

Variables	Total cases of TN n = 39	Classic or idiopathic TN n = 24	Secondary TN n = 15
Treatments received before STN			
Number of treatments: $1 \geq 2$	8/31	7/17	1/14
Carbamazepine or oxcarbazepine	37	22	15
Treatments received during STN (dosage range)			
Carbamazepine (450/2000 mg/day)	30	19	11
Oxcarbazepine (450/1200 mg/day)	8	4	4
Gabapentine (900–4800 mg/day)	6	3	3
Baclofene (15–80 mg/day)	12	11	1
Pregabalin (100–1500 mg/day)	8	7	1
Lamotrigine (75–300 mg/day)	4	4	0
Clonazepam (orally or intravenously, 0.3–6 mg/day)	15	9	6
Amitriptyline (orally or intravenously, 20–50 mg/day)	6	5	1
Lidocaine (intravenously; 90 mg–165 mg/day)	12	6	6
Lacosamide (intravenously, 200 mg/day)	8	7	1
Total number of treatments received: $1/2-3/\geq 4$	2/26/11	2/17/5	0/9/6
Poor treatment tolerance	23	13	10
Patient ability to take oral treatment during STN: possible/difficult/impossible	23/11/5	15/5/4	8/6/1

19 patients and gamma-knife radiosurgery in 10 patients. Five of these patients underwent gamma-knife radiosurgery after failure of two balloon compressions.

## Discussion

Our study is the largest descriptive study focused on the clinical features of acute exacerbations of TN. There are few descriptions of this condition in the literature. The umbrella term “acute exacerbation of TN” usually refers to TN patients requiring in-hospital treatment, intravenous treatments or rehydration.[7] Other authors, using different terms (“status of trigeminal neuralgia”, “status trigeminus”, “trigeminal neuralgia crisis”) [3,20–23], provided clinical descriptions: “the most severe manifestation of a trigeminal neuralgia exacerbation” (Megdiatov et al.), “a rapid succession of tic-like spasms triggered by seemingly any stimulus” (Greenberg), “incessant twinges” (Straus et al.), and “severe pain episodes, patients may be unable to eat, drink, or even swallow oral medication, requiring in-hospital treatment” (Schnell et al.). In our study, we used the term “status trigeminal neuralgia” in reference to other neurological conditions refractory to medical treatments: “status migrainosus” and “status epilepticus”.

Our study population is broadly similar to the various descriptions in the literature [24,25]. The age of onset in our study (50 years old) was slightly younger than that in the literature (53–60 years old). This could be explained by the difference in the incidence of secondary TN to multiple sclerosis in our study. We found a high number of patients with hypertension in our population (21%). This link has been established by Pan et al. [26]. Regarding the topography of TN pain, there was a predominance of involvement of the V2 territory, which was affected in two-thirds of our patients, which is consistent with the data in the literature [27]. On the other hand, interestingly, there was a significant difference between the “classic or idiopathic” and “secondary” TN groups. The V3 territory was significantly more affected in secondary TN (predominantly affected in 73.3% of patients versus 20% in classic or idiopathic TN,  $P = 0.001$ ), and the V1 territory was very frequently affected in the classic or idiopathic TN group (41.7%), which is not the common territory in the literature. This must be weighed against the fact that in our study, we did not analyze the associated involvement of several territories, which would be interesting to look at. Furthermore, the presence of a trigger zone was found more rarely in secondary TN (69.2%) than in classic or idiopathic TN (90.9%). Although this result was not significant ( $P = 0.16$ ), this trend was consistent with the literature, where the absence of a trigger zone should prompt a search for secondary TN.

