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Bilateral cortical stimulation for bilateral refractory atypical trigeminal neuropathic pain: Case report

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Abstract

BACKGROUND: Atypical trigeminal neuropathic pain (aTNP) is a disabling clinical entity. If conservative treatment fails neuromodulation could be indicated. Motor cortex stimulation (MCS) has emerged as an alternative advanced management of such cases.
CASE REPORT: We report a case of a patient with bilateral aTNP effectively treated with bilateral MCS. We describe case history, preoperative planning, surgical technique, follow-up and stimulation settings. The surgical technique and the settings used were both gradually adjusted according to current knowledge.
CONCLUSIONS: The bilateral MCS led to substantial pain relief in a patient for whom previous pharmacological management had failed. Initial VAS 10/10 with attacks of acute pain was reduced to median VAS 2/10 (maximum VAS 5/10) without acute attacks since the second electrode parameters were set. The reported results for MCS treatment of TNP in the literature demonstrate good long-term efficacy with low complication rates. Although MCS remains to be an off-label procedure, our case demonstrates that in a well-chosen candidate this option could provide impressive results. Although no clear evidence is currently given, we believe that future studies will elucidate indication criteria, surgical technique and stimulation parameters for MCS so it could be offered in a regular basis to patients with refractory pain.

INTRODUCTION

Refractory pain, resulting from various causes, represents a clinical challenge as responding poorly to all types of available pharmacological therapies. Invasive neurostimulation enabled by a development of neuromodulation techniques brought an option to treat the refractory pain and is currently applied at various sites of the peripheral and central nervous system. Stimulation of the precentral gyrus and motor cortex areas was firstly described by Tsubokawa *et al.* in 1991 (Monsalve, 2012) and after almost 30 years represents an effective treatment method with an indication list including post-stroke pain, brachial plexus avulsion, phantom pain, trigeminal neuropathic or deafferentation pain and pain induced by spinal cord injury and post-radicular plexopathy. (Mo *et al.* 2019)

C A S E R E P O R T

CASE REPORT

History

This 42 year-old woman injured both temporomandibular joints after a fall from a swing when she was 5 year-old. Whole childhood she had problems with chewing, opening of mouth and had repeated luxations. When she was 25 she suddenly could not open her mouth. She underwent repeated surgeries of both joints but the function was not sufficiently preserved so at 29 years of age she underwent bilateral total temporomandibular joint replacement. The left one was surgically reviewed because of pain in trigeminal area and suspection of screw irritation. Joint function was saved, however atypical trigeminal neuralgic pain developed in all branches of trigeminal nerve on the left side and third branch on the right. The pain gradually increased up to VAS 10/10 and attacks of neuralgia were accompanied by tonic clonic attacks spreading from the left side to the right and generalizing with no response to benzodiazepines. Medical treatment (NSAIDs, pregabalin, rivotril, carbamazepine, valproic acid, buprenorfin or fentanyl) did not relieve the pain. Only the convulsions responded to application of morphin by injection.

The patient was firstly consulted in the neuromodulation program when she was 31. Neurological examination revealed dysesthesias in the regions of all branches of left trigeminal nerve and right mandibular nerve and a neuralgic attacks starting after a touch on trigeminal trigger points on both sides provoked up to 10 times a month. EEG ruled out epileptic origin of convulsions. Psychological and psychiatric examinations were without gross pathology and excluded somatoform disorder. Electrophysiological examination indicated an incomplete blockade of trigeminal nerve bilaterally and left glossopharyngeal nerve associated with regional pain syndrome and an absence of indirect response of R2 of blink reflex on both sides. Patient was then reffered to rTMS. RTMS was done in a standard double-blinded protocol with a duration of two months and was applied using an aircooled, 70-millimeter coil creating a magnetic field of 1-2 Tesla in a time interval of 100-200 ms using a Magstim Super Rapid stimulator (Magstim, Whitland, United Kingdom) with an intensity of 95% of the motor threshold (720 pulses/session). The motor threshold intensity was set at the lowest intensity of the device, an intensity at which at least 5 of the 10 stimuli were recorded with electromyography and produced a visually detectable response to stimulation represented by masseter contraction. During placebo (sham stimulation), an inactive rTMS was used as a sham coil and was placed in the identical area as the active coil. Patient responded well to 20 Hz active stimulation (from VAS 10 to VAS 3) with no response to sham stimulation. As the improvement after active stimulation lasted only few days and the repeated transfers to the pain center would be difficult in this case the patient was offered an implantation of cortical stimulators bilaterally.

