Nervus intermedius and the surgical management of geniculate neuralgia

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OBJECTIVE Geniculate neuralgia (GN) is an uncommon craniofacial pain syndrome attributable to nervus intermedius (NI) dysfunction. Diagnosis and treatment can be challenging, due to the complex nature of ear sensory innervation, resulting in clinical overlap with trigeminal neuralgia (TN) and glossopharyngeal neuralgia (GPN).

METHODS A retrospective review of a prospective neurosurgical database at our institution was performed, 2000–2017, with a corresponding systematic literature review. Pain outcomes were dichotomized as *unfavorable* for unchanged/worsened symptoms versus *favorable* if improved/resolved. Eight formalin-fixed brains were examined to describe NI at the brainstem.

RESULTS Eleven patients were surgically treated for GN—9 primary, 2 reoperations. The median age was 48, 7 patients were female, and the median follow-up was 11 months (range 3–143). Seven had ≥ 2 probable cranial neuralgias. NI was sectioned in 9 and treated via microvascular decompression (MVD) in 2. Five patients underwent simultaneous treatment for TN (4 MVD; 1 rhizotomy) and 5 for GPN (3 MVD; 2 rhizotomy). Eleven reported symptomatic improvement (100%); 8 initially reported complete resolution (73%). Pain outcomes at last contact were *favorable* in 8 (73%)—all among the 9 primary operations (89% vs 0%, $p = 0.054$). Six prior series reported outcomes in 111 patients.

CONCLUSIONS GN is rare, and diagnosis is confounded by symptomatic overlap with TN/GPN. Directed treatment of all possible neuralgias improved pain control in almost all primary operations. Repeat surgery seems a risk factor for an unfavorable outcome. NI is adherent to superomedial VIII at the brainstem; the intermediate/cisternal portion is optimal for visualization and sectioning.

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KEYWORDS nervus intermedius; geniculate neuralgia; retrosigmoid approach; microvascular decompression; functional neurosurgery

GENICULATE neuralgia (GN) or nervus intermedius (NI) neuralgia is an uncommon craniofacial pain syndrome that typically causes severe shock-like neuralgic paroxysms centered in the deep ear canal.^{6,10–12,15} The etiology of GN has been related to NI pathology, in particular microvascular compression and herpes zoster infection.^{15,17} The NI contains 3 types of fibers: general somatic afferent sensory from the surface of the ear canal, tympanic membrane, retro-auricular skin, and regions within the pharynx; special visceral afferent (taste) from the anterior two-thirds of the tongue, floor of the mouth, and palate; and general visceral efferent (parasympathetic

output) to the lacrimal, sublingual, submandibular, and nasopalatine glands.¹⁷ The neuron cell bodies of the gustatory and sensory fibers form the geniculate ganglion.^{8,12} Within the ear canal, NI sensory innervation is complemented by contributions from the trigeminal, glossopharyngeal, and vagus nerves. Definitive diagnosis of GN is challenging, and features suggestive of both trigeminal neuralgia (TN) and glossopharyngeal neuralgia (GPN) are frequently described alongside deep ear pain, inviting speculation regarding the true nerve or nerves driving the pain syndrome.

Management of GN typically consists of several initial

ABBREVIATIONS BMI = body mass index; CN = cranial nerve; GN = geniculate neuralgia; GPN = glossopharyngeal neuralgia; MVD = microvascular decompression; NI = nervus intermedius; TN = trigeminal neuralgia.

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pharmacological trials prior to neurosurgical intervention, at which time either rhizotomy or microvascular decompression (MVD) of NI is carried out.^{7,8} If the patient's history is concerning for additional or alternative neuralgias, procedures targeting other potentially complicit cranial nerves, such as the trigeminal nerve (MVD or rhizotomy) or glossopharyngeal nerve (MVD or rhizotomy of the glossopharyngeal nerve and superior vagal rootlets, "cranial nerve complex IX–X partial rhizotomy"), may be incorporated into the operative plan. However, this practice is not universal and has not been studied previously. Additionally, although GN is notoriously challenging to treat, few studies have examined the outcomes in recurrent GN after reoperation. The primary objective of the present study was to review the presentation, management, and outcomes of surgically treated GN at our institution, with a focus on operative techniques that may result in a better clinical outcome and a comparison of outcomes after primary surgery versus reoperation. Additionally, a systematic review of prior series was conducted. An anatomical study of the NI at the brainstem, to better inform surgical techniques for correctly identifying NI and treating GN, was also performed.

