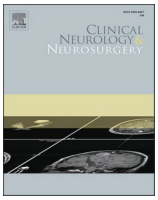
Clinical Neurology and Neurosurgery 219 (2022) 107343

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro



Neural activity in trigeminal neuralgia patients with sensory and motor stimulations: A pilot functional MRI study

Wen-Ching Liu [a,d,*], Nolan K. Winslow [b,d], Lisa Chao [d,1], Hrachya Nersesyan [c,d], Michael T. Zagardo [d], Patrick T. Tracy [b,d]

[a] Department of Radiology, OSF HealthCare System, OSF Saint Francis Medical Center, Peoria, IL, USA
[b] Department of Neurosurgery, OSF HealthCare System, OSF Saint Francis Medical Center, Peoria, USA
[c] Department of Neurology, Illinois Neurological Institute, OSF HealthCare System, Peoria, USA
[d] University of Illinois College of Medicine at Peoria, Peoria, USA

ARTICLE INFO

Keywords:
Trigeminal neuralgia
FMRI
Pain
Radiofrequency rhizotomy
Sensory
Motor stimulation

ABSTRACT

Objective: Trigeminal neuralgia (TN) is a neuropathic pain syndrome that typically exhibits paroxysmal pain. However, the true mechanism of pain processing is unclear. We aim to evaluate the neural activity changes, before and after radiofrequency rhizotomy, in TN patients using functional MRI (fMRI) with sensory and motor stimulations.

Methods: Six patients with classical TN participated in the study. Each patient underwent two boxcar paradigms of fMRI tasks: air-sensation and jaw-clenching around 1–3 weeks before and after the surgical intervention. McGill Pain Questionnaire (MPQ) was used to evaluate the pain intensity prior to fMRI study.

Results: Before rhizotomy, the jaw-clenching stimulation yielded reduced brain activation in primary motor (M1) and primary (SI) and secondary somatosensory (SII) cortices. Following intervention, activation in those regions returned to near normal levels observed in healthy subjects. For air-sensation stimulation, several pain and pain modulation regions such as right thalamus, right putamen, insula, and brainstem, were activated before the intervention, but subsided after the intervention. This correlated well with the change of MPQ scores ($p < 0.01$).

Conclusions: In our study, we observed significant pain reduction accompanied by increased motor activities after rhizotomy in patients with TN. We hypothesize that the reduced motor activities identified in fMRI may be reversed after the treatment with radiofrequency rhizotomy. More research is warranted.

1. Introduction

Trigeminal neuralgia (TN, tic douloureux) is a neuropathic orofacial pain syndrome characterized by episodic and shock-like unilateral facial pain in one or more branches of the trigeminal nerve (5th cranial nerve) [1]. Sensory impairment has been documented using quantitative and neurophysiological methods [2,3]. Demyelination, central sensitization, and amplified responses to non-noxious stimuli are known phenomena in TN, which, in conjunction with after-discharges and neighboring neuron coupling, comprise part of the paroxysmal nature of the disease mechanism. The true underlying mechanism of pain, however, remains unknown. The root entry zone theory cites vascular contact with the trigeminal nerve as the primary offense and etiology for pain [4]. Subsequent studies have shown the demyelination of the trigeminal nerve and root atrophy to be associated with physical contact [5]. Furthermore, the arterial compression with a nerve is more frequently reported in surgical and cadaveric studies than venous contact. Besides changes in the nerve itself, specific gray matter volumes have been shown to be altered in TN including somatosensory cortex, motor cortex and other regions [6]. A study measuring cortical thickness and volume in 24 patients with TN demonstrated increased gray matter volume in the contralateral primary somatosensory cortex (SI), and primary motor cortex (M1) [7]. Evidence also illustrated that some gray matter abnormalities detected on MRI scans are reversible following effective treatment of chronic pain and after microvascular decompression [8,9].

In TN, when cases are not controlled by pharmacotherapy, percutaneous radiofrequency rhizotomy (RFR) can produce superior results. This method maintains 50–60% pain relief for 5 years [10].

* Correspondence to: Department of Radiology, OSF HealthCare Saint Francis Medical Center, 515 NE Glen Oak Ave, Suite 209, Peoria, IL 61637, USA.
E-mail address: Wenching.Liu@osfhealthcare.org (W.-C. Liu).
[1] Current address: Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, TX, USA.

https://doi.org/10.1016/j.clineuro.2022.107343
Received 30 October 2021; Received in revised form 2 May 2022; Accepted 29 May 2022
Available online 18 June 2022
0303-8467/© 2022 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Blood oxygenation level dependent functional magnetic resonance imaging (BOLD fMRI) is a non-invasive technique to detect brain activity during an execution of a designed task or stimulation [11]. Its feasibility in visualizing neuro-anatomical locations with task-related stimulus has been demonstrated.

