Internal Neurolysis for the Treatment of Trigeminal Neuralgia: A Systematic Review

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■ INTRODUCTION: **Trigeminal neuralgia (TN) remains a challenging disease with debilitating symptoms and variable efficacy in terms of treatment options. Microvascular decompression (MVD) with internal neurolysis (IN) is an alternative treatment that might benefit patients but has limited understanding. We performed a systematic review of IN for the treatment of TN.**

■ METHODS: **Studies from 2000 to 2021 that had assessed IN for TN were aggregated and independently reviewed.**

■ RESULTS: **A total of 520 patients in 12 studies were identified, with 384 who had undergone IN (mean age, 53.8 years; range, 46–61.4 years; mean follow-up, 36.5 months). Preoperative symptoms had been present for ~55.0 months before treatment, and pain was predominantly in V2 and V3 (26.8%), followed by other distributions. Of the patients, 83.7% (range, 72%–93.8%) had had an excellent to good outcome (Barrow Neurological Institute pain scale score [BNI-PS], I–II). The pain outcomes at 1 year were excellent for 58%–78.4%, good or better for 77%–93.75%, and fair or better for 80%–93.75% of the patients. On average, facial numbness after IN was experienced by 96% of the patients. However, at follow-up, facial numbness remained in only 1.75%–10%. Most of the remaining numbness was not significantly distressing to the patients. Subgroup comparisons of IN versus recurrent MVD, IN versus radiofrequency ablation, the effects of IN in the absence of vascular compression, and IN with and without MVD were also evaluated.**

■ CONCLUSIONS: **IN represents a promising surgical intervention for TN in the absence of vascular compression and for potential cases of recurrence. Complications were limited in general but require further study.**

INTRODUCTION

Trigeminal neuralgia (TN) is a pain syndrome characterized by recurrent episodes of lancinating facial pain. The first-line therapy for treatment is medical management; however, many patients may require surgery because of refractory symptoms or intolerable side effects from medication.[1,2] The mainstay surgical treatment of TN has been microvascular decompression (MVD) when neurovascular compression (NVC) is found.[2]

Although the association between NVC and TN is strong, the pathophysiology is not completely understood.[1] TN is known to occur and recur in the absence of NVC, and many individuals with NVC will not manifest TN.[3-5] In their literature review, Lee et al.[3] suggested that 10%–20% of patients with TN will not have NVC. Also, in their own data, they found that 28.8% of those with TN type I and 18.4% of those with TN type II had no NVC.[3] They reported significant variation depending on the imaging modality, study era, type of TN, and study inclusion criteria.[3] Additionally,

Key words
- Facial pain
- Internal neurolysis
- Trigeminal neuralgia

Abbreviations and Acronyms
BNI-HS: Barrow Neurological Institute hypesthesia scale
BNI-PS: Barrow Neurological Institute pain scale
IN: Internal neurolysis
MRI: Magnetic resonance imaging
MVD: Microvascular decompression
NVC: Neurovascular compression
PRISMA: Preferred reporting items for systematic reviews and meta-analyses
PSR: Partial sensory rhizotomy
RF: Percutaneous radiofrequency rhizotomy
SRS: Stereotactic radiosurgery
TN: Trigeminal neuralgia

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for MVD, differences exist in the outcome based on the severity of NVC and whether the compression is arterial or venous.[2,5-11] Furthermore, although high-resolution magnetic resonance imaging (MRI) and magnetic resonance angiograph are reliable tests for verifying NVC with a sensitivity of 96% for TN type I and II and a specificity of 90% for TN I and 66% for TN II, false-positive results still occur, with no NVC seen at surgery.[3]

The treatment of patients presenting with TN in the absence of NVC or with low-grade arterial or venous compression has been more difficult, with higher postoperative treatment rates. Percutaneous radiofrequency rhizotomy (RF), glycerol rhizotomy, balloon compression, stereotactic radiosurgery (SRS), and partial sensory rhizotomy (PSR) have been the traditional second-line surgical therapies for this patient population.[1,12-22]

Internal neurolysis (IN) has emerged as an attempt to provide long-term pain relief to patients with refractory TN. IN, also known as "nerve-combing," is the process of microsurgical parallel dissection of the cisternal portion of the trigeminal nerve into multiple nerve fasicles.[1] Although the first reports seemed promising, the efficacy, durability, and complication pattern remain to be fully defined.[23] In the present report, we have provided a systematic review of the available literature on the efficacy of IN for treating patients with TN.

METHODS

The PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines were followed for reporting our systematic review.[24]

