Chasing Map Plasticity in Neuropathic Pain

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Key words
- Eye
- fMRI
- Implant
- Perception
- PET
- Phantom
- Somatosensory reorganization

Abbreviations and Acronyms
AD: Anesthesia dolorosa
BOLD: Blood-oxygen-level dependence
fMRI: Functional magnetic resonance imaging
IPG: Internal pulse generator
PET: Positron emission tomography
SI: Primary somatosensory cortex
SII: Secondary somatosensory cortex
TMS: Transcranial magnetic stimulation

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OBJECTIVE: **Recently, somatosensory cortex stimulation has been proposed as a possible treatment for neuropathic deafferentation pain, based on a simple 4-step concept: (1) pain is associated with increased activity in the somatosensory cortex, (2) allodynia-evoked blood-oxygen-level dependence functional magnetic resonance imaging (fMRI) activation depicts the area involved in the pain, (3) if fMRI-guided, neuronavigation-based transcranial magnetic stimulation can transiently suppress the pain, then (4) an extradural electrode can be implanted targeting the same area.**

CASE DESCRIPTION: **A patient who was successfully treated with this approach for over 6 years for trigeminal anesthesia dolorosa associated with a subjectively malpositioned eye after multiple recurrent facial skin tumor removals developed new pain after more extensive surgery. Reprogramming the implanted electrode was unsuccessful. The presence of the electrode yielded too many artifacts on a renewed fMRI, and therefore a positron emission tomography (PET) scan was performed under evoked allodynia. Fusing the previous fMRI with the new PET images depicted 2 novel targets for stimulation, 1 anterior and 1 posterior of the previous target and beyond the spatial configuration of the implant. After the addition of 2 new electrodes, the pain could again be controlled in a placebo-controlled way, but only when the 2 electrodes were activated.**

CONCLUSIONS: **Combining fMRI and PET scanning can potentially demonstrate continuing map plasticity under progressive somatosensory deafferentation. The functional imaging data can be used as target for pathophysiology-based somatosensory cortex stimulation.**

INTRODUCTION

Anesthesia dolorosa (AD) is a form of deafferentation pain belonging to the group of neuropathic pain syndromes. It is most commonly iatrogenic in nature, following surgically induced lesions of the trigeminal nerve. It can occur after glycerol injection, partial nerve sections, radiofrequency rhizotomy, gamma knife surgery, balloon compressions, and microvascular decompression. AD is characterized by a painful anesthesia often associated with numbness. The neuropathic pain is associated with allodynia (feeling of pain on touch) and hyperalgesia (exaggerated reaction to painful stimuli). It can be continuous with superimposed lancinating paroxysms. AD typically presents as a burning feeling associated with or without numbness, itching, and a feeling of coldness.

It is typically very treatment resistant, and therefore is often treated by neuromodulatory approaches such as motor cortex stimulation (22), somatosensory cortex stimulation (8), or deep brain stimulation (18).

We present a case of AD in the ophthalmic division of the trigeminal nerve that developed after multiple resections of a basal cell carcinoma of the forehead. It was initially successfully treated by functional magnetic resonance imaging (fMRI)—guided stereotactic somatosensory cortex stimulation (7), but after more surgery for tumor recurrences, became intractable. A successful approach using positron emission tomography (PET)-guided implantation of 2 extra electrodes with successful stimulation is described.

CASE REPORT

A 53-year-old woman presented at the BRAI²N clinic with a 10-year history of persistent lancinating pain in the right supraorbital region. The pain arose a few weeks after a surgical excision of basal cell carcinoma on the right side of the forehead. Initially she suffered a normal postoperative pain progressively evolving to a constant, sharp lancinating pain. Multiple surgical procedures that followed caused aggravation of the symptoms (Figure 1). The pain was initially treated with medication consisting of paracetamol 500 mg/codeine 10 mg, up to 8 tablets per day. The patient subsequently also took

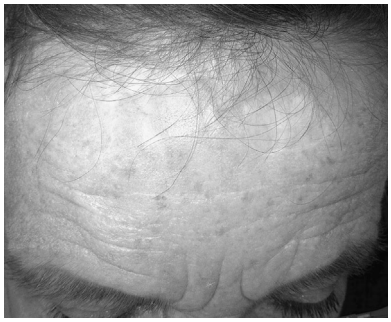

Figure 1. Multiple old scars can be detected on the right forehead, as well as a skin transplant (*light color*) crossing the midline.

tramadol 4 × 50 mg, amitriptyline 50 mg, zolmitriptan 2.5 mg, valproic acid chrono 2 × 500 mg, carbamazepine 3 × 200 mg, and gabapentin 3 × 300 mg, all to no avail. Transcutaneous electrical nerve stimulation was applied without success, and a stellate block brought no pain relief. Finally the right supraoptic nerve was cut, inducing AD.

Aside from the pain, she also developed a sensation of her right eye being located on her right maxillary arc. Despite a normal vision as demonstrated by an extensive neuro-ophthalmological workup, the subjective eye misplacement often induced a misperception of the position of surrounding objects, causing her to run into obstacles ipsilateral to the phantom sensation.