This study aims to evaluate the neural activities in patients with TN using BOLD fMRI sensory (air-sensation) and motor (jaw-clenching) tasks, for the periods before and after RFR.

2. Materials and methods

2.1. Participants

Two male and four female patients with classical trigeminal neuralgia, ages 57–81 years, average 73.3 ± 10.1, were treated with percutaneous radiofrequency rhizotomy and provided consent to be included in the study. Local institutional review board approval was obtained for the study.

Radiofrequency ablation was performed at the temperatures varying from 70 to 95° C. In order to assess patient's pain intensity, McGill pain questionnaire [12] was administered prior to each fMRI study.

2.2. Imaging acquisition

A GE 3 T whole body MR scanner (Discovery 750 W, GE Medical Systems, Milwaukee, WI), with a high-res 8 channel head coil was used to perform fMRI data acquisition. Before the fMRI study, each subject rehearsed study tasks to ensure that they could tolerate the participation. In the scanner, a set of 3D brain images (3D-FSPGR sequence) was acquired first. The imaging acquisition parameters were: TR/TE = 7.82/3.0 ms, flip angle = 12°,field of view = 25 cm, matrix size = 256 × 256, slice thickness = 1 mm, with the spatial resolution of 0.97 × 0.97 × 1 mm^3, and 150 or more slices to cover the whole brain. A T2 * -weighted gradient echo, echo planar imaging (EPI) sequence was used to acquire the functional data. The pulse sequence parameters for blood oxygenation level–dependent (BOLD) imaging were: TR/TE = 3000/30 ms, flip angle = 90°, matrix = 64 × 64, field of view = 24 cm, slices thickness = 3 mm, with the voxel size of 3.75 × 3.75 × 3 mm^3, and around 50 slices to cover the entire brain.

All fMRI data sets utilized a boxcar paradigm consisting of a 15 second baseline, followed by 10 cycles of 15 s ON (task participation) and 15 s OFF (no task participation). The stimulus cue was instructed first for jaw clenching, then air sensation. The reason for this delivery order was to reduce the potential reluctance to continue, caused by the pain induced from sensory stimulation. For the jaw clenching paradigm, patients performed a biting-down action (ON), then jaw relaxation (OFF). The air-sensation paradigm was delivered passively via a nasal cannula tube blowing air at patient's face ipsilateral to the lesion, at a rate of 2 Liter/min for ON, and no air for OFF.

2.3. Brain mapping

Imaging data was pre-processed with FSL software (https://fsl.fmrib.ox.ac.uk/fsl/ fslwiki/FSL)[13], including smoothing (5 × 5 × 5 mm^3 kernel), motion correction, and normalization of images to a standardized brain template. Motion corrections were performed for image alignment, with respect to the first set of head images, using FMRIB's Linear Image Registration Tool (McFLIRT). Normalization was modeled using 12 parameters model affine transformation in FLIRT. All the functional information was later transformed and overlaid on to a standard template from FSL. The contrast of fMRI data was estimated by FMRI Expert Analysis Tool (FEAT). The fMRI time course was analyzed using General Linear Modeling on a voxel-by-voxel basis for activation. Individual data were processed for 1st level analysis initially and later combined for high level group analysis (for within-group and between-group comparisons) with fixed effects model [13]. To compare the fMRI activation between groups of pre- and post-rhizotomy intervention, a two tailed, paired student t-test was used. Statistical significance was threshold with a cluster threshold of $Z > 3.0$ and corrected $p < 0.005$.

For region of interest analysis (ROI analysis) at anatomical locations, definitions from Julich Histological Atlas [14] and the Harvard-Oxford Subcortical and Cortical Atlas of Neuroanatomy were selected. Cluster analysis of voxels was performed using the Featquery program provided by FSL.

3. Results

A total of 6 patients participated in the study (Table 1). Pre-operative fMRI was obtained 2–3 weeks prior to the intervention; follow up imaging was obtained 1–2 weeks after the intervention. Average McGill pain score before rhizotomy was 50.67 ± 17.79 and significantly decreased to 19.5 ± 5.35 after the procedure ($p < 0.01$).

The group BOLD activation for pre- and post-RFR intervention with the jaw clenching task are displayed in Fig. 1-A, and detail activated regions are listed in Table 2. When compared to pre intervention group (post > pre condition), significant increase activation was observed in the right primary motor cortex (M1), bilateral primary (SI) and secondary somatosensory cortices (SII), Anterior Cingulate cortex (ACC), superior and middle temporal gyrus, right amygdala and right cerebellum, as shown in Fig. 1-B and detailed in Table 3.