Surgical Technique and Follow-up

Before the surgery an fMRI was performed (Figure 1). The first electrodes (Lamitrode S8 (3286), St. Jude Medical™) were implanted subdurally on the right side in December 2010. The craniotomy and durotomy was guided with neuronavigation, one of the electrodes was placed to the precentral gyrus and second to the postcentral gyrus with a use of phase reversal and direct cortical stimulation with an experienced neurophysiologist. The pulse generator (St. Jude Medical™, Abbott Neuromodulation) was implanted to the left subclavicular area. The postoperative course was uneventful without a change in neurological status. After implantation of the electrodes, The St. Jude Medical™ Invisible Trial System (Abbott Neuromodulation) was used for 3 months to find stimulation parameters that produced the best pain relief without side effects. The final setting was continous stimulation with contacts 2+,3- (ramp time – 4 s, frequency – 60 Hz, Pulse width 200 μs, Perception – 0.7 mA, Comfort – 1.4 mA, Maximum – 6 mA, 86 steps – step size of 0.05 mA). In this final setting the VAS score of the chronic component on the left side decreased by 40% with no neuralgic attacks triggered on the left side. Dosage of the medication was reduced by more than a half to MQS Score 22.3 (buprenorfin, carbamazepine, escitalopram and fentanyl citrate). (Harden *et al.* 2005) The patient however continued to have mandibular nerve pain on the right side with acute attacks. The chronic component was getting worse and attacks more frequent - up to one time a day. These attacks were treated by nasal application of 50 μg of fentanyl citrate. The contralateral implantation was planned on August 2013 but had to be postponed due to the presence of multiple teeth infections. Gangrenous teeth were extracted, but since malnutrition developed contralateral electrodes could not be implanted. The state was complicated by a discharge of a battery of the pulse generator (4 years after implantation). The pain went back to the preoperative status with more frequent attacks by up to 3 times a day. The analgesic medication had to be increased up to MQS Score of 41.8. The patient underwent long-term nutritional program and multiple surgical sanations of teeth. Almost nine years after the first implantation multidisplinary team (neurosurgeon, psychiatrist, pain treatment specialist, neurologist and imunologist) decided to plan the contralateral implantation and change of the pulse generator.

Implantation of the left electrode (Lamitrode S8 (3286), St. Jude Medical™) was performed in February 2020 together with a replacement of the generator due to the discharged battery and all electrodes were connected to it. The technique was similar to the implantation on the right, but the electrodes were placed epidurally. The postoperative course was uneventful (Figure 2). Stimulation parameters were set 14 days after the