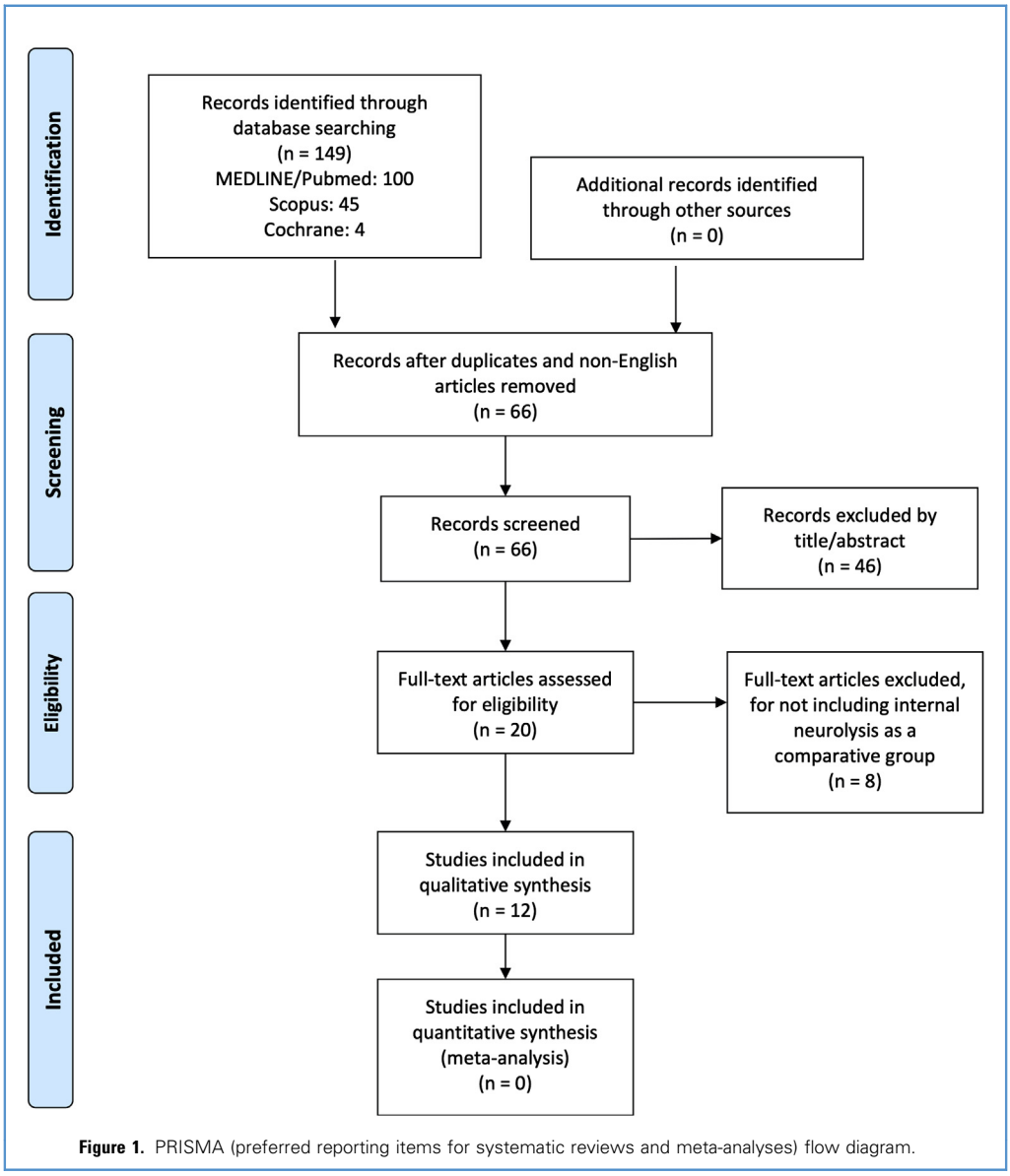

Figure 1. PRISMA (preferred reporting items for systematic reviews and meta-analyses) flow diagram.

Eligibility Criteria

We included studies reporting IN as surgical treatment of TN (Figure 1). The inclusion criteria were 1) outcome assessments of IN with or without a comparative group; 2) pain control outcomes reported with ≥1 year of follow-up; 3) any study design; 4) studies reported in English; 5) studies reported from 2000 to 2021; and 6) a minimum of 1 year of follow-up. Series that had not differentiated the results of IN from those of other treatments were excluded.

Information Sources and Search Strategy

The MEDLINE (PubMed), Scopus, and Cochrane databases were queried from January 1, 2000 to April 8, 2021. Ongoing studies were searched for in the ClinicalTrials.gov registry, the controlled-trials.com registry, and the Trials Central databases. The references from the included studies were screened for additional studies. The search strategy included the following terms and indexation terms: "trigeminal neuralgia, neurolysis," "trigeminal neuralgia, internal neurolysis," and "trigeminal neuralgia, microvascular decompression, neurolysis." No restrictions were placed on the study design or outcomes in the search strategy.

Study Selection and Data Extraction

Three authors (V.S., J.M., J.H.) independently screened the titles and abstracts after removing the duplicates and non-English studies. Full-text reports were reviewed for eligibility. If any discrepancies were found between any of the reviewers, the third reviewer's decision was the tie-breaker.

The patient demographics, perioperative outcomes, surgical outcomes, Barrow Neurological Institute pain scale (BNI-PS) scores, Barrow Neurological Institute hypesthesia scale (BNI-HS) scores, numerical pain rating scale scores, and complication profile were obtained (Table 1). Three studies had classified the outcomes into 4 tiers: excellent, good, pain-free recurrence, and poor.[23,25,26] Patients with excellent outcomes had had complete pain relief without medication. Those with good outcomes had experienced intermittent pain relief with medication. Patients with pain-free recurrence had experienced relief for 1 month but subsequent recurrence. Finally, those with poor outcomes included those without pain relief despite medication.

Outcomes Measures

The primary outcome was the postoperative pain score as defined by the BNI-PS or other equivalent scale. The outcomes were stratified as excellent (BNI-PS score I or excellent), good (BNI-PS score I—II or excellent/good), or fair (BNI-PS score I—III and excellent/good). The secondary outcomes included the recurrence rate and complications.

Risk of Bias in Individual Studies

A specific analysis of the bias risk was not performed because these studies were all retrospective, nonrandomized trials without a blinded assessment of the outcomes. Where relevant, missing data were reported in the summary tables. No specific method was used to assess the risk of bias in the individual studies.

Table 1. Outline of Barrow Neurological Institute Pain and Hypesthesia Scales

Scale Score	Description
BNI-PS*	
I	No pain, no medications
II	Occasional pain, no medications required
III	Some pain, adequately controlled with medications
IIIa	No pain, continued medication
IIIb	Persistent pain, controlled with medication
IV	Some pain, not adequately controlled with medications
V	Severe pain or no pain relief
BNI-HS	
I	No facial numbness
II	Mild facial numbness that is not bothersome
III	Somewhat bothersome facial numbness
IV	Very bothersome facial numbness

BNI-HS, Barrow Neurological Institute hypesthesia scale; BNI-PS, Barrow Neurological Institute pain scale.
*A BNI-PS score of I—III was originally considered a good outcome; however, we defined the outcomes as excellent (BNI-PS score I or excellent), good (BNI-PS score I—II or excellent to good), or fair (BNI-PS score I—III or excellent to good).

Summary Measures

Weighted averages for the patients who had undergone IN were generated for continuous variables, including patient demographics, outcomes, and complications, when available. The averages for outcomes used the study definitions of a good outcome or otherwise considered a BNI-PS score of I—II (excellent to good) as a good outcome. The average complication rates, such as the number of patients reporting facial numbness, at the last known follow-up were noted. Subgroups of patients with only IN were also analyzed for the outcomes and complications. For studies that did not report the mean age, the median age was used. The variable ranges are reported when available.