For the air sensation stimulation, the within group activation, before and after the intervention, was presented in Fig. 2-A and Table 4. Activation associated with pain or pain modulation, before the intervention, was identified in the right thalamus, right putamen, insular cortex, and brainstem, including periaqueductal gray matter (PAG). Interestingly, most of the activation subsided after the intervention. In order to see the group comparison map (pre > post), we have to reduce the threshold to $Z > 2.5$ and $p < 0.05$ as displayed in Fig. 2-B and Table 5. The significant subsided activation was in the right amygdala, bilateral hippocampus, right thalamus, right insula, brainstem and bilateral cerebellum.

4. Discussion

Prior to RFR intervention, the jaw-clenching stimulation generated

Table 1
Patient demographics and clinical characteristics.

Age/ gender	Symptom Laterality	Additional history	Lesion	McGill Pain Score (pre/ post)	Post-operative course
57/M	Right	Tortuous Basilar Artery	V3	36/13	Recurrent pain Repeat RFR
77/F	Left	None	V3	67/25	Decreased V2–3 sensation. No pain
79/F	Left	RFR (4 years prior) -Gamma Knife radiosurgery (1 year prior)	V1–2	37/26	Mild recurrent V1 pain
78/F	Left	None	V3	78/15	Recurrent pain Repeat RFR
62/M	Left	Multiple sclerosis	V2	38/21	Recurrent pain Repeat RFR
81/F	Right	None	V3	48/17	Recurrent pain Repeat RFR