Clinical Examination

The presence of hyperalgesia and a loss of sensation of temperature and vibration in the right V1 dermatoma were noted. Tactile stimulation of the medial cornea and upper eyelashes of the right eye were sensed at the subjectively malpositioned eye at the right maxillary arc (Figure 2B). Tactile stimulation of the medial cornea and medial upper and lower eyelashes of the misplaced eye were referred to the corresponding areas at the ipsilateral eye. A corneal reflex could not be elicited by striking at the subjectively malpositioned eye. Further clinical examinations were normal.

fMRI

fMRI was performed on a 3-T magnetic resonance system using the blood-oxygen-level dependence (BOLD) method and consisted of acquisition of whole-brain fast field echo-echo planar imaging (resolution of 3 × 3 × 4 mm, TE/TR = 33/3000 ms) as well as high-resolution T1-weighted anatomical images. The stimulation paradigm was a blocked fMRI design alternating 30-second epochs of sensory stimulation (the patient rubbed the painful right V1 skin area using her left hand) with 30-second epochs of non-stimulation (rest). Statistical comparison

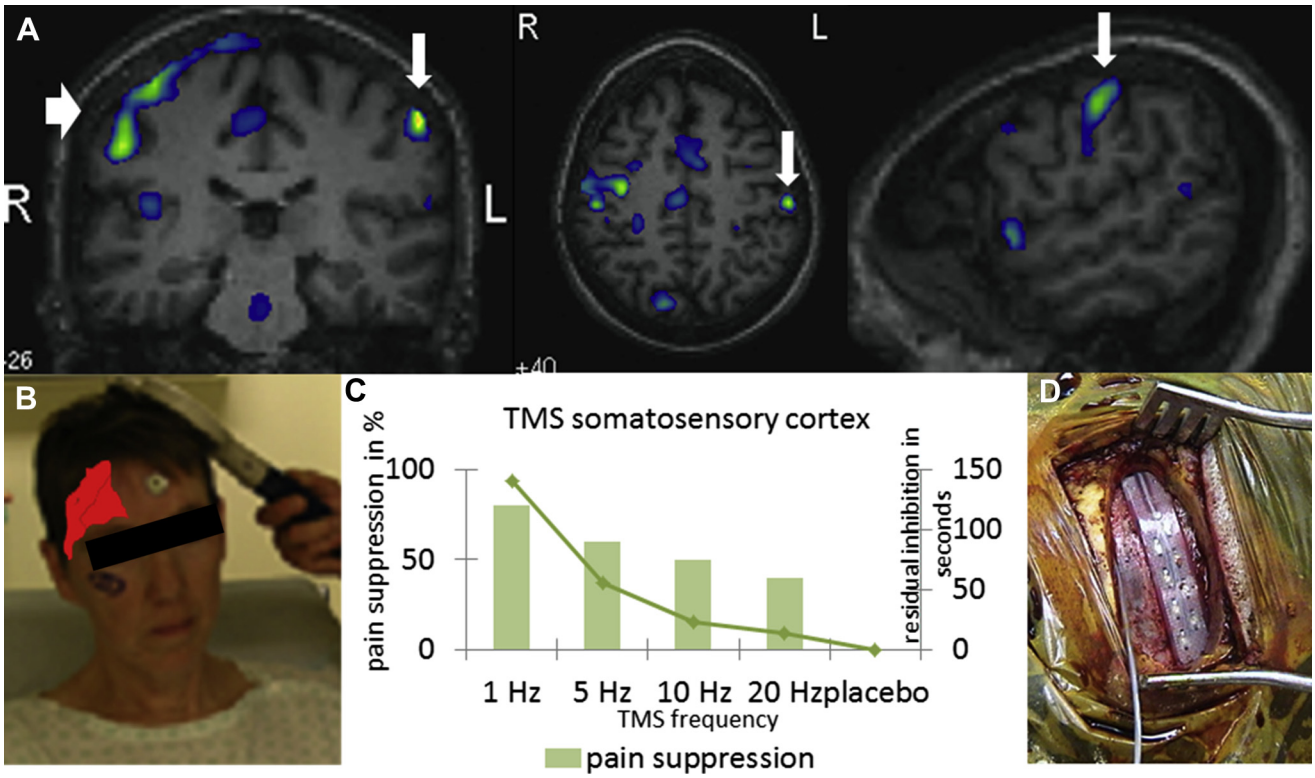

Figure 2. (**A**) Functional magnetic resonance imaging activation elicited by allodynia of the V1 dermatoma (*downward arrow*). The motor cortex activation is the result of using her left hand in the MRI machine to rub her right forehead (*horizontal thick arrow*). (**B**) The area of anesthesia dolorosa with allodynia is represented by *red coloring* in the area on her forehead. The phantom eye is drawn on her right cheek. (**C**) The amount of transcranial magnetic stimulation (TMS)–related pain suppression for each frequency is depicted by the *boxplot*, the residual inhibition for each TMS stimulation frequency by the *green dots connected by a line*. (**D**) Extradural implant. This corresponds to the middle electrode on Figure 4. Figure adapted from De Ridder et al. (7).