Methods

A prospectively maintained neurosurgical operative database at our tertiary academic referral center was retrospectively queried for all patients treated surgically for GN from 2000 to 2017. Included patients underwent secondary chart review to capture demographics (sex, age at surgery), preoperative baseline characteristics (body mass index [BMI], smoking status, prior treatments, hearing status, symptomatology), operative details (approach, extent of cranial nerve sectioning and/or MVD), and follow-up details (symptomatology, hearing/facial nerve status, requirement for additional therapies, follow-up time). For patients with pre- and postoperative audiograms, hearing status was reported using the American Academy of Otolaryngology–Head and Neck Surgery guidelines. In patients without a formal audiometric study, binary subjective assessment of hearing status relative to preoperative baseline at time of last clinical contact was used, and facial nerve function was reported using the House-Brackmann grading system.^{3,5}

The primary study outcome was pain outcome at last clinical contact, relative to preoperative baseline. Pain outcomes were specific to neuralgia pain and were documented using the visual analog scale or subjective patient assessment of symptoms, as available in the medical record. Data were captured at multiple time points, including last preoperative consultation, early postoperative period, and last clinical contact. Pain outcome was dichotomized as favorable if pain had resolved or decreased versus unfavorable if the pain score had increased or remained unchanged. Patients were also classified based on potential underlying craniofacial neuralgia syndromes using patient-reported symptoms and the operating surgeon's documented preoperative diagnoses (GN, GN/TN, GN/GPN, GN/TN/GPN).

Systematic review of the literature was carried out by

searching MEDLINE, Embase, and Google Scholar databases since 1960, using MeSH/keywords "geniculate" or "nervus intermedius" together with "neuralg*". An initial search identified 83 candidate citations. Non-English language publications, articles not reporting primary data (e.g., isolated reviews, meta-analyses, or national database projects), and series reporting on fewer than 3 patients were excluded. Bibliographies of included publications were reviewed in detail to identify and include any additional citations meeting criteria. Included publications were reviewed in detail to confirm the diagnosis of GN and, as available, to capture data points including total sample size, presenting symptoms and other suspected neuralgias, pertinent surgical history, operative approach and intraoperative procedures, early and late pain outcomes, cranial nerve and wound complications, and total follow-up duration.

Fourteen sides of 8 formalin-fixed, cadaveric brains were studied. The cranial nerve (CN) VII–VIII complex was not preserved in 2 sides, which therefore could not be used for dissection. Direct examination was carried out using an operative microscope to evaluate, and describe in detail, the location of the NI at the brainstem, the relationships between the nerve and the adjacent fibers of the facial and vestibulocochlear nerves, and all surrounding vascular structures.

Summary statistics were generated, including median and range for continuous variables or frequency counts and percentages for categorical variables. Analysis was conducted using SAS 9.4 and JMP 13.0.0 (SAS Institute Inc., 1989–2017). Fisher's exact and Student t-tests were used for categorical and continuous data, respectively; all tests were two sided, and p values < 0.05 were considered statistically significant. All pertinent study components were fully approved by our institutional review board and biospecimens subcommittee.

Results

Clinical Analysis

During the study period, 2000–2017, 11 patients were surgically treated for GN at our institution; 9 were primary operations and 2 were reoperations (Table 1). The overall median age of the patients was 48 years, 7 patients were female (64%), and the median follow-up was 11 months (range 3–143 months). Seven patients (64%) presented with complex symptoms and were identified by a neurologist or neurosurgeon at our institution as exhibiting features consistent with GN and at least one additional cranial neuralgia. Therefore, 4 patients presented with isolated GN (36%), while concomitant symptoms potentially consistent with TN, GPN, or all 3 craniofacial neuralgias were described in 3, 2, and 2 patients, respectively.