RESULTS

Patient Demographics

A total of 520 patients had been included in the 12 studies, 384 (73.8%) of whom had undergone IN (Table 2).[1,23,25-34] The mean or median age for all the studies was 53.8 years (range, 46—61.4 years), and mean or median follow-up time was 36.5 months (range, 12—90 months). The preoperative symptom duration was reported in 8 studies and averaged 55.0 months (range, 40.4—70.8 months). The average TN distribution was most common for V2—V3 (26.8%), followed by V1—V2 (16.1%), V1—V3 (16.1%), and V3 (15.6%). Five studies had reported previously attempted surgical treatments.

Table 2. Study Demographics and Patient Characteristics

Investigator	Treatment Group	Patients (*n*)	Mean or Median Age (years)	Female Gender (%)	Mean or Median Follow-up (months)	Preoperative Symptom Duration (months)	TN Type (%)	TN Distribution (%)							Surgical or Procedural History (%)
								V1	V2	V3	V1–V2	V2–V3	V1, V3	V1–V3	
Sabourin et al.,[27] 2020	MVD + IN	19	61	78.1	23	NA	I, 79; II, 21	0	15.8	21.1	10.5	47.4	5.3	NA	32 (MVD, SRS, RF)
	IN	13	59	61.5	15	NA	I, 85; II, 15	0	15.4	30.8	30.8	23.1	0	NA	54 (MVD, SRS, RF)
Wu et al.,[28] 2020	IN	21	57	52.3	12	63.6	I, 100	NA	42.9	28.6	4.8	23.8	NA	NA	NA
Durnford et al,[29] 2020	IN	8	55	87.5	38	69	I, 75; II, 25	25	12.5	NA	25	12.5	NA	25	NA
Wu et al.,[30] 2018	IN with TCR	23	50.12	70	36.2	47.8	I, 100	NA	29.6	18.5	NA	51.9	NA	NA	44.4 (MVD, RF, SRS)
	IN without TCR	4	56.33			58.2	I, 100								
Hussain et al.,[31] 2018	R-MVD	19	54	79	36 (median pain improvement period)	NA	NA	NA	NA	NA	NA	NA	NA	NA	MVD, 100
	IN	11	54	82		NA	NA	NA	NA	NA	NA	NA	NA	NA	
Liang et al.,[32] 2017	IN	37	50.19	67.6	29.5	40.4	I, 100	2.7	10.8	8.1	16.2	43.2	10.8	8.1	NA
Zhao et al.,[33] 2017	IN	15	61.4	60	≥48	41.2	NA	NA	27	13.3	20	33	NA	6.7	NA
Zhang et al.,[34] 2017	R-MVD	62	58.4	61	12	NA	NA	9.7	9.7	13	22.5	29	NA	16.1	MVD, 100
	R-MVD + IN	86	59.8	64	12	NA	NA	6	12	10	23	23	NA	26	
Zhou et al.,[26] 2016	IN	50	48.9	44	90	67.2	NA	4	12	16	16	NA	24	28	NA
	RF	55	49.3	45		70.8	NA	9.1	18.2	20	9.1	NA	25.4	18.2	NA
Ko et al.,[1] 2015	IN	27	46.9	74	39.1	NA	I, 100	3.8	7.7	15.4	7.7	30.8	NA	34.6	38.5 (MVD, SRS, RF)
Jie et al.,[25] 2013	IN without NVC	28	50.6	36	52	52	NA	3.6	7.1	21.4	25	28.6	NA	14.3	NA
	IN with NVC	32	46	63	56	50	NA	6.3	NA	25	15.6	37.5	NA	15.6	NA
Ma et al.,[23] 2009	IN	10	60.4	60	36	45	NA	NA	10	20	20	40	NA	10	NA
Weighted average for IN cases	NA	384	53.8	61	36.5	55.0	NA	3.7	13.3	15.6	16.1	26.8	4.4	16.1	NA

TN, trigeminal neuralgia; MVD, microvascular decompression; IN, internal neurolysis; NA, data not available or not applicable; SRS, stereotactic radiosurgery; RF, percutaneous radiofrequency thermocoagulation; TCR, trigeminocardiac reflex; R-MVD, reexploration or revision microvascular decompression; NVC, neurovascular compression.

Table 3. Study Description with Outcome Metrics and Treatment Outcomes

Investigator	Study Description	Outcome Metrics	Treatment Groups	Overall Results
Sabourin et al.,[27] 2020	Retrospective study comparing patients who had undergone IN with or without MVD	BNI-PS and BNI-HS; BNI-PS score: I, no pain; excellent, II; successful, IIIa; adequate, IIIb; poor, ≥IV	IN + MVD	For BNI-PS: patients with IN + MVD showed no pain (58%), excellent (11%), successful (11%), adequate (22%), and poor (0%) outcomes at last follow-up
			IN	For BNI-PS, patients with IN showed no pain (38%), excellent (0%), successful (38%), adequate (8%), and poor (15%) outcomes at last follow-up
Wu et al.,[28] 2020	Retrospective study evaluating IN for type 1 TN; quantitative diffusion MRI used to evaluate response to IN	BNI-PS; outcomes of combined BNI-PS scores: excellent, II; good, III; fair, IV; poor, ≥V	IN Healthy control for MRI comparison	At 1-year follow-up, 52.4% showed excellent outcomes, 23.8%, good outcomes, 14.3%, fair outcomes, and 0.95%, poor outcomes; compared with controls, IN resulted in reduced mean fractional anisotropy and apparent diffusion coefficient; fractional anisotropy did not correlate with BNI-PS score but decreased apparent diffusion coefficient correlated with improved BNI-PS scores
Durnford et al.,[29] 2020	Retrospective study evaluating IN for patients without NVC	BNI-PS and BPI-F	IN	All patients had BNI grade V; at last follow-up, 6 were pain free (BNI grade I) and 2 had developed recurrence; median preoperative BPI-F score, 115; at last follow-up, 20; both face-specific and general scores were reduced on follow-up
Wu et al.,[30] 2018	Retrospective study evaluating outcomes of IN and relationship to TCR; IN performed for patients without NVC seen intraoperatively; TCR defined as any change in heart rate or mean arterial pressure of ≥20% owing to direct manipulation of trigeminal nerve	BNI-PS and BNI-HS; outcomes of combined BNI-PS and BNI-HS: excellent, II; good, III; fair, IV; poor, ≥V	IN with TCR; IN without TCR	Study found that 85.2% of patients who had undergone IN developed TCR intraoperatively; at a median follow-up of 36.2 months, overall outcomes were excellent, 67.7%; good, 19.4%; fair, 12.9%; atrophy of trigeminal nerve was a significant risk factor for TCR due to IN ($P < 0.05$); no significant differences were found in BNI-PS scores between TCR and non-TCR groups