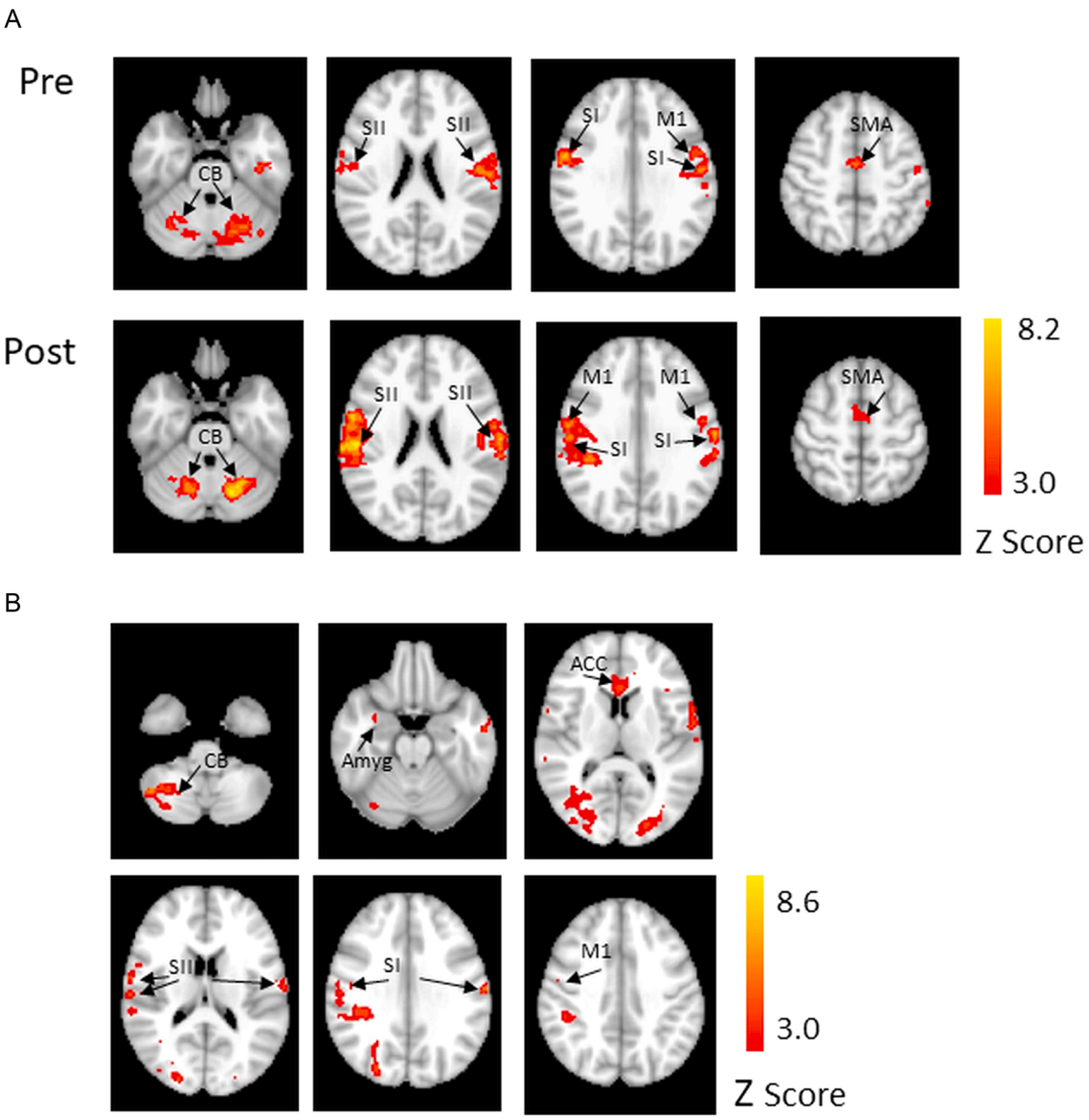


Fig. 1. A. Jaw-Clenching Group Map. FMRI group activation map (within group analysis) was generated for pre and post intervention condition, respectively. B. Jaw-Clenching Comparison Map. Through a two-tailed, paired student t-test, a between groups comparison map (post > pre intervention) was obtained.

Table 2
Activation areas from Jaw-Clenching group map.

	Pre-Intervention					Post-Intervention				
Areas	Vol	x	Y	z	Z-max	Vol	x	y	z	Z-max
SMA	162	4	-8	48	5.31	344	6	-2	62	5.32
M1-L	526	-48	-14	26	7.00	288	-54	-4	26	5.65
M1-R	273	56	0	34	7.78	463	60	-6	26	6.70
SI-L	1093	-56	-16	20	7.02	925	-62	-14	30	6.55
SI-R	461	56	0	34	7.78	1109	50	-12	26	6.76
SII-L	939	-56	-16	20	7.02	1307	-62	-14	30	6.55
SII-R	486	66	-12	12	5.15	2012	56	-20	22	8.44
STG-a	67	68	-8	0	4.44	158	62	4	-4	5.19
STG-p	159	68	-14	12	5.14	475	68	-24	20	6.73
TFC-a	92	-38	-16	-32	5.48					
TFC-p	195	-38	-16	-32	5.48					
CB-L	581	-20	-60	-24	5.68	481	-18	-68	-28	7.83
CB-R	305	34	-62	-28	4.72	429	14	-66	-26	6.56

Vol: activated voxel number; (x,y,z): standard coordinates in mm unit; Z-max: max Z score
Abbreviation: SMA= Supplementary motor cortex; M1-L (R) = Left (Right) Primary motor cortex; SI-L (R) = Left (Right) Primary sensory cortex; SII-L (R) = Left (Right) Secondary sensory cortex; STG-a (p) = Anterior (Posterior) Superior temporal gyrus
TFC-a (p) = Anterior (Posterior) temporal fusiform cortex; CB-L (R) = Left (Right) Cerebellum.

Table 3
Activation areas from Jaw-Clenching comparison map (post > pre).

Areas	Vol	X	Y	Z	Z-max
M1-R	49	60	-2	22	4.18
SI-L	241	-62	-14	30	5.74
SI-R	245	62	-4	16	4.54
SII-L	319	-62	-14	30	5.74
SII-R	738	56	-20	24	5.54
ACC	195	-6	34	4	5.03
Ins	56	38	-6	-4	4.51
STG-a	127	-62	-10	-10	4.77
MTG-a	439	-54	0	-32	7.53
Amyg-R	22	26	2	-10	3.68
LOC-s	326	28	-80	30	5.22
LOC-i	682	30	-84	2	4.86
CB-L	121	34	-56	-30	6.56
CB-R	209	46	-60	-44	5.78

ACC = Anterior Cingulate cortex; Ins = Insula cortex;
STG-a = Anterior Superior temporal gyrus; MTG-a = Anterior Middle temporal gyrus;
Amyg-R = Right Amygdala; LOC-s (-i) = Superior (Inferior) Lateral occipital cortex.

decreased activation in the right M1, bilateral SI, bilateral SII, right amygdala, and bilateral cerebellum. The jaw-clenching task has been studied elsewhere in both healthy subjects [15,16] and patient groups [17,18]. It stimulated the bilateral M1, supplementary motor (SMA), SI and SII, thalamus, and cerebellum [16] in normal controls. Nevertheless, patients with temporomandibular joint disorder (TMD) [17] showed decrease activation in the left primary motor cortex, inferior temporal gyrus, and cerebellum, when compared to controls. For bruxism patients, a decreased activation pattern was also observed in right inferior parietal lobule and dorsal posterior cingulate areas [18]. The study from DeSouza et.al reported a reversal effect in insular and microstructure nerve abnormalities following effective surgical treatment [8]. In our study, TN patients showed a decreased activation in the motor cortex before the intervention, which returned to close to normal levels shown in the literature after treatment [15,16]. We hypothesize that motor cortex altered activity may be associated with dysfunctional sensory afferent pathways and that surgical intervention may be able to reverse the reduced motor activation. However, it is possible that due to the pain before the intervention, the patients might not perform the jaw clenching as hard as later. In our study, the clenching force was not quantified.