A retrosigmoid approach was performed in all cases. GN was treated by MVD in 2 (18%) and NI rhizotomy in 9 (82%); TN was treated by MVD in 4 (80%) and by rhizotomy in 1 (20%); and GPN was treated by MVD in 2 (50%) and by rhizotomy of CN IX/partial rhizotomy of CN X in 2 (50%). All patients experienced clinically significant pain relief in the early postoperative period, with complete resolution of neuralgia symptoms in 8 (73%). Five patients experienced a symptomatic recurrence (45%), in

TABLE 1. Study cohort overview

Case No.	Age (yrs)	Sex	BMI	Active Smoker	Preop Sx (mos)	Tried Pharmacological Therapy	Pain Location	Preop Diagnosis	Primary Op or Reop	NI Treatment	TN Treatment	GPN Treatment	Early Postop Pain Relief	Pain Outcome			Medication at Last Clinical Contact	Total FU (mos)
														Recurrence	Contact	Stable	Yes	
1	35	F	26.6	Yes	18	C, G, B, NOR	Deep ear	GN	Primary	Rhizotomy	—	—	Complete	No	Favorable	Stable	Yes	143
2	44	F	25.1	Yes	12	C, G, O, TOP, NSAID	Deep ear	GN	Primary	Rhizotomy	—	—	Complete	Yes, permanent	Unfavorable	Stable	Yes	16
3	31	F	26.6	Yes	84	C, G, L, O	Deep ear	GN	Primary	Rhizotomy	—	—	Complete	Yes, transient	Favorable	Worsened	Yes	102
4	70	M	29.9	No	10	C	Deep ear, throat	GN, GPN	Primary	Rhizotomy	—	Rhizotomy	Incomplete	No	Favorable	Stable	No	11
5	48	M	25.9	Yes	79	C, G, B, O	Deep ear, tongue, oropharynx	GN, TN*	Primary	MVD	MVD	—	Complete	No	Favorable	Stable	No	3
6	53	M	27.3	No	108	C, G, O, NSAID, SSRI	Deep ear, auricle, periauricular face/scalp	GN, TN	Primary	Rhizotomy	MVD	—	Complete	No	Favorable	Stable	Yes	3
7	62	F	29.7	Yes	240	C, G, B, NSAID	Deep ear (w/ facial triggers)	GN, TN	Primary	Rhizotomy	MVD	MVD†	Complete	No	Favorable	Stable	Yes	4
8	46	M	23.9	No	50	Ox, L, G, B, O	Deep ear, face, throat	GN, TN, GPN	Primary	MVD	MVD	MVD	Incomplete	No	Favorable	Stable	No	29
9	62	F	32	No	26	Ox, O, TOP	Deep ear, face, oropharynx, throat	GN, TN, GPN	Primary	Rhizotomy	Rhizotomy	MVD	Complete	Yes, transient	Favorable	Stable	No	4
10	54	F	20.4	No	60	C, B, O	Deep ear	GN	Repeat	Rhizotomy	—	—	Incomplete	Yes, permanent	Unfavorable	Stable	Yes	3
11	33	F	33.6	Yes	8	C, G, B, AMY	Deep ear, throat	GN, GPN	Repeat	Rhizotomy	—	Rhizotomy	Complete	Yes, permanent	Unfavorable	Stable	No	90

AMY = amitriptyline; B = baclofen; C = carbamazepine; FU = follow-up; G = gabapentin; L = lamotrigine; NOR = nortriptyline; NSAID = nonsteroidal antiinflammatory drug; O = opioid; Ox = oxcarbazepine; SSRI = selective serotonin reuptake inhibitor; Sx = symptoms; TOP = topiramate.

* Neuralgic pain symptoms noted with radiographic compression of CNs VII–VIII and sensorineural hearing loss; operating surgeon's final preoperative diagnosis was GN versus atypical TN.

† Preoperative consideration for GPN low; however, large vascular loop compression of CNs IX–X was identified intraoperatively and therefore decompressed.

FIG. 1. Flow diagram demonstrating clinical trajectories for 11 patients treated for GN.

2 of whom it subsequently improved (40%). At last clinical contact, 8 patients reported favorable pain outcomes (73%), all of whom were among the 9 who had undergone primary operations (89%), and 4 of whom were able to discontinue all pharmacotherapy (44% of primary operations, 50% of favorable outcomes). Clinical trajectories are diagrammed in Fig. 1. Due to the small cohort size, differences between the groups did not reach statistical significance; however, a marked trend was noted, in which 8 of 9 primary surgeries resulted in a favorable pain outcome, whereas both patients who underwent reoperation experienced debilitating, permanent recurrences resulting in unfavorable pain outcomes (89% vs 0%, $p = 0.054$).