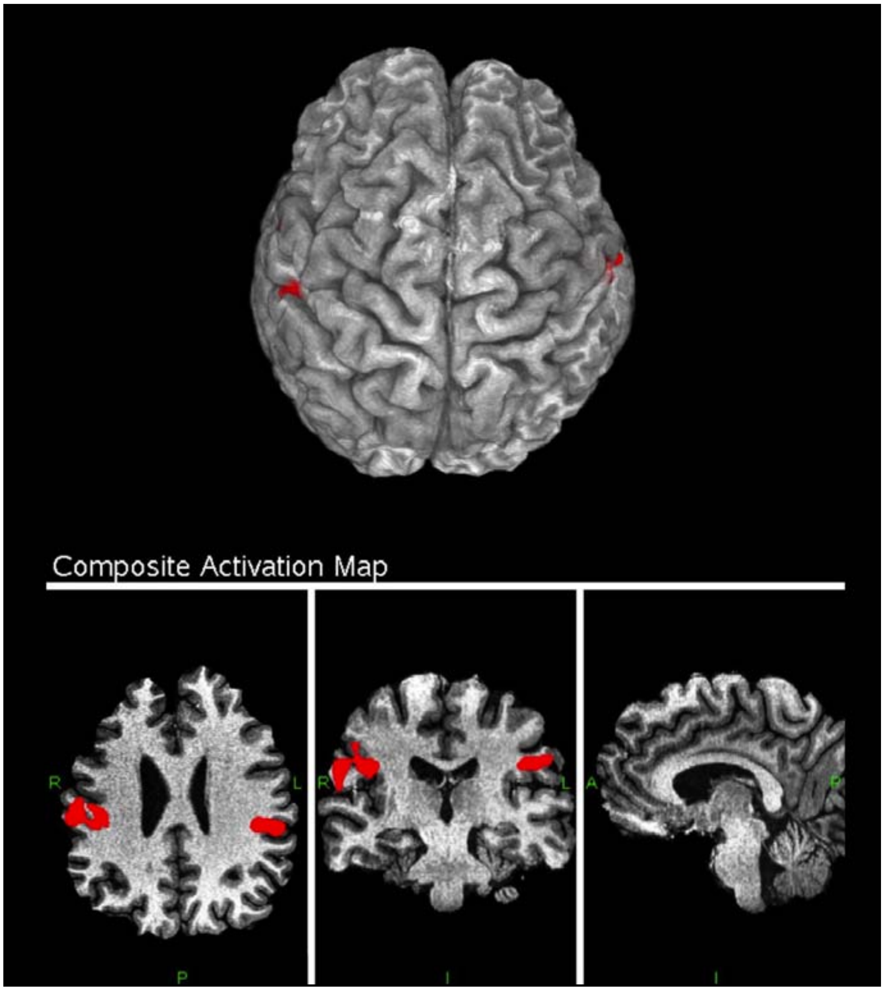

Fig. 1. fMRI of the brain performed on a GE Signa HDx device 3.0 T, s / nWB0022. Examination performed with EPI sequences, block design. Processed using Brainwave PA with correction motion artifacts, smoothing 8x8x8 mm, statistical analysis using GLM and spatial co - registration of a functional map on segmented 3D T1W anatomical sequence (FSPGR 3D). Thresholding Z-maps were chosen for p <0.01 with correction for repeated measurements. Examination performed during chewing movements (red). Activations were rather weak, chewing causes pain, activation more pronounced only after repetition. Areas of bilateral activation are visible especially in caudal parts of MI/SI, on the right more rostrally than on the left. Also active are bilateral small districts of the upper temporal lobe.

implantation to with contacts 2+,3- (ramp time – 4 s, frequency – 60 Hz, Pulse width 200 µs, Perception – 1.0 mA, Comfort – 2.0 mA, Maximum – 6 mA, 60 steps – step size of 0.10 mA). In June 2020 the parameters were set to cyclic on both sides as cyclization in responders prolong battery life and delay the need for INS replacement and may improve pain relief. (Ivanishvili *et al.* 2017) The current settings are with contacts 1-,2-,3+ on the right/2+/3- on the left with parameters: On – 20min, Off 120 min, ramp time – 4 s, frequency – 50 Hz, Pulse width 200 µs, Perception – 1.0 mA, Comfort – 1.0 mA, Maximum – 1 mA, 20 steps – step size of 0.05 mA. – and provide substantial pain relief (max VAS 5, median VAS2). The clinical observation continues.

DISCUSSION

We present a case with bilateral atypical TNP effectively treated with bilateral cortical stimulation with almost 10 years of follow-up after the first operation and 7 months after the second implantation. Atypical TNP is often misdiagnosed with typical neuralgia. Typical neuralgia is often idiopathic and clinically manifests as paroxysmal sharp „electrical“ facial pain confined to the distribution of trigeminal nerve emerging after stimulation of tigger points. Atypical TNP on the other hand has in addition to the paroxysms a constant component with an aching quality and most often occurs as a result of trigeminal injury. (Shankland, 1993)

Although no clear evidence is currently given, the reported results for MCS treatment of TNP in the literature (Mo *et al.* 2019, Monsalve, 2012, Rasche & Tronnier, 2016) demonstrate good long-term efficacy with low complication rates. Rasche *et al.* (Rasche & Tronnier, 2016) published a sample of 36 patients with TNP treated with MCS with a responder rate of 72%. Monsalve *et al.* (Monsalve, 2012) published a literature review of 118 patients with chronic neuropathic facial pain and MCS with a responder rate of 84% and Mo *et al.* (Mo *et al.* 2019) in the systematic literature review presented an overall pain improvement of 46.5% in patients with TNP. The explanations for the outcomes may be related to the size of a facial area in the motor cortex. (Rasche & Tronnier, 2016) Taking into account that our patient was refractory to any prior treatment, the pain improvement is remarkable. Holsheimer *et al.* (Holsheimer *et al.* 2007) stated that better results could be achieved if cathode is placed in front of the central sulcus and anode postcentrally. We tried this setting as

Fig. 2. A-P radiograph after 2nd implantation of the contralateral electrodes. Ideal position of the electrodes was achieved without any surgical complications.

the first option, however, a better result in this case was achieved with the opposite setting (difference in VAS 1/10, complete elimination of acute attacks). Despite the inconsistency among studies (Mo *et al.* 2019) the rTMS protocol proved well to predict the pain relief of cortical stimulation in this case. However, prospective, randomized, controlled, multicenter trials with standardized protocols on indication, surgical technique, and stimulation parameters are urgently needed to provide evidence for this type of therapy as well as research to discover the underlying mechanisms.

ACKNOWLEGMENT

Authorship Statement

Dr. Masopust diagnosed and treated the patient. Dr. Skalický prepared the written manuscript with a supporting literature search and important intellectual input from Dr. Masopust. Both authors contributed substantially in writing and editing of the paper and had complete access to patient data.

Conflict of interest statement

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