Systematic reviews and analyses have shown that surgical motor cortex stimulation provides pain relief in trigeminal neuropathic syndromes [19]. Although the specific mechanism is not known, reciprocal connections between the primary motor cortex and other brain regions (somatosensory cortex, anterior cingulate, and thalamus) suggest a role in affective or emotional modulation of pain signaling [19,20]. Hagenacker et al. studied transcranial anodal direct current stimulation of the primary motor cortex in 10 classical trigeminal neuralgia patients and patients with other persistent facial pain diagnoses [21]. They found that intensity of pain was ameliorated by 29% in the TN group, but no pain improvement was seen with stimulation in atypical syndromes. No patients in their data had previous invasive procedures for pain (rhizotomy, surgery, radiation). Their work suggested that motor circuit activation could inhibit or modulate abnormal sensory processing. The thalamic nucleus is known to receive information from the primary motor cortex, which would support the possibility of motor cortex

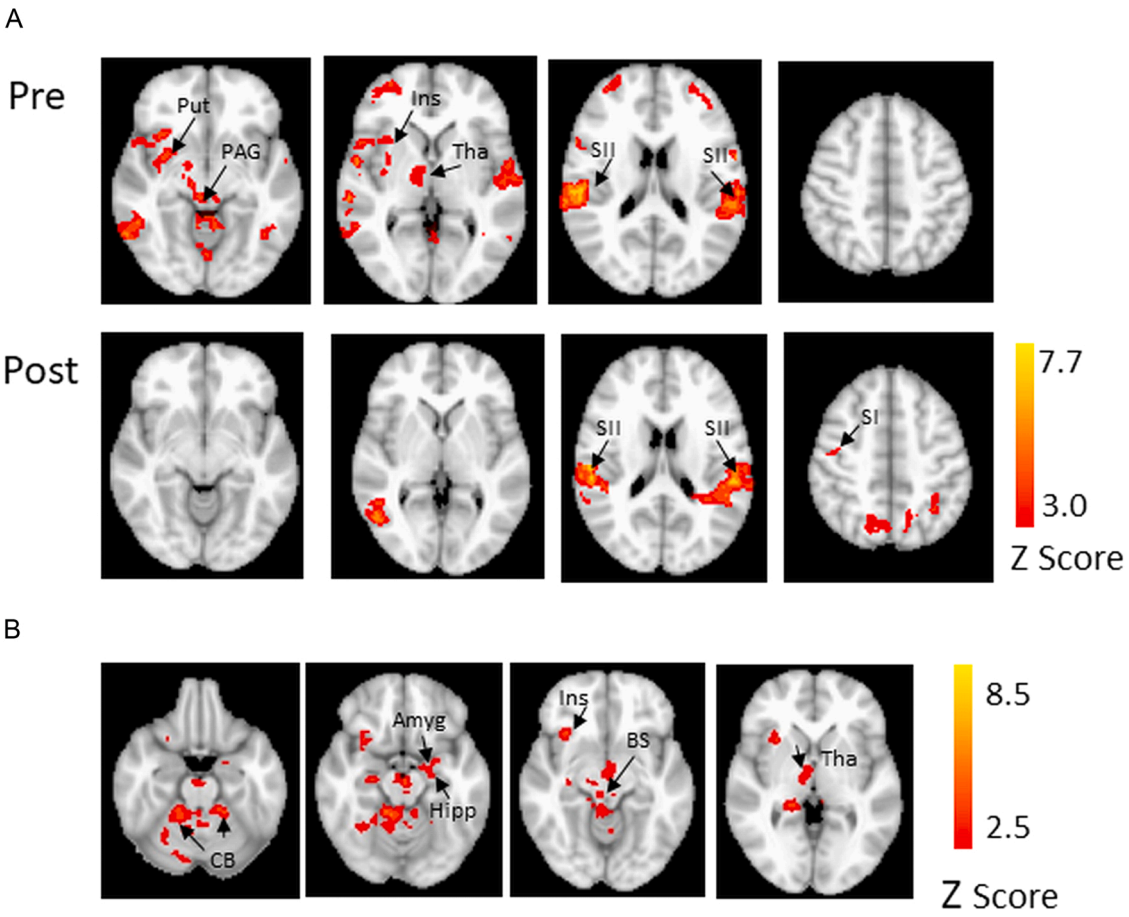


Fig. 2. A. Air-Sensation Group Map. Within-group analysis was performed for Air-Sensation stimulation. B. Air-Sensation Comparison Map. Between-group comparison map (pre > post) for Air-Sensation stimulation.