All patients had intact House-Brackmann grade I facial nerve function pre- and postoperatively. One patient reported a subjective decrease in ipsilateral hearing postoperatively; formal audiometric assessment was declined, but the operative report documented loss of wave 5 of the brainstem auditory evoked potential response during manipulation of the NI. No other hearing deficits were noted, and trigeminal distribution facial hypesthesia was noted only in one patient who underwent trigeminal rhizotomy. No CSF leaks or wound infections were noted. No patient experienced dysphagia or dysphonia in our series. Two patients experienced a clinically significant medical complication (18%), including one instance each of acute kidney injury and chronic obstructive pulmonary disease exacerbation, both of which were treated appropriately and both

of which resolved. Detailed summary statistics regarding baseline demographics, medical management, neuralgia presentation, operative technique, and outcomes are summarized and compared by primary versus repeat surgery (Table 2), as well as by outcome group (Table 3).

Systematic Review

Six prior publications met study criteria and were included (Table 4). One hundred eleven patients were reported in addition to the 11 in our series for a total of 122 patients, followed for a median of 11–68 months. GN was treated by NI rhizotomy in 108 (88.5%) and MVD in 14 (11.5%). Formal diagnoses of TN/GPN were not explicitly documented in most publications, but concerning symptoms were reported in 15 (12%) for TN and 9 (7%) for GPN, with roughly equal fractions treated via MVD or rhizotomy of the nerve in question. Pain outcomes included early postoperative pain relief in 86%, and favorable pain outcome at last contact in 96% of primary surgeries and 86% of reoperations. Cranial nerve injuries and wound complications occurred in 4% and 6% of patients, respectively.

Cadaveric Analysis

NI was successfully and unambiguously identified in all 14 brainstem sides studied. In all instances, NI was found to be densely adherent to the superomedial aspect of

CN VIII at its brainstem origin, prior to the point at which its fibers joined CN VII in the cerebellopontine cistern. A small vein < 1 mm in caliber was identified between the CN VIII–NI complex and CN VII on the brainstem surface in 13 sides (93%); in all 13 instances, the NI was located immediately lateral to this vein (Fig. 2).

Discussion

GN is a rare cranial neuralgia syndrome, with fewer than 150 reported cases in the literature. Understanding of the natural history and optimal management of GN is incomplete, and prior outcome studies after surgical treatment have been small and heterogeneously described.^{4,7,11,13,14,18} We report a series of 11 patients treated surgically for GN, including 9 primary surgeries and 2 reoperations, which is among the largest single-institution cohorts describing this rare entity, accompanied by the first true systematic review.

Although GN treatment begins with medical management, this frequently fails, and two surgical options may be considered: MVD or sectioning of the NI. Previous studies and our own analysis have not identified a significant difference between these treatment strategies; however, they have all been based on limited, inconsistent data and small patient cohorts.^{15,17} When obvious neurovascular compression of NI is encountered, the anterior inferior cerebellar artery is often the offending vessel.⁹ In these cases, the decision to proceed with isolated MVD or to section the NI is at the discretion of the operating surgeon. Optimistic results have been reported with isolated MVD, as Goulin Lippi Fernandes et al. demonstrated in a recently published series of 8 GN patients, 7 of whom had persistently favorable outcomes at a median of 35 months after surgery.⁴

In the present series, all patients except two underwent NI sectioning, with none reporting subsequent dry eye or loss of taste. In the majority of patients, additional cranial nerve–directed treatments, including MVD or rhizotomy of CN V or IX–X, were also included in the operative procedure, typically due to clinical concern for an alternative or additional underlying or comorbid craniofacial pain syndrome. All patients experienced immediate postoperative pain relief (complete or incomplete), favorably supporting the efficacy of NI sectioning and MVD. However, we also hold that our practice of aggressive, extensive, and symptom-driven treatments for patients reporting symptoms potentially attributable to TN/GPN likely contributed to our generally favorable outcomes, particularly among patients undergoing primary operations.

