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## Pain Management Using 19-Electrode Z-Score LORETA Neurofeedback

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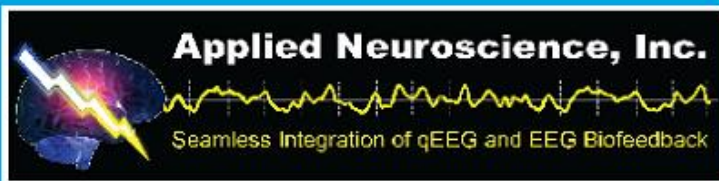
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## PAIN MANAGEMENT USING 19-ELECTRODE Z-SCORE LORETA NEUROFEEDBACK

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**Z-score LORETA neurofeedback (NFB) has been found in case reports to be an effective and promising form of neuromodulation, relieving many neuropsychiatric symptoms. LORETA imaging that identifies dysregulation in the structures of the brain that are involved in pain regulation has made it possible to design a targeted NFB therapy. This article describes the effective delivery of targeted LORETA NFB to treat chronic pain in four selected patients.**

### INTRODUCTION

Previous reports from our clinic have described LORETA Z-score NFB as highly effective in the treatment of many individuals with neuropsychiatric disorders (Koberda, 2012; Koberda, Moses, & Koberda, 2012; Koberda, Moses, Koberda, & Koberda, 2012). The International Association for the Study of Pain (n.d.) defined pain as “an unpleasant sensory and emotional experience arising from actual or potential tissue damage.” The neural substrates of pain perception have been intensively explored with neuroimaging techniques, such as fMRI and positron emission tomography (Hanakawa, 2012). Many imaging studies have consistently revealed a set of brain regions as substrates of pain perception (Moisset & Bouhassira, 2007; Moont, Crispel, Lev, Pud, & Yarnitsky, 2012). These regions include the anterior cingulate cortex, the insula, the parietal operculum including the second somatosensory cortex, and the thalamus, which are collectively called the pain matrix. Sawamoto and colleagues (2000) showed that the anterior cingulate cortex and parietal operculum/insula area are activated during a painful stimulus. On a QEEG, most pain conditions produce an elevation of beta power in a response to painful stimulation (Jensen, Hakimian, Sherlin, & Fregni, 2008;

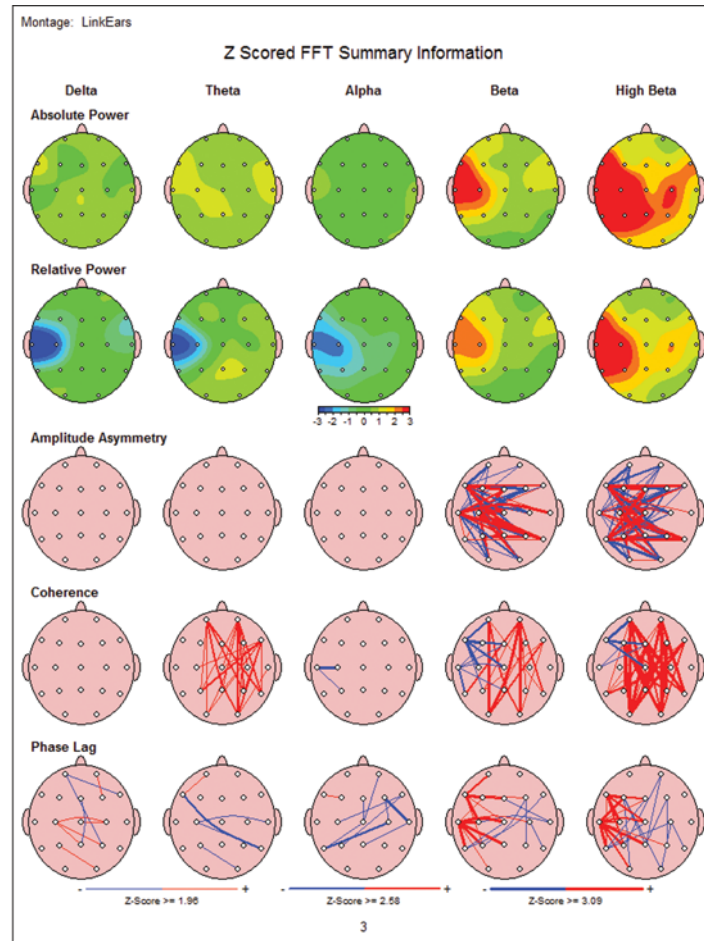
Stern, Jeanmonod, & Sarnthein, 2006; Walker, 2011).