Table 4
Activation areas from Air-Sensation group map.

	Pre-Intervention					Post-Intervention				
Areas	Vol	X	Y	Z	Z-max	Vol	X	Y	Z	Z-max
M1-R						191	56	2	24	5.13
SI-L	101	-60	4	22	5.79	389	-64	-20	30	5.63
SI-R	4	64	-14	26	3.76	265	56	2	24	5.13
SII-L	1004	-56	-32	12	8.43	1342	-56	-24	14	7.04
SII-R	1012	52	-22	22	7.86	699	56	-20	22	7.75
Tha-R	174	12	-16	-2	5.15					
Put-R	133	32	4	-6	4.88					
Ins	341	36	18	-2	5.16					
MTG-tc	537	60	-58	-8	5.65	240	50	-64	2	5.648
CB-L	1958	-36	-56	-30	6.10					
CB-R	1826	10	-44	-18	6.39					
BS	256	4	-30	-10	5.33					

Tha-R = Right Thalamus; Put-R = Right Putamen; MTG-tc = Temporo-occipital Middle temporal gyrus; BS = Brainstem.

Table 5
Activation areas from Air-Sensation comparison map (pre > post).

Areas	Vol	X	Y	Z	Z-max
Amyg-L	166	-16	-6	-16	3.15
Hipp-L	26	-20	-8	-18	3.05
Hipp-R	139	16	-32	-4	4.37
Tha-R	141	16	-32	-2	4.44
Ins-R	211	34	20	-6	4.75
BS	205	4	-40	-14	3.89
CB-L	357	-18	-40	-20	3.56
CB-R	885	14	-42	-18	4.85

Hipp-L (R) = Left (Right) Hippocampus.

stimulation influencing multiple sensory and associative pathways [20]. The link between activation of motor pathways and pain relief is not fully understood but likely relies on the diffuse connections of primary motor cortex to other neural matrices. Our findings of reduced fMRI sensorimotor activity before intervention may be a compensatory mechanism in adaption to the chronic pain.

For air-sensation stimulation, before the intervention, we saw brainstem activation, more specifically in PAG, which plays a major role in pain modulation. The insular cortex manifests a large portion of somatosensory inputs including tingling, electric, warm, and cold sensations. Both non-painful and painful stimuli can generate insular activation [22]. The putamen activation may also associate with pain and its modulation. Interestingly, in our study, the activation, associated with pain and/or pain modulation such as from PAG, insula, and amygdala, subsided after the intervention. The working mechanism of rhizotomy is to create a thermal lesion to the root or roots of trigeminal nerve using radiofrequency. With each lesion, there is a known risk of losing tactile sensitivity. However, the degree of this loss after the procedure has not been reported.

Air-puff tactile stimulation on the face has been used in task-specific fMRI studies with normal subjects [23]. Activations typically localized to bilateral primary and secondary somatosensory cortices, primary motor cortex, and middle temporal cortices. Our results support these published patterns.

Blatow et al. utilized fMRI with the air-puff paradigm to examine finger and lip sensation in TN patients [24]. The authors observed general reduction of SI and SII in TN patients that was independent of side of symptoms or stimulus, which suggested that reduced activity of the cortical thalamic feedback network could result from long-term modulation of somatosensory function to potentially painful stimulation. Moisset et al. studied trigeminal TN patients with and without evoked pain using fMRI via a cotton swab tactile stimulation [25]. Painful stimulation was associated with increased activity in multiple areas, including spinal trigeminal nucleus, thalamus, primary and secondary somatosensory cortices, anterior cingulate cortex, insula, premotor/motor cortex, putamen, and PAG. This increased activation was no longer seen in areas outside of SI and SII after successful procedural treatment of TN [25]. The authors considered that the pathological hyperexcitability of the trigeminal nociceptive system and activation of PAG might represent a compensatory mechanism attempting to involve increased pain modulation. Although the above mentioned Blatow and Moisset studies propose different responses of pain processing to long stimulus history, both are plausible theories. Our patient group showed decreased somatosensory activation overall prior to effective rhizotomy, supporting the theory of induction of compensatory mechanisms to lessen the affective aspect of chronic pain. Recently, the regional cerebral blood flow (rCBF) in PAG has been shown to positively correlate with pain experience in both normal control and chronic low back pain groups using positron emission tomography (PET) [26]. In another PET study, Petrovic et al. reported that brush stimuli to the allodynic region activated PAG more than the stimulus to control regions [27]. A study from Lee et al. showed that the brainstem played a maintenance role in central sensitization during noxious stimulation in humans [23]. These studies seem to favor the idea of increased activation of modulatory pain pathway components as compensation for stimulus. It is likely that both mechanisms, decreased somatosensory activation, and increased activation of pain modulation pathways, play a role in neural adaptation to chronic pain.