This possibility is well supported by prior reports, including several captured by our systematic review. Lovely and Jannetta advocated the prophylactic MVD of CNs V and IX–X in all patients undergoing NI sectioning for suspected GN, which resulted in favorable outcomes among 90% (9 of 10) of primary operations at 1 year.⁷ As they discuss in detail, this practice was motivated by the risk of an alternative diagnosis driving the pain syndrome, which is remarkably high in apparent GN. Simultaneously, the potential for treatment-related morbidity is relatively low, particularly when limited to an extensive MVD. Rupa et al. recommended an even more aggressive

TABLE 2. Summary statistics of primary versus repeat operations

Variable	Primary (n = 9)	Reop (n = 2)	p Value
Demographics & patient baseline information			
Median age at op (range), yrs	48 (31–70)	44 (33–54)	0.54
Female sex	5 (56%)	2 (100%)	0.49
Median BMI at op (range)	26.6 (23.9–32.0)	27.0 (20.4–33.6)	0.89
History of smoking	4 (44%)	1 (50%)	1.0
Median duration of Sx (range), mos	50 (10–240)	34 (8–60)	0.53
Medical management prior to surgery			
Carbamazepine	7 (78%)	2 (100%)	1.0
Gabapentin	7 (78%)	1 (50%)	0.49
Opioid	6 (67%)	1 (50%)	1.0
Baclofen	4 (44%)	2 (33%)	0.45
Lamotrigine	2 (22%)	0 (0%)	1.0
Oxcarbazepine	2 (22%)	0 (0%)	1.0
NSAIDs	4 (44%)	0 (0%)	0.49
Neurological presentation			
GN alone	3 (67%)	1 (50%)	1.0
GN/TN	3 (33%)	0 (0%)	1.0
GN/GPN	1 (11%)	1 (50%)	0.35
GN/TN/GPN	2 (22%)	0 (0%)	1.0
Surgical technique			
Retrosigmoid approach	9 (100%)	2 (100%)	1.0
NI MVD	2 (22%)	0 (0%)	1.0
NI rhizotomy	7 (78%)	2 (100%)	1.0
CN V MVD	4 (44%)	0 (0%)	0.49
CN V rhizotomy	1 (11%)	0 (0%)	1.0
CN IX–X MVD	3 (33%)	0 (0%)	1.0
CN IX–X partial rhizotomy	1 (11%)	1 (50%)	0.35
Early postop outcomes			
Any pain relief	9 (100%)	2 (100%)	1.0
Complete pain relief	7 (78%)	1 (50%)	1.49
Decline in ipsilateral hearing	1 (11%)	0 (0%)	1.0
CSF leak	0 (0%)	0 (0%)	1.0
Wound infection	0 (0%)	0 (0%)	1.0
Medical complication	2 (22%)	0 (0%)	1.0
FU outcomes			
Favorable overall pain outcome	8 (89%)	0 (0%)	0.054
Transient pain recurrence	2 (22%)	0 (0%)	1.0
Permanent pain recurrence	1 (11%)	2 (100%)	0.054
Total median FU (range), mos	11 (3–143)	47 (3–90)	0.73
Continued pain med at last FU			
Any continued neuralgia	5 (56%)	1 (50%)	1.0
Continued gabapentin	3 (33%)	1 (50%)	1.0
Continued carbamazepine	2 (22%)	0 (0%)	1.0
Continued narcotics	2 (22%)	0 (0%)	1.0