Neurofeedback (NFB) is becoming an increasingly popular modality of therapy utilized for reduction of beta activity and potential pain amelioration (Walker, 2011). In addition to localized beta activity reduction by standard 1- or 2-electrode NFB, a more specific NFB method called Low Resolution Electromagnetic Tomography (LORETA) is capable of targeting specific pain matrix anatomical structures and may help in diminishing pain (Koberda et al., 2012; Thatcher, 2013). For example, the insular cortex and anterior cingulate have been identified as potential NFB target sites to improve pain control (Moisset & Bouhassira, 2007). An additional enhancement in NFB specificity is the use of continuous comparisons to an age-matched normative database resulting in “live” or real-time z scores (Thatcher, 1999, 2000). The recent introduction of 19-electrode Z-score LORETA NFB equipment has generated hopes for an improvement in NFB efficiency (Koberda et al., 2012; Thatcher, 2013).

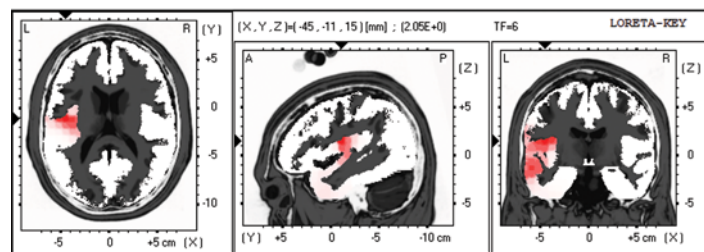
In Z-Score NFB, a real-time comparison to an age-matched population of healthy subjects simplifies protocol generation and allows clinicians to target modules and hubs that indicate dysregulation and instability in networks related to symptoms (Thatcher, 2013). Z-score

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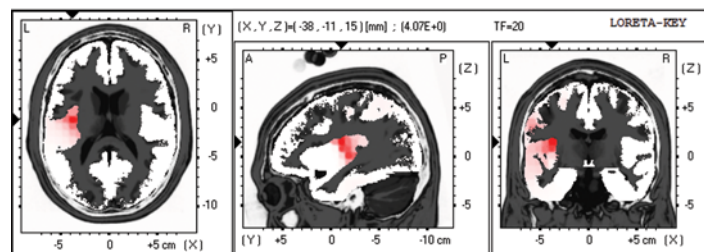
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(A)



(B)



(C)

**FIGURE 1.** (A) Case 1: Pretreatment QEEG. (B) Case 1: Pretreatment LORETA findings in the theta frequency band. (C) Case 1: Pretreatment LORETA findings in the beta frequency band. (Color figure available online.)

neurofeedback increases specificity in operant conditioning and provides a guide that links extreme z-score outliers to symptoms and then reinforces z-score shifts toward states of greater homeostasis and stability. The goal is increased efficiency of information processing in brain networks related to the patient's symptoms (Thatcher, 2013).

In this article, we report four different cases of chronic pain patients seen in our clinic that exhibited a good response to surface/LORETA 19-electrode Z-score NFB therapy.

## METHODOLOGY

This report describes the treatment of four selected pain cases from our neurological clinic using both 19-channel surface Z-score NFB and 19-channel LORETA Z-score NFB (NF1 and NF2; NeuroGuide program, Applied Neuroscience, Inc.). Protocol selection was based on the patient's symptoms using a "symptom checklist," as well as QEEG/LORETA characteristics. Patients with defined pain matrix LORETA dysregulations were frequently subject to specifically targeted LORETA NFB therapy if they were resistant to the "symptom checklist" treatment