Our study poses certain limitations, such as small number of study subjects, which did not allow for insight into ipsilateral/contralateral sensory comparison. The mixed laterality of TN symptoms in our patient population is another limitation; it is possible that the process of averaging our data may have masked effects of right-versus left-sided disease and associated functional brain changes. Particularly for jaw-clenching task, the bilateral activation in M1/SMA and right SI/SII in normal subjects [16] makes the laterality less important.

5. Conclusion

Our findings provide evidence of altered motor map in patients with TN. We hypothesize that the reduced motor response is induced by the dysfunctional sensory afferents in patients with trigeminal neuralgia and these changes may be improved after radiofrequency rhizotomy. Further studies are warranted to better explore the activated regions.

Funding

OSF HealthCare Illinois Neurological Institute Research Program.

CRediT authorship contribution statement

Wen-Ching Liu: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – review &

editing, Visualization. **Nolan Winslow:** Formal analysis, Investigation, Writing-original, Writing - review & editing. **Lisa Chao:** Conceptualization, Methodology, Investigation. **Hrachya Nersesyan:** Conceptualization, Methodology, Investigation, Writing – review & editing. **Michael Zagardo:** Methodology, Validation. **Patrick Tracy:** Conceptualization, Methodology, Resources, Supervision, Project administration, Funding acquisition.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgements

We would like to express our gratitude to the members of the MRI facility in the Radiology department at OSF HealthCare Saint Francis Medical Center, our research staff, and our patients without whom our project would not have been possible.