TABLE 3. Summary statistics by outcome group

Variable	Outcome		
	Favorable (n = 8)	Unfavorable After Primary Op (n = 1)	Unfavorable After Reop (n = 2)
Demographics & patient baseline information			
Median age at op (range), yrs	51 (31–70)	44 (33–54)	44 (33–54)
Female sex	4 (50%)	1 (100%)	2 (100%)
Median BMI at op (range)	26.9 (23.9–32.0)	25.1 (—)	27.0 (20.4–33.6)
History of smoking	4 (50%)	1 (100%)	1 (50%)
Median duration of Sx (range), mos	65 (10–240)	12 (—)	34 (8–60)
Medical management prior to surgery			
Carbamazepine	6 (75%)	1 (100%)	2 (100%)
Gabapentin	6 (75%)	1 (100%)	1 (50%)
Opioid	5 (63%)	1 (100%)	1 (50%)
Baclofen	4 (50%)	0 (0%)	2 (100%)
Lamotrigine	2 (25%)	0 (0%)	0 (0%)
Oxcarbazepine	2 (25%)	0 (0%)	0 (0%)
NSAIDs	3 (38%)	1 (100%)	0 (0%)
Neurological presentation			
GN alone	2 (25%)	1 (100%)	1 (50%)
GN/TN	3 (38%)	0 (0%)	0 (0%)
GN/GPN	1 (13%)	0 (0%)	1 (50%)
GN/TN/GPN	2 (25%)	0 (0%)	0 (0%)
Surgical technique			
Retrosigmoid approach	8 (100%)	1 (100%)	2 (100%)
NI MVD	2 (25%)	0 (0%)	0 (0%)
NI rhizotomy	6 (75%)	1 (100%)	2 (100%)
CN V MVD	4 (50%)	0 (0%)	0 (0%)
CN V rhizotomy	1 (13%)	0 (0%)	0 (0%)
CN IX–X MVD	1 (13%)	0 (0%)	0 (0%)
CN IX–X partial rhizotomy	3 (38%)	0 (0%)	1 (50%)
Early postop outcomes			
Any pain relief	8 (100%)	1 (100%)	2 (100%)
Complete pain relief	6 (75%)	1 (100%)	1 (50%)
Decline in ipsilateral hearing	1 (13%)	0 (0%)	0 (0%)
CSF leak	0 (0%)	0 (0%)	0 (0%)
Wound infection	0 (0%)	0 (0%)	0 (0%)
Medical complication	2 (25%)	0 (0%)	0 (0%)

approach, frequently incorporating multiple rhizotomies into the operative procedure for equivocal cases.¹³ This approach may be excessive, and in cases in which a secondary process is less likely, an MVD may better balance the mandate to treat a potentially dysfunctional nerve against the need to minimize treatment-related morbidity.

The possible benefit of an isolated MVD is again supported by the encouraging recent results from Goulin Lip-

pi Fernandes et al., which confirmed durable symptomatic relief after MVD of the NI in 7 of 8 patients a median 35 months after primary surgery for uncomplicated GN.⁴ Taking these results together with our own experience, we recommend addressing all possible sources of neuralgia pain identified by the clinical history with MVD, where appropriate, or considering rhizotomy if symptoms indicate probable TN/GPN but obvious neurovascular compression is not encountered intraoperatively. Furthermore, even in patients who are taken to surgery with a history of unambiguous GN (e.g., isolated deep ear pain), we recommend exploration of CNs V and IX–X, given the minimal risk of morbidity, and MVD if there is clear microvascular compression.

Although our clinical results were convincing overall, the contrast in favorable pain control between primary surgery and reoperation in our series was remarkable, with 89% sustained improvement after a first operation, compared to the severe, permanent recurrences noted in both patients after repeat operation. Prior reports are somewhat equivocal, particularly given the rarity with which repeat surgery is reported. Several older series reported positive outcomes, most notably Pulec's 64-patient experience with universally favorable outcomes among 16 reoperations, although this study's criteria were not clearly defined.¹¹ Others, including Rupa et al., did not parse outcomes with an analysis such as ours in mind; of their 18 patients, 5 had unfavorable outcomes, but it is not clear how many of them are among the 12 reoperations.¹³ Lovely and Jannetta reported an experience similar to our own: among 4 reoperations, there was 1 true treatment failure and 3 patients with partial relief, but in spite of these relatively optimistic results, they wrote at length about the inherent challenges and frustrations of treating this patient population.⁷ Ultimately, a larger cohort is required to definitively assess the potential for good clinical outcomes after repeat operation for GN; however, based on our experience and our interpretation of the literature, we strongly advise consideration of repeat surgery only in the most refractory of patients, and with guarded patient counseling and unambiguous management of expectations prior to surgery.