All patients were already being treated at the onset of STN. The vast majority had at least the reference treatment of carbamazepine or oxcarbazepine [28]. Moreover, the majority of patients were even being treated with several lines of TN therapy at the onset of TN exacerbation. The initial severity profile of these patients showed a tendency toward drug resistance or tolerance. This profile is found during STN, making it very difficult to manage and leading to worsening pain. In fact, initial treatment will most often consist of

**Table 4 – Proposed diagnostic criteria for status trigeminal neuralgia.**

A. Facial pain fulfilling both criteria for trigeminal neuralgia (ICHD-3 classification, criterion 13.1.1) and all the following criteria
B. Neuralgiform attacks, with the following two features: <ol style="list-style-type: none"> <li>1 – high frequency attacks or sub-continuous attacks</li> <li>2 – severe or very severe intensity</li> </ol>
C. Involving significant functional repercussions, with at least two of the following five criteria: <ol style="list-style-type: none"> <li>1 – Difficulty eating</li> <li>2 – Difficulty hydrating</li> <li>3 – Difficulty expressing oneself</li> <li>4 – Weight loss</li> <li>5 – Anxiety and depression</li> </ol>
D. Duration > 3 days

increasing the dose of oral or intravenous medication whenever possible. This treatment was often poorly tolerated and insufficiently effective, requiring a surgical procedure in most of the cases. This picture of drug resistance and drug tolerance therefore initially seemed to us to be an important feature of the STN. However, we decided not to include it in our proposed diagnostic criteria, as a patient may start out with TN and immediately enter a STN without being previously treated with anti-neuralgic therapy. The efficacy of subcutaneous or intranasal sumatriptan, previously reported in the algorithm treatment of STN, was not assessed in our study [18].

In Table 4, we propose criteria for STN, which were individually respected in our population. These criteria can be divided into three categories: the characteristics of pain, the functional impairment and the duration of STN. Our study also suggests some modifications of clinical pictures during STN, summarized below: the extension of a pain beyond the usual territory and the appearance of a painful background between attacks or cranial autonomic symptoms during attacks. The incidence of these symptoms is insufficient to be considered as a diagnostic criterion but deserves to be evaluated in further prospective studies.

### Characteristics of pain during STN

The high intensity of pain was a constant clinical feature in our patients. The exact frequency of attacks was very difficult to assess in these patients, who were in a state of extreme suffering. At least 81% of patients experienced “very frequent or constant” attacks, but it was impossible to obtain an objective number of attacks per hour or even per day. Indeed, the frequency of attacks was so high that it was impossible to quantify them.

### Functional impairment of STN

In terms of functional impact, we were interested in the following three points: drinking, eating and speaking. These three essential actions, when they trigger attacks, become impossible for the patient to perform, which is what makes the crisis so serious.

Food intake was reported as a triggering factor in 98% of patients. In this context, weight loss was observed in two-

thirds of patients. This is an objective reflection of the inability to eat but is not always noticed by patients, especially when the crisis lasts only a few days. A median weight loss of 4 kg was observed in the 13 patients whose weight loss could be quantified, with extremes ranging from 2 to 12 kg. It is very likely that a greater proportion of patients are affected by weight loss in the face of major eating difficulties but that for a weight loss of less than 2 kg, this is not noticed by patients. A prospective study with systematic weighing of patients is needed to assess this precise item.

Drinking was difficult in 54% of patients. Over one-fifth of patients received intravenous hydration.

In 90% of cases, speech was a factor triggering attacks, with major functional repercussions.

In addition, the impact of anxiety and depression, which was found in at least 57% of patients, is likely underestimated in our study due to the absence of a depression and anxiety assessment scale and, above all, because practitioners do not systematically seek out this information during consultations. This issue needs to be assessed more systematically in the future.

### **Duration of STN**

We propose a minimum duration criterion of three days, which is the minimum duration of STN in our patients. However, due to the retrospective nature of this study, these data should be interpreted with caution. In medical records, the beginning of STN was considered when patients were suffering from a particularly debilitating condition, had difficulty speaking, eating or talking. In fact, there were two types of patients: (i) those who reported initial progressive clinical worsening, over several days or weeks, with failure of therapeutic modifications, before entering the phase of STN, a clinical phase rarely lasting more than a few days that led them to seek emergency care; and (ii) those who reported sudden worsening of their neuralgia, with rapid entry over a few days or even a few hours into the phase known as STN. This is why in our study, there were missing data concerning the duration of STN in eight patients who presented alternating periods of major worsening and then lulling. In our STN criteria proposition, we defined an arbitrary cutoff for STN duration, suggested by the minimum duration of exacerbations in our study.