IN, internal neurolysis; MVD, microvascular decompression; BNI-PS, Barrow Neurological Institute pain scale; BNI-HS, Barrow Neurological Institute hypesthesia scale; MRI, magnetic resonance imaging; BPI-F, brief pain inventory facial scale; TCR, trigeminocardiac reflex; NVC, neurovascular compression; R-MVD, revision or reexploration microvascular decompression; RF, radiofrequency rhizotomy; REZ, root entry zone; PFR, pain-free recurrence; PFPS, Penn facial pain scale.

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Table 3. Continued

Investigator	Study Description	Outcome Metrics	Treatment Groups	Overall Results
Hussain et al.,[31] 2018	Retrospective study analyzing outcomes of R-MVD for recurrent TN; IN performed for patients without NVC intraoperatively; preoperatively, all patients had had BNI-PS score IV—V	BNI-PS; BNI-PS score I—III, good outcome; BNI-PS score, IV—V, poor outcome	R-MVD; IN	Median pain improvement period, 36 months; IN subgroup had BNI-PS score I, 63.6%; BNI-PS score III, 27.3%; BNI-PS score IV, 9.1%; good outcome, 90.9%; poor outcome, 9%; R-MVD group: BNI-PS score I, 15.8%; BNI-PS score II, 26.3%; BNI-PS score III, 42.1%; BNI-PS score IV, 10.5%; BNI-PS score V, 5.3%; good outcome, 84.2%; poor outcome, 15.8%
Liang et al.,[32] 2017	Retrospective study analyzing outcomes of IN for patients with TN and no NVC; preoperatively, all patients had had BNI-PS score IV—V	BNI-PS; numerical pain rating scale, 0—10; 0, no pain; to 10, the worst pain; quality of life outcomes assessed using numerical rating scale; 0, worst imaginable state of health; to 100, the best imaginable state of health; recurrence defined as transition from BNI-PS score I or II to III—V	IN	Immediate postoperative results: BNI-PS score I, 94.6%; BNI-PS score II, 5.4%; numerical pain rating scale decreased from 8.24 to 0.32; quality of life score increased from 30.43 to 91.81; postoperative results at 1 year: BNI-PS score I, 78.4%; BNI-PS II score, 8.1%; BNI-PS score III, 5.4%; BNI-PS score IV, 5.4%; BNI-PS score V, 2.7%; pain had recurred in 13.5% of patients at 1 year; pain of patients with BNI-PS score III was adequately controlled with medication; at an average follow-up of 29.5 months: BNI-PS score I, 64.9%; BNI-PS score II, 13.5%; BNI-PS score III, 0.8%; BNI-PS score IV, 5.4%; BNI-PS score V, 5.4%; overall recurrence rate, 21.6%; pain for all patients with BNI-PS score III was adequately controlled with medication; overall average numerical pain rating scale score, 1.49; quality of life score, 82.54

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Table 3. Continued

Investigator	Study Description	Outcome Metrics	Treatment Groups	Overall Results
Zhao et al.,[33] 2017	Retrospective study analyzing outcomes of IN for patients with TN and no NVC	Excellent recovery: pain had resolved immediately after surgery, without medication; good recovery: pain had resolved late postoperatively, with medication required; partial recovery: pain recovery rate, 75% with or without medication; poor result: pain recovery rate, 25% or no pain resolution	IN	Minimum follow-up, 48 months: excellent outcome, 73.3%; good outcome, 13.3%; partial recovery, 6.7%; poor result, 6.7%; overall recurrence rate, 6.7%; partial recovery not considered failure because no medication was required for pain relief
Zhang et al.,[34] 2017	Retrospective study analyzing outcomes of R-MVD vs. R-MVD and IN for patients with failed prior MVD for TN; when NVC found intraoperatively, MVD was performed; if no NVC found, previously inserted Teflon replaced and IN performed	BNI-PS; BNI-PS score I, excellent response; BNI-PS score II, good response; BNI-PS score I—II, success; BNI-PS score $\geq$III, poor outcome; recurrence defined as transition from an excellent response to a good response or from success to a poor outcome	R-MVD; R-MVD + IN	R-MVD success rates at 1 day and 1 year postoperatively: 80.65% and 78.95%, respectively; at 1 day and 1 year postoperatively, R-MVD and IN success rates, 97.67% and 93.75% respectively; despite defining recurrence, recurrence rates were not reported; extrapolation revealed a recurrence rate of 1.7% for R-MVD and 3.92% for R-MVD + IN; however, these could have been underestimated because the transition from an excellent response to a good response was unknown
Zhou et al.,[26] 2016	Retrospective analysis of IN vs. RF for patients with TN; 58% of patients found on MRI to have blood vessels near REZ	Four-tier system with excellent/good considered good outcome; excellent, complete pain relief without medication; good, pain free with medication or mild pain not requiring medication; PFR, no pain for $\geq$1 month, followed by pain recurrence; poor, minimal or no pain relief	IN; RF	Mean follow-up, 90 months; IN satisfactory, 82%; IN PFR, 10%; IN poor outcome, 8%; RF satisfactory, 76.4%; RF PFR, 14.5%; RF poor outcome, 9.1%; no statistically significant differences between IN and RF outcomes

IN, internal neurolysis; MVD, microvascular decompression; BNI-PS, Barrow Neurological Institute pain scale; BNI-HS, Barrow Neurological Institute hypesthesia scale; MRI, magnetic resonance imaging; BPI-F, brief pain inventory facial scale; TCR, trigeminocardiac reflex; NVC, neurovascular compression; R-MVD, revision or reexploration microvascular decompression; RF, radiofrequency rhizotomy; REZ, root entry zone; PFR, pain-free recurrence; PFPS, Penn facial pain scale.