From an anatomical perspective, the observed clinical benefits of supplementing NI sectioning with TN/GPN-directed treatments are attributable to the difficulty of definitive diagnosis in GN, to multifactorial pain syndromes driven by multiple cranial nerves, or to a combination of both. Neuropathic ear pain is potentially attributable to multiple craniofacial neuralgia syndromes mediated via CN V (through the auriculotemporal nerve), CN IX (through Jacobson's nerve), or CN X (through Arnold's nerve).¹³ Jacobson's nerve receives sensation from the middle ear, and Arnold's nerve from the posterior aspect of the auricle and ear canal. GPN is also typically accompanied by pain in the back of the throat and tongue; however, highly variable clinical presentations have been reported. This sensory pattern underlies the difficulty in distinguishing between these neuralgias in the clinical setting, particularly when deep ear pain is accompanied by intermittent facial or pharyngeal paroxysms that raise the specter of atypical TN or GPN. The diagnostic challenge is further augmented by the paucity of supplemental diag-

TABLE 4. Detailed results of systematic literature review

Authors & Year	No. of Cases	Repeat Ops	Rhizotomy for GN	MVD for GN	Sx of TN	Sx of GPN	MVD for TN/GPN	Rhizotomy for TN/ GPN	Complete					Favorable Outcome at Last					Wound Complication (CSF leak, infection)	Median FU (mos)		
									Any Early			Early		Contact			Medication				CN Injury	
									Postop Pain Relief	Postop Pain Relief	Postop Pain Relief	All Ops	Primary Op	Reop	Contact	All Ops	Primary Op	Reop				
Sachs, 1968	4	0 (0%)	4 (100%)	0 (0%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)	4 (100%)	4 (100%)	4/4 (100%)	—	0 (0%)	1 (25%)	0 (0%)	68						
Rupa et al., 1991	18	12 (67%)	17 (94%)	1 (7%)	2 (11%)	2 (11%)	7 (39%)	14 (77.8%)	—	—	—	—	—	2 (11%)	2 (11%)	31						
Lovely & Jannetta, 1997	14	4 (29%)	11 (79%)	3 (21%)	6 (43%)	2 (14%)	13 (92%)	1 (7%)	10 (71%)	3 (21%)	9/10 (90%)	3/4 (75%)	—	0 (0%)	3 (21%)	26						
Pulec, 2002	64	16 (25%)	64 (100%)	0 (0%)	—	—	—	16 (25%)	—	—	47/48 (98%)	16/16 (100%)	—	1 (2%)	0 (0%)	—						
Ulubil et al., 2009	3	0 (0%)	3 (100%)*	0 (0%)	—	—	—	0 (0%)	—	—	3/3 (100%)	—	0 (0%)	—	—	30						
Goulin Lippi Fer- nandes et al., 2017	8	0 (0%)	0 (0%)	8 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (88%)	6 (75%)	7/8 (88%)	—	—	0 (0%)	2 (25%)	35						
Present study	11	2 (18%)	9 (82%)	2 (18%)	5 (45%)	4 (36%)	5 (45%)	3 (27%)	11 (100%)	8 (73%)	8/9 (89%)	0/2 (0%)	6 (55%)	1 (9%)	0 (0%)	11						
Summary	122	34 (28%)	108 (86%)	14 (11%)	15 (12%)	9 (73%)	25 (20%)	34 (28%)	32 (86%)	21 (57%)	78/81 (96%)	19/22 (86%)	6 (33%)	5 (4%)	7 (6%)	11–68						

— = No data available in the publication.

For columns with incomplete data, summary statistics are reported as a fraction of those papers reporting that outcome.

* Sensory auricular branch of CN VII sectioned.

FIG. 2. Anterior view of the left cerebellopontine angle in an anatomical specimen. The NI is consistently located at the superomedial aspect of CN VIII at its origin in the brainstem before joining CN VII. A small venous vessel is most of the time encountered between CN VII and the CN VIII–NI complex at the brainstem (asterisk). Figure is available in color online only.

nostic studies, which are effectively limited to cocaineization of the tonsillar fossa, which supports the diagnosis of GPN if pain resolves after application, or high-contrast T2-weighted MRI sequences (e.g., CISS and FIESTA), which are supportive of a diagnosis when obvious neurovascular compression is identified but not reliably confirmatory, regardless of whether the study is positive or negative.

Correspondingly, given the ultimate treatment goal of sustained pain relief, when taking patients to surgery for a probable diagnosis of GN, any suspicion of concomitant TN or GPN warrants directed treatment via MVD or rhizotomy—a strategy that is anatomically supported and clinically validated, in both our own experience and that of our predecessors. By the same token, if patients present with atypical TN or GPN, the history should be probed for possible features of GN, and an intraoperative exploration of the NI may be considered.