### **Modifications of the clinical picture during STN**

During STN, more than one-third of patients had an extension of the pain territory beyond the usual one. Similarly, *de novo* autonomic symptoms, i.e., those not ever reported in TN attacks, appeared in 23% of patients. This phenomenon was described by Megdiatov et al. in 1993 [20]. One hypothesis would be that the prolonged duration of STN increases the risk of developing cranial autonomic symptoms. Ipsilateral lacrimation was present in all our patients with dysautonomia. Interestingly, this *de novo* dysautonomia during STN was found only in the classic and idiopathic TN group, whereas it was absent in secondary TN cases. This difference is significant ( $P = 0.02$ ) and may be explained by the fact that in cases of secondary TN, the anatomical zone stimulated

most in our study was the V3 territory, which is less prone to dysautonomia. Excessive salivation, a cranial autonomic symptom involving the third branch of the trigeminal nerve, is difficult to observe during STN, and was possibly underestimated in our study [29]. It has been described that autonomic signs tend to be more frequent in patients with pain involving V1 [29]. In our study, 46% of patients with autonomic symptoms prior to STN had pain involving the V1 territory. This was also the case for half of patients with autonomic symptoms during STN. There was also frequently a painful background between attacks, found in 35% of cases, reflecting the clinical severity. This painful background in STN must be differentiated from TN with concomitant continuous pain, a subform for idiopathic trigeminal neuralgia in the IHS classification [19]. In STN, the background pain disappeared after the resolution of the episode. Initially, we hypothesized a possible multiplication of the number of trigger zones during STN, but this hypothesis has not been validated. In fact, multiple trigger zones ( $\geq 2$ ) were found during STN in only five patients. In all of them, this phenomenon had already been described during previous attacks of TN.

The appearance of facial hypoesthesia in the area affected by TN was not demonstrated in our study. Most of the time, sensitivity testing was not carried out because of the extreme pain presented by patients and the risk of triggering attacks at the time of the examination. We were therefore unable to evaluate this item in our study.

We consider to have excluded from our study patients with a diagnosis of SUNCT or SUNA, syndromes defined as moderate to severe headache attacks, strictly unilateral, lasting from a few seconds to a few minutes, occurring at least once a day and usually associated with significant tearing and redness of the ipsilateral eye (for SUNCT) or at least one ipsilateral autonomic symptom (for SUNA) [19]. Distinguishing between these two entities and TN can be difficult when associated autonomic symptoms are present, particularly when the V1 territory is involved [29,30]. In fact, 13 patients had a rapid onset of TN, with the presence of one (most often, 55% of cases) or more autonomic symptoms, including four only during the most severe attacks. However, these patients also fulfilled all the ICHD-3 criteria for TN, in particular the presence of a trigger zone (except in one patient), so that the diagnosis of TN was retained. In the literature, autonomic symptoms are present in the course of TN in at least 30% of cases [25,29,30]. The only patient without a trigger zone had multiple sclerosis and was therefore diagnosed as having secondary TN. Moreover, it was difficult to determine at what point in the evolution of TN these signs had appeared (from the first attacks or after several years or post-surgery) in this context of retrospective collection, given the lack of information concerning these precise data.

### **Limitations**

The retrospective nature of the study may have led to several biases, in particular recall and selection bias. Moreover, the small number of patients, which is inherent to the rarity of the pathology, and the monocentric design of the study. The absence of a consensual definition for STN may be a selection bias in our study. We deliberately excluded 27 patients from



the analysis because TN exacerbation was not considered severe enough to be called STN. This reflects the need to clarify the definition of TN exacerbation. With this selection criterion, we obtained a relatively small population of STN. In comparison, we found 300 patients coded TN (13.1) or classical TN (13.1.1) between June 2015 to February 2023 in our headache center. Finally, objective measures of functional impairment would have allowed for a more objective selection of patients.

### Perspectives

These diagnostic criteria constitute the first proposal for defining STN. A prospective evaluation of these criteria is needed to validate them. We believe that the establishment of these criteria is necessary for the elaboration of further clinical studies in this area.

### Conclusion

The occurrence of STN in the course of TN disease is rare. We propose a clinical definition of this condition. However, further prospective studies are needed to validate our criteria proposition and other clinical modifications pictures, as shown in our study. This may be a prerequisite for larger-scale studies to develop effective therapeutic strategies.