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Table 3. Continued

Investigator	Study Description	Outcome Metrics	Treatment Groups	Overall Results
Ko et al.,[1] 2015	Retrospective analysis of patients with TN and no NVC who had undergone IN	BNI-PS; BNI-PS score I—II, success; recurrence measured as significant or any recurrence; significant recurrence: BNI-PS score I—II change to ≥III (from success to failure); any recurrence: significant recurrence or BNI-PS score change from I to II (from pain free to good response); quality of life metrics analyzed using BPI-facial, also known as PFPS	IN	Immediate postoperative results: BNI-PS score I, 85%; success rate, 96%; overall BNI-PS score I at 1 year, 58%; at 2 years, 52%; 5 years, 47%; overall long-term success outcomes: 77% at 1 year, 72% at 2 years, 72% at 5 years; Kaplan-Meier plot: overall BNI-PS score I—III at 1 and 5 years: ≈80%; patients without previous treatment showed 94% success at 1 year and was maintained at ≤5 years of follow-up; patients with a history of previous treatment had significantly worse ($P = 0.006$) median recurrence time than their counterparts; 8.7 vs. 24.4 months; success for previously treated patients: 40% at 1 year, which became good for 40% at 2, 3, and 5 years; significant pain recurrence at 1 year, 17%; any pain recurrence at 1 year, 42%; both continued to increase at a rate of ∼2% annually equating to an ∼25% and ∼50% recurrence for significant and any pain, respectively, at 5 years
Jie et al.,[25] 2013	Retrospective analysis of patients with TN with or without NVC who had undergone IN	Four-tier system with excellent/good considered good outcomes; excellent: complete pain relief without medication; good: pain free with medication or mild pain not requiring medication; PFR, no pain for ≥1 month followed by pain recurrence; poor, minimal or no pain relief	IN without NVC IN with NVC	Average follow-up: 52 months; patients without NVC had excellent outcome, 82.1%; good outcome, 7.1%; PFR, 3.6%; poor outcome, 3.6% after IN; average follow-up: 56 months; patients with NVC at REZ: excellent outcome, 62.5%; good outcome, 25%; PFR, 6.25%; poor outcome, 6.25% after IN

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Table 3. Continued

Investigator	Study Description	Outcome Metrics	Treatment Groups	Overall Results
Ma et al.,[23] 2009	Retrospective analysis of patients with TN without NVC at REZ who had undergone IN	Four-tier system with excellent/good considered good outcomes; excellent: complete pain relief without medication; good: pain free with medication or mild pain not requiring medication; PFR, no pain for ≥1 month followed by pain recurrence; poor, minimal or no pain relief	IN	Follow-up: 3 years; outcomes: excellent, 70%; good, 10%; PFR, 10%; poor, 10%

IN, internal neurolysis; MVD, microvascular decompression; BNI-PS, Barrow Neurological Institute pain scale; BNI-HS, Barrow Neurological Institute hypesthesia scale; MRI, magnetic resonance imaging; BPI-F, brief pain inventory facial scale; TCR, trigeminocardiac reflex; NVC, neurovascular compression; R-MVD, revision or reexploration microvascular decompression; RF, radiofrequency rhizotomy; REZ, root entry zone; PFR, pain-free recurrence; PFPS, Penn facial pain scale.

Overall Pain Outcomes

Of the 520 patients, 83.7% (range, 72%–93.8%) had had excellent to good outcomes (BNI-PS score I–II; Table 3). The immediate postoperative results were excellent for 85%–94.6%, good or better for 96%–100% and fair or better for 96%–100% of the patients. The 1-year postoperative pain outcomes were excellent for 58%–78.4%, good or better for 77%–93.75%, and fair or better for 80%–93.75% of the patients. The primary outcome for all the studies, irrespective of the follow-up time, was excellent for 47%–82.1%, good or better for 62.5%–87.1%, and fair or better for 80%–100% of patients.

Recurrence

The 1-year recurrence rates for any pain, including a transition of the BNI-PS score from I to II, ranged from 3.92% to 42%, with an overall rate of 3.6%–50%. However, when considering only a significant recurrence of pain, defined as a change from a BNI-PS score of I–II to III–V, the 1-year recurrence rates ranged from: 3.92% to 17%, and the overall recurrence rates ranged from 3.6% to 25%.

IN Outcomes with NVC Present

Three studies had included data on IN for patients with NVC. Zhou et al.[26] reported that 58% of the patients were found on MRI to have a blood vessel near the root entry zone, with an overall satisfactory result of 82% after IN as defined by their study. Additionally, Jie et al.[25] compared the results of IN for patients with and without NVC. They reported that with >4 years of follow-up, patients without NVC had had a 19.6% higher rate of an excellent outcome and overall lower rates of recurrence and poor outcomes in the pain scores.[25] Sabourin et al.[27] showed good outcomes for 80% of patients with IN and MVD compared with 76% for patients with IN alone, suggesting a very limited difference between these 2 groups of patients.

Reexploration MVD with and without IN

Two studies specifically evaluated reexploration MVD with and without IN for recurrent TN. Hussain et al.[31] found that patients who had undergone IN (84.2%) had similar overall rates of a good outcome compared with those who had undergone reexploration MVD (90.9%). However, the patients who had undergone IN had had a 47.8% higher rate of BNI-PS score I.[31] Zhang et al.[34] found that at 1 year patients who had undergone revision MVD and IN had a 14.8% higher rate of success as defined by the study compared with the patients who had undergone revision MVD alone.[31,34]

IN Outcomes in Relation to Previous Treatments of TN

Five studies had reported a patient population with previous treatments, with a range of 32%–100% of patients who had undergone previous treatments (Table 2). Ko et al.[1] stratified patients with prior MVD and found that patients with a history of previous treatment had had significantly worse outcomes than others. Patients with a history of previous treatment had had a 40% success rate (BNI-PS score I–II) at 1 year, which had become a 40% rate of good outcomes (BNI-PS score of ≥III) at 2, 3, and 5 years of follow-up.[1] Patients without a history of previous treatment had had a 94% success rate at 1 year, which had been maintained at 2, 3, and 5 years of follow-up. The median time to recurrence for the patients with a history of a previous procedure was 8.7 months compared with 24.4 months for those without such a history.[1]

IN Compared with RF

One study had compared IN and RF and found a trend toward greater satisfactory rates, lower recurrence rates, and lower rates of a poor outcome for IN compared with RF. However, the differences were not statistically significant.[26]