With those recommendations in mind, we sought to provide a clinically oriented assessment of NI anatomy at the brainstem, to assist in rapid, safe identification of the NI for treatment of GN. The NI has been classically described as part of CN VII and was the subject of one of Dr. Rhoton's first studies, which analyzed in rigorous detail the nerve's anatomical course.¹³ The NI has 3 components in its cisternal portion: a proximal segment, densely adherent to CN VIII; an intermediate segment, in which it is free from adhesions and travels from CN VIII to join CN VII; and a distal segment, interdigitated with CN VII.^{2,12} One to 4 rootlets constitute the NI at the intermediate segment.

In our anatomical study, we focused on the proximal segment of the cisternal portion and identified NI at the brainstem, where we observed it to be very consistently located in a superomedial position relative to CN VIII. In almost all specimens, we also observed a small vessel between CN VII and the CN VIII–NI complex at the brainstem, immediately medial to the NI. In contrast to the highly preserved origin of the NI at the brainstem, the anatomy of the more distal cisternal segment was variable. This accords with Dr. Rhoton's analysis, which demonstrated the adhesive proximal section of the NI to be approximately 8 mm in length and lacking a true free segment in 20% of cases, potentially predisposing it to a challenging dissection and sectioning. In this study, the NI was usually formed by a single trunk, but in some cases it was composed of up to 6 rootlets.¹²

Under most circumstances, the NI is readily identified by direct dissection of the cisternal segment. If there is any doubt regarding the anatomy, we recommend identification of the NI origin at the brainstem between the small vessel adjacent to CN VII medially and CN VIII laterally, at the superomedial aspect of the CN VIII origin—a technique that may benefit from endoscopic assistance to avoid excessive retraction on the CN VII–VIII complex. Once the NI origin is established, it can be followed distally to the intermediate segment, where the NI is safely divided between the proximal adhesion to CN VIII and distal integration with CN VII. Should both techniques fail, we recommend exposure of the internal acoustic canal and

retrograde tracing of the NI; however, this should be reserved as a last resort, given the potential for increased risk of facial nerve injury, deafness, vestibulopathy, and CSF leak due to temporal bone drilling.^{1,7,13,15,16}

The results of our study are subject to several significant limitations, including small cohort sizes in both the primary and repeat surgery groups, short median follow-up of 11 months, and the inherent risks of bias and confounding that are associated with any retrospective analysis. With respect to the systematic review, the included studies were scattered over a broad range of years and techniques, outcomes were reported inconsistently and heterogeneously, and the small sample sizes and inconsistent data prohibited formal statistical analysis. In spite of these shortcomings, our analysis represents one of the longest and most detailed reviews of GN and its operative treatment, which highlights the frequency of concomitant diagnoses, and therefore a small but essential step forward in our understanding of the natural history and optimal management of this rare and debilitating neurosurgical disease.

Conclusions

GN is an uncommon craniofacial pain syndrome that frequently overlaps with other cranial neuralgias, including TN and GPN. Surgical treatment, including MVD or sectioning of the NI, is beneficial in cases that are refractory to medical treatment. When performing surgery for isolated GN, extensive exploration and possible MVD of CNs V and IX–X should be considered; if concomitant TN or GPN is suspected, it should be aggressively treated with MVD/rhizotomy. Favorable outcomes at last follow-up in our series were achieved in 89% of primary operations and 0% of reoperations. Anatomically, the NI is densely adherent to the superomedial aspect of the vestibulocochlear nerve at the brainstem and is frequently identified lateral to a small vessel interposed between CNs VII and VIII on the lateral surface of the pontomedullary junction. The intermediate segment of the cisternal portion of the NI is optimal for visualization and sectioning of the nerve.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Peris-Celda. Acquisition of data: Oushy, Perry, Graffeo, Carlstrom. Analysis and interpretation of data: Peris-Celda, Carlstrom. Drafting the article: Peris-Celda, Graffeo. Critically revising the article: Link, Perry, Graffeo. Reviewed submitted version of manuscript: Link, Peris-Celda, Oushy. Approved the final version of the manuscript on behalf of all authors: Link. Statistical analysis: Peris-Celda, Oushy, Graffeo. Study supervision: Link, Zimmerman, Meyer, Pollock.

Supplementary Information

Previous Presentations

Portions of this work were presented at the annual scientific meeting of the North American Skull Base Society, Coronado, CA, February 16–18, 2018.

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