### Declaration of interest

Z. Pouillet and R. Gravier-Dumoncau declare that they have no competing interest. S. Redon reports disclosure with Teva, A. Donnet reports disclosure with Allergan/AbbVie, Lilly, Lundbeck, Novartis, Pfizer, Teva.

### REFERENCES

- [1] Cheshire WP. Trigeminal neuralgia: for one nerve a multitude of treatments. *Expert Rev Neurother* 2007;7:1565–79. <http://dx.doi.org/10.1586/14737175.7.11.1565>.
- [2] Cheshire WP. Fosphenytoin. *J Pain Symptom Manag* 2001;21:506–10. [http://dx.doi.org/10.1016/S0885-3924\(01\)00269-X](http://dx.doi.org/10.1016/S0885-3924(01)00269-X).
- [3] Schnell S, Marrodan M, Acosta JN, Bonamico L, Goicochea MT. Trigeminal neuralgia crisis – intravenous phenytoin as acute rescue treatment. *Headache* 2020;60:2247–53. <http://dx.doi.org/10.1111/head.13963>.
- [4] Juniper RP, Glynn CJ. Association between paroxysmal trigeminal neuralgia and atypical facial pain. *Br J Oral Maxillofac Surg* 1999;37:444–7. <http://dx.doi.org/10.1054/bjom.1999.0135>.
- [5] Zakrzewska JM, Wu J, Mon-Williams M, Phillips N, Pavitt SH. Evaluating the impact of trigeminal neuralgia. *Pain* 2017;158:1166–74. <http://dx.doi.org/10.1097/j.pain.0000000000000853>.
- [6] Xu R, Xie ME, Jackson CM. Trigeminal neuralgia: current approaches and emerging interventions. *JPR* 2021;14:3437–63. <http://dx.doi.org/10.2147/JPR.S331036>.
- [7] Bendtsen L, Zakrzewska JM, Abbott J, Braschinsky M, Di Stefano G, Donnet A, et al. European Academy of Neurology guideline on trigeminal neuralgia. *Eur J Neurol* 2019;26:831–49. <http://dx.doi.org/10.1111/ene.13950>.
- [8] Jones MR, Urits I, Ehrhardt KP, Cefalu JN, Kendrick JB, Park DJ, et al. A comprehensive review of trigeminal neuralgia. *Curr Pain Headache Rep* 2019;23:74. <http://dx.doi.org/10.1007/s11916-019-0810-0>.
- [9] Sindrup SH, Jensen TS. Pharmacotherapy of trigeminal neuralgia. *Clin J Pain* 2002;18:22–7. <http://dx.doi.org/10.1097/00002508-200201000-00004>.
- [10] Pinto MJ, Gomes A, Pinto M, Abreu P, Costa A. Treatment of acute exacerbations of trigeminal neuralgia in the emergency department: a retrospective case series. *Headache* 2022;62:1002–6. <http://dx.doi.org/10.1111/head.14373>.
- [11] Tate R, Rubin LM, Krajewski KC. Treatment of refractory trigeminal neuralgia with intravenous phenytoin. *Am J Health Syst Pharm* 2011;68:2059–61. <http://dx.doi.org/10.2146/ajhp100636>.
- [12] Andersen ASS, Heinskou TB, Asghar MS, Rossen B, Noory N, Smilkov EA, et al. Intravenous fosphenytoin as treatment for acute exacerbation of trigeminal neuralgia: a prospective systematic study of 15 patients. *Cephalalgia* 2022;42:1138–47. <http://dx.doi.org/10.1177/03331024221094536>.
- [13] Noro S, Seo Y, Honjo K, Okuma M, Asayama B, Amano Y, et al. Intravenous fosphenytoin therapy for rescue of acute trigeminal neuralgia crisis in patients awaiting neurosurgical procedures: a cross-sectional study. *J Clin Neurosci* 2021;94:59–64. <http://dx.doi.org/10.1016/j.jocn.2021.09.040>.
- [14] Arai Y-CP, Hatakeyama N, Nishihara M, Ikeuchi M, Kurisuno M, Ikemoto T. Intravenous lidocaine and magnesium for management of intractable trigeminal neuralgia: a case series of nine patients. *J Anesth* 2013;27:960–2. <http://dx.doi.org/10.1007/s00540-013-1641-5>.
- [15] Xu R, Nair SK, Shah PP, Kannapadi N, Materi J, Alomari S, et al. A potential role for steroids in acute pain management in patients with trigeminal neuralgia. *World Neurosurg* 2022;167:e1291–8. <http://dx.doi.org/10.1016/j.wneu.2022.09.025> [S1878875022012918].
- [16] Solaro CM, Ferriero G. Refractory trigeminal neuralgia successfully treated by combination therapy (pregabalin plus lamotrigine). *Mult Scler Relat Disord* 2018;25:165–6. <http://dx.doi.org/10.1016/j.msard.2018.07.027>.
- [17] Cruccu G, Gronseth G, Alksne J, Argoff C, Brainin M, Burchiel K, et al. AAN-EFNS guidelines on trigeminal neuralgia management: trigeminal neuralgia management. *Eur J Neurol* 2008;15:1013–28. <http://dx.doi.org/10.1111/j.1468-1331.2008.02185.x>.
- [18] Moore D, Chong MS, Shetty A, Zakrzewska JM. A systematic review of rescue analgesic strategies in acute exacerbations of primary trigeminal neuralgia. *Br J Anaesth* 2019;123:e385–96. <http://dx.doi.org/10.1016/j.bja.2019.05.026>.
- [19] Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia* 2018;38:1–211. <http://dx.doi.org/10.1177/0333102417738202>.
- [20] Megdiatov RS, Karlov VA, Tebloev IK, Kalashnikov ID, Savin AA, Stulin ID, et al. [Status of trigeminal neuralgia and its pathogenetic therapy]. *Zh Nevropatol Psikhiatr Im S S Korsakova* 1990;90:13–6.
- [21] Greenberg MS. Greenberg's handbook of neurosurgery. 10th ed. New York/Stuttgart/Dehli: Thieme; 2023. <http://dx.doi.org/10.1055/b000000751>.
- [22] Straus DC, Ko AL, Sekhar LN. Trigeminal neuralgia. *Principles of neurological surgery*. Elsevier; 2018: 745–52 [e1]. <https://doi.org/10.1016/B978-0-323-43140-8.00053-6>.