Complications

The primary complication of IN is facial numbness (e.g., hypesthesia, hypoesthesia; Table 4). The rate of facial numbness after IN was as high as 96% in the immediate postoperative period. However, with long-term follow-up, the rate had decreased to ~38.8% on average. Studies varied significantly in their follow-up length and timing of complication assessments. Long-term numbness was often reported as mild and not distressing (BNI-HS score I–II) in most studies and was present in 1.75%–10% of patients at last follow-up. Because IN is a technique involving direct manipulation of the trigeminal nerve, other important complications to consider include corneal hypesthesia, corneal ulcer, loss of corneal reflex, and anesthesia dolorosa. The overall rate of corneal hypesthesia and ulcer was 1.2%, and 1 case of anesthesia dolorosa was reported (0.31%). Several other surgical complications were reported in the studies we reviewed, including facial nerve dysfunction, cerebrospinal fluid leak, and meningitis. However, these complications were related more to the surgical approach.

DISCUSSION

To the best of our knowledge, our systematic review is the first to address the surgical results of posterior fossa exploration with IN of the trigeminal nerve for TN. Overall, excellent to good outcomes (BNI-PS score I–II) were seen, on average, for 83.7% of the patients who had undergone IN. The recurrence rates for clinically significant changes in pain (change from a BNI-PS score of I–II to a score of III–V) ranged from 3.6% to 25%. Improved BNI-PS score I outcomes after IN were comparable to those after reexploration MVD alone. Patients without any history of prior TN seemed to fare better. Some, but not all, studies showed that patients who had undergone reexploration MVD had better results if IN had also been performed. However, the heterogeneity between the studies did not allow for clear answers regarding the concomitant role of MVD and IN or the role of IN alone for recurrent disease. The consequences of trigeminal nerve manipulation included high rates of postoperative facial hypesthesia (≤96% of patients) in some studies. Numbness was experienced, average, by 38.8% of the patients after various lengths of follow-up and 1.75%–10% at the last follow-up. Corneal ulceration and anesthesia dolorosa were rare.

We believe these data are supportive of IN as an alternative first-line treatment of patients without NVC, for whom IN can be used in conjunction with MVD (Figure 2). In addition, IN could be an option for patients with recurrent TN who had previously undergone MVD. These data suggest IN as a reasonable alternative to other TN treatments, such as SRS and RF. The main limitation in the studies evaluating IN was the limited follow-up length, and further research is needed. Ultimately, any treatment approach requires discussion with the patient and should include an explanation of the risks, benefits, and durability of each approach. Multiple theories have been suggested to explain the pathophysiology of TN, and more recent functional MRI and volumetric brain data have suggested the presence of complex changes in patients with TN.[35] The therapeutic mechanism of IN remains unclear, similar to the challenges of understanding how nerve vascular decompression improves neuralgic pain in those with classic TN. IN can produce a further lesioning effect, which might account for the higher rates of facial numbness. However, additional research is required to better understand where IN can fit in the treatment algorithm of TN.

IN Versus MVD Outcomes

MVD for type I TN remains a durable surgical treatment option, and comparisons of IN outcomes are limited. IN can be considered for patients without NVC found on imaging studies or direct surgical observation. One study showed overall good outcomes for 83.7% of their patients with a mean follow-up of 36.5 months.[2] However, they suggested that the various follow-up lengths in the available studies confounded the definitive comparison of outcomes with MVD versus MVD with IN. Sindou et al.[6,10] evaluated patients with NVC at various severity levels. At 1 and 15 years, the BNI-PS score I cure rates stratified by the NVC grade were 96.6% and 88.1% (grade III [adhesion]), 90.2% and 78.3% (grade II [touching and indentation]), and 83.3% and 58.3% (grade I [touching]), respectively. Venous compression decreased the pain control rates compared with arterial compression, with BNI-PS score I rates of 8.1% and 14.3% at 1 and 15 years, respectively.[6] However, these longer follow-up lengths are simply not available for IN and especially not for first-time IN treatment.

The results after MVD for grade III compression appeared superior to those after IN. However, the outcomes after MVD for lower grade NVC or venous compression appear comparable to those after IN. Two studies reported on IN for patients with NVC. However, only 1 study had clearly delineated the NVC status and neither had reported the NVC severity. Although most patients who undergo IN will not have NVC, the potential for adding IN to treat patients with milder NVC with recurrent pain could be a promising option.

Another indication for IN is to treat recurrent pain after MVD. Zhang et al.[34] reported a 1-year success rate of 93.75% after revision MVD with IN. Hussain et al.[31] suggested similarly good outcomes between revision MVD and IN at the last follow-up (90.9% vs. 84.2%). The rate of excellent results after revision MVD without IN was 50%–60%, 40%–50%, and ~42% at 1, 5, and 10 years, respectively.[2] These results indicate that reexploration with IN should be considered for patients with pain recurrence after MVD. Whether this strategy is better than SRS or RF remains to be determined.

IN Versus SRS

A systematic review of SRS for TN showed that the average rates of initial freedom from pain with or without medication after a latency period were 84.8% for gamma knife radiosurgery, 87.3% for linear particle accelerator, and 79% for CyberKnife, without any significant differences between the radiation modalities.[15] The average rates of freedom from pain after SRS without medication were 53.1% for gamma knife radiosurgery, 49.3% for linear particle accelerator, and 56.3% for CyberKnife, again without any significant differences between the treatment modalities.[15] The review also found 2 studies that had reported a rate of freedom from pain without medication at 10 years of 30% and 45.3% and that previous surgery was a negative predictor for pain relief after SRS.[15,19,36] Within the limits of the