References

[1] L. Bendtsen, J.M. Zakrzewska, T.B. Heinskou, et al., Advances in diagnosis, classification, pathophysiology, and management of trigeminal neuralgia, Lancet Neurol. 19 (2020) 784–796, https://doi.org/10.1016/S1474-4422(20)30233-7.
[2] D. Bowsher, J.B. Miles, C.E. Haggett, P.R. Eldridge, Trigeminal neuralgia: a quantitative sensory perception threshold study in patients who had not undergone previous invasive procedures, J. Neurosurg. 86 (1997) 190–192, https://doi.org/10.3171/jns.1997.86.2.0190.
[3] M. Leandri, C.I. Parodi, E. Favale, Early trigeminal evoked potentials in tumours of the base of the skull and trigeminal neuralgia, Electroencephalogr. Clin. Neurophysiol. Evoked Potentials 71 (1998) 114–124, https://doi.org/10.1016/0168-5597(88)90069-X.
[4] W.E. Dandy, An operation for the cure of TIC douloureux partial section of the sensory root at the pons, Arch. Surg. 18 (1929) 687–734.
[5] P.R.L. Leal, J.A. Roch, M. Hermier, et al., Structural abnormalities of the trigeminal root revealed by diffusion tensor imaging in patients with trigeminal neuralgia caused by neurovascular compression: a prospective, double-blind, controlled study, Pain 152 (2011) 2357–2364, https://doi.org/10.1016/j.pain.2011.06.029.
[6] Y.H. Tsai, R. Yuan, D. Patel, et al., Altered structure and functional connection in patients with classical trigeminal neuralgia, Hum. Brain Mapp. vol. 39 (2018) 609–621, https://doi.org/10.1002/hbm.23696.
[7] D.D. DeSouza, M. Moayedi, D.Q. Chen, et al., Sensorimotor and pain modulation brain abnormalities in trigeminal neuralgia: a paroxysmal, sensory-triggered neuropathic pain, PLoS One 8 (2013), https://doi.org/10.1371/journal.pone.0066340.
[8] D.D. DeSouza, K.D. Davis, M. Hodaie, Reversal of insular and microstructural nerve abnormalities following effective surgical treatment for trigeminal neuralgia, Pain 156 (2015) 1112–1123, https://doi.org/10.1097/j.pain.0000000000000156.
[9] D.A. Seminowicz, T.H. Wideman, L. Naso, et al., Effective treatment of chronic low back pain in humans reverses abnormal brain anatomy and function, J. Neurosci. 31 (2011) 7540–7550, https://doi.org/10.1523/JNEUROSCI.5280-10.2011.
[10] J.S. Cheng, D.A. Lim, E.F. Chang, N.M. Barbaro, A review of percutaneous tre atments for trigeminal neuralgia, Neurosurg 10 (2014) 25–33, https://doi.org/10.1227/NEU.0000000000001687.
[11] S. Ogawa, T.M. Lee, A.R. Kay, D.W. Tank, Brain magnetic resonance imaging with contrast dependent on blood oxygenation, Proc. NatI. Acad. Sci. USA 87 (1990) 9868–9872, https://doi.org/10.1073/pnas.87.24.9868.
[12] R. Melzack, The McGill Pain Questionnaire: major properties and scoring methods, Pain 1 (1975) 277–299, https://doi.org/10.1016/0304-3959(75)90044-5.
[13] S.M. Smith, M. Jenkinson, M.W. Woolrich, et al., Advances in functional and structural MR image analysis and implementation as FSL, NeuroImage 23 (2004) 208–219, https://doi.org/10.1016/j.neuroimage.2004.07.051.
[14] S.B. Eickhoff, K.E. Stephan, H. Mohlberg, et al., A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data, NeuroImage 25 (2005) 1325–1335, https://doi.org/10.1016/j.neuroimage.2004.12.034.
[15] T. Iida, M. Kato, O. Komiyama, et al., Comparison of cerebral activity during teeth clenching and fist clenching: a functional magnetic resonance imaging study, Eur. J. Oral. Sci. 118 (2010) 635–641, https://doi.org/10.1111/j.1600-0722.2010.00784.x.
[16] C.S. Lin, Meta-analysis of brain mechanisms of chewing and clenching movements, J. Oral Rehabil. 45 (2018) 627–639, https://doi.org/10.1111/joor.12657.
[17] S.S. He, F. Li, T. Gu, et al., Altered neural activation pattern during teeth clenching in temporomandibular disorders, Oral Dis. 22 (2016) 406–414, https://doi.org/10.1111/odi.12465.
[18] S. Yilmaz, To see bruxism: a functional MRI study, Dentomaxillofac. Radiol. 44 (2015), https://doi.org/10.1259/dmfr.20150019.
[19] J.J. Mo, W.H. Hu, C. Zhang, et al., Motor cortex stimulation: a systematic literature-based analysis of effectiveness and case series experience, BMC Neurol. 19 (2019) 1–9, https://doi.org/10.1186/s12883-019-1273-y.
[20] S.M. Sherman, Thalamus plays a central role in ongoing cortical functioning, Nat. Neurosci. 19 (2016) 533–541, https://doi.org/10.1038/nn.4269.
[21] T. Hagenacker, V. Bude, S. Naegel, et al., Patient-conducted anodal transcranial direct current stimulation of the motor cortex alleviates pain in trigeminal neuralgia, J. Headache Pain 15 (2014) 1–9, https://doi.org/10.1186/1129-2377-15-78.
[22] K.B. Jensen, C. Regenbogen, M.C. Ohse, et al., Brain activations during pain: a neuroimaging meta-analysis of patients with pain and healthy controls, Pain 157 (2016) 1279–1286, https://doi.org/10.1097/j.pain.0000000000000517.
[23] M.C. Lee, L. Zambreanu, D.K. Menon, et al., Identifying brain activity specifically related to the maintenance and perceptual consequence of central sensitization in humans, J. Neurosci. 28 (2008) 11642–11649, https://doi.org/10.1523/JNEUROSCI.2638-08.2008.
[24] M. Blatow, E. Nennig, E. Sarpaczki, et al., Altered somatosensory processing in trigeminal neuralgia, Hum. Brain Mapp. 30 (2009) 3495–3508, https://doi.org/10.1002/hbm.20773.
[25] X. Moisset, N. Villain, D. Ducreux, et al., Functional brain imaging of trigeminal neuralgia, Eur. J. Pain. 15 (2011) 124–131, https://doi.org/10.1016/j.ejpain.2010.06.006.
[26] S.W.G. Derbyshire, A.K.P. Jones, F. Creed, et al., Cerebral responses to noxious thermal stimulation in chronic low back pain patients and normal controls, NeuroImage 16 (2002) 158–168, https://doi.org/10.1006/nimg.2002.1066.
[27] P. Petrovic, M. Ingvar, S. Stone-Elander, et al., A PET activation study of dynamic mechanical allodynia in patients with mononeuropathy, Pain 83 (1999) 459–470, https://doi.org/10.1016/S0304-3959(99)00150-5.