- [23] Sanchez ASL, Gonzalo PR. Descompresión microvascular para el tratamiento de la neuralgia del trigémino. *Gac Med Bol [Internet]* 2020;43(1):67–73 [citado 2023 Jul 17. n.d].
- [24] Katusic S, Beard CM, Bergstralh E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945–1984. *Ann Neurol* 1990;27:89–95. <http://dx.doi.org/10.1002/ana.410270114>.
- [25] Maarbjerg S, Gozalov A, Olesen J, Bendtsen L. Trigeminal neuralgia – a prospective systematic study of clinical characteristics in 158 patients. *Headache* 2014;54:1574–82. <http://dx.doi.org/10.1111/head.12441>.
- [26] Pan S-L, Yen M-F, Chiu Y-H, Chen L-S, Chen H-H. Increased risk of trigeminal neuralgia after hypertension: a population-based study. *Neurology* 2011;77:1605–10. <http://dx.doi.org/10.1212/WNL.0b013e3182343354>.
- [27] Donnet A, Simon E, Cuny E, Demarquay G, Ducros A, De Gaalon S, et al. Recommandations pour le diagnostic et la prise en charge de la névralgie trigéminal classique. *Neurochirurgie* 2018;64:285–302. <http://dx.doi.org/10.1016/j.neuchi.2018.04.001>.
- [28] Zakrzewska JM, Linskey ME. Trigeminal neuralgia. *BMJ* 2014;348:g474. <http://dx.doi.org/10.1136/bmj.g474>.
- [29] Simms HN, Honey CR. The importance of autonomic symptoms in trigeminal neuralgia: clinical article. *JNS* 2011;115:210–6. <http://dx.doi.org/10.3171/2011.4.JNS101843>.
- [30] Araya EI, Claudino RF, Piovesan EJ, Chichorro JG. Trigeminal neuralgia: basic and clinical aspects. *Curr Neuropharmacol* 2020;18:109–19. <http://dx.doi.org/10.2174/1570159X17666191010094350>.