Table 4. Complications

Investigator	Treatment Group	Complications
Sabourin et al.,[27] 2020	MVD + IN	For BNI-HS: patients with IN + MVD showed no numbness (21%), mild numbness (74%), some numbness (5%), and bothersome numbness (0%) at last follow-up
	IN	For BNI-HS: patients with IN showed no numbness (39%), mild numbness (42%), some numbness (0%), and bothersome numbness (0%) at last follow-up
Wu et al.,[28] 2020	IN	NA
Durnford et al.,[29] 2020	IN	12.5% of patients showed an absent corneal reflex postoperatively, which had recovered at 3 months; all patients reported postoperative facial numbness but only 50% of patients showed some facial numbness at last follow-up
Wu et al.,[30] 2018	IN with TCR	88.9% of patients had hypesthesia postoperatively; long-term rates of hypesthesia not reported
	IN without TCR	
Hussain et al.,[31] 2018	R-MVD	Hypesthesia rate not reported; no significant complications occurred in patient group; CSF leak and wound complication rates were comparable to those for patients undergoing first-time MVD
	IN	
Liang et al.,[32] 2017	IN	91.9% of patients experienced facial numbness postoperatively; 8.8% of patients developed corneal hypesthesia; of the patients who had developed numbness, numbness had resolved for 26.5% within 6 months, with numbness persisting for 73.5% for >6 months; no other long-term rates of hypesthesia or other significant complications were reported
Zhao et al.,[33] 2017	IN	20% of patients experienced facial numbness, all of which had resolved after 4 months; 1 patient had loss of corneal reflex
Zhang et al.,[34] 2017	R-MVD	No significant differences in rates of facial numbness between R-MVD and R-MVD + IN groups; however, a trend was found toward R-MVD + IN group having greater rates of numbness at all recorded time points; at 1-day postoperatively, hypesthesia rate in R-MVD group, 48.39%; hypesthesia rate in R-MVD + IN group, 60.47%; at 1 year, hypesthesia rate had decreased in the R-MVD group to 1.75% and 3.75% in the R-MVD + IN group; other complications included cerebellar ataxia in 2 patients in R-MVD group and 1 patient in R-MVD + IN group; 2 patients in R-MVD + IN group had increased difficulty opening their eyes postoperatively; 1 patient in R-MVD group and 2 in R-MVD + IN group had taste hypoesthesia without affecting patients' quality of life; all had improved postoperatively during follow-up
	R-MVD + IN	
Zhou et al.,[26] 2016	IN	Significant differences in rates of facial dysesthesia seen between IN (16%) and RF (3.6%) groups and between rates of facial nerve lesions (14%, IN; 1.8%, RF); all other complications were not significantly different between IN and RF groups
	RF	
Ko et al.,[1] 2015	IN	96% of patients experienced facial numbness immediately postoperatively; numbness rates at last follow-up not reported; 5 patients (22%) had had dysesthesia postoperatively, with 4 of 5 having had pain in same distribution preoperatively and 1, a clear new case of anesthesia dolorosa after IN postoperatively; all 5 patients had undergone previous treatments; only other postoperative complication noted was CSF leak in 1 patient
Jie et al.,27 2013	IN without NVC	17.9% of patients in IN without NVC group and 12.5% of patients in IN with NVC group reported facial numbness; other complications included EOM palsy, CSF leak, transient hearing loss, and meningitis
	IN with NVC	
Ma et al.,[23] 2009	IN	90% of patients experienced facial numbness postoperatively, which had completely resolved in 8 of 9 patients by 6 months; 1 patient experienced permanent facial numbness that was still present at 36 months postoperatively; no patient experienced motor dysfunction, loss of corneal reflex, or any other significant complications

MVD, microvascular decompression; IN, internal neurolysis; BNI-HS, Barrow Neurological Institute hypesthesia scale; NA, not available; TCR, trigeminocardiac reflex; R-MVD, revision or reexploration microvascular decompression; CSF, cerebrospinal fluid; RF, radiofrequency rhizotomy; NVC, neurovascular compression; EOM, extraocular muscle.

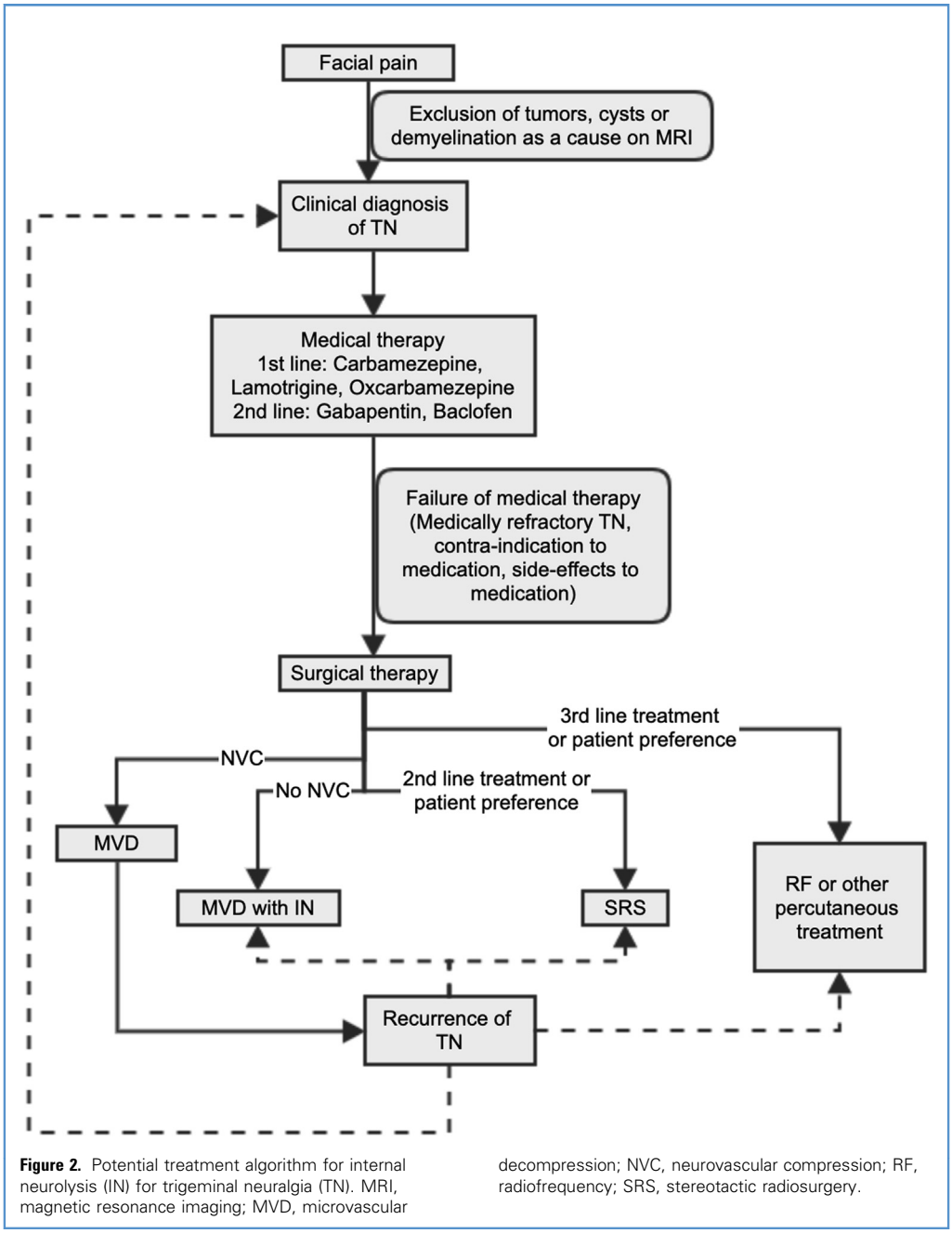

Figure 2. Potential treatment algorithm for internal neurolysis (IN) for trigeminal neuralgia (TN). MRI, magnetic resonance imaging; MVD, microvascular decompression; NVC, neurovascular compression; RF, radiofrequency; SRS, stereotactic radiosurgery.

data for IN that exist, IN appears to have a higher success rate compared with SRS at short-term follow-up and remains to be determined for long-term follow-up.

IN Versus Percutaneous Procedures

Many retrospective cohort studies have described the success rates for the different percutaneous procedures. Success has usually ranged from 90% to 97% for pain relief in the immediate post-operative period but with a recurrence rate as high as 75% at long-term follow-up.[20,27,31,32] When comparing the different techniques, RF appeared to provide the best pain relief of the percutaneous procedures but also showed a potentially higher complication profile.[21] One review found a trend toward higher rates of anesthesia dolorosa as a complication after RF compared with after glycerol rhizotomy or balloon compression.[21]

One study compared the results of RF versus IN. Zhou et al.[26] found a trend toward IN producing greater rates of satisfactory results, lower recurrence rates, and lower rates of poor outcomes, as defined by the study, at an average follow-up of 90 months. However, because of the significantly higher complication rate seen with IN than with RF and a nonsignificant difference in treatment outcomes, they concluded that RF was the

preferred procedure.[26] The greater rate of complications seen with IN included facial dysesthesia in 16% of patients and facial nerve injury in 14% of patients.[26] These rates of facial nerve injury with posterior fossa exploration were higher than those from most reported studies, which have usually ranged from 0.5% to 3%.[2] In our systematic review, the rate of facial dysesthesia was ~4%. The actual degree of facial hypoesthesia versus dysesthesia was also unclear in the studies comparing RF and IN. In addition, some patients might tolerate facial numbness with improved pain control. When considering the results of these studies, IN appears to be as effective and potentially more effective than percutaneous procedures. It seems especially indicated for patients without NVC and without any prior TN treatment.

IN Versus PSR

PSR has been used as a surgical option and as an alternative to MVD in the absence of intraoperative NVC, for patients with venous compression, and during revision surgery for failed MVD.[17,37-40] One series that used these criteria for PSR found excellent, good, and poor results for 48%, 22%, and 30% of patients, respectively.[17] Also, 42% of patients had undergone prior treatment for TN, 76% had had no NVC intraoperatively and 23% were found to have NVC and had undergone either isolated PSR or PSR with MVD. The results for the patients with no prior surgery were excellent for 64% at 1 year and for 55%–60% at 5 years. In contrast, the patients with prior surgery had had worse results (excellent for 38% at 1 month and 1 year and for 10%–15% at 5 years).[17]

Regarding IN, patients with previous surgery fared worse with PSR. However, the overall excellent result of 48% for PSR at 5 years was within the lower range seen for IN, and the outcome of 55%–60% excellent results after PSR for patients without previous surgery was much lower than the 94% excellent results seen with IN for patients without previous treatment.[1]

Complications

Facial numbness is an expected complication of IN resulting from the increased manipulation of the trigeminal nerve. The results from our review suggest that significant recovery will occur over time for patients who have undergone IN, from 96% of patients immediately postoperatively to 1%–10% at the last follow-up. Furthermore, the results from these studies suggested that the incidence of painful numbness was low (BNI-HS score I–II). The relationship between postoperative facial numbness and long-term pain relief must be further established. Major complications related to trigeminal nerve dissection, including corneal ulceration and anesthesia dolorosa, were rarely reported in the included studies. The rest of the complication profile appears similar to that for MVD. More studies are warranted to better define the postoperative incidence of, distribution of, and recovery from facial hypesthesia.

Study Limitations

All 12 studies included in the present review had a retrospective design with unblinded assessments of the outcomes and were, thus, subject to a high risk of bias. The degree of heterogeneity in the patient populations within the different studies was also high, which could have created variability in the pain relief outcomes. Some included studies had been from the same institution and could have included the same patient twice in the analysis.[28,30,33,34] However, we could not identify such patients and exclude them from the analysis. Thus, the actual size of our meta-analysis might be smaller. Additionally, the follow-up times for the included studies were relatively short compared with reported studies of other treatment modalities for TN, which also made it difficult to compare the results.

CONCLUSIONS

IN for TN is effective for providing pain relief. IN can be as effective as MVD for patients with low-grade NVC. Furthermore, for patients without NVC and for those with recurrence after MVD, IN seems to provide at least similar, if not better, short-term outcomes compared with other surgical options, especially considering that these cases are notably more difficult to treat and have higher recurrence rates. IN is another treatment option that might allow for better long-term pain relief than SRS or percutaneous treatment options. Future studies are required to better define long-term pain relief, ideal patient populations, and the complication profile of IN.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Victor Sabourin: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft. **Pascal Lavergne:** Data curation, Writing – review & editing. **Jacob Mazza:** Data curation, Writing – review & editing. **Jeffrey Head:** Data curation, Writing – review & editing. **Fadi Al-Saiegh:** Data curation, Writing – review & editing. **Tony Stefanelli:** Data curation, Writing – review & editing. **Michael Karsy:** Formal analysis, Methodology, Software, Validation, Writing – review & editing. **James J. Evans:** Conceptualization, Methodology, Supervision, Writing – review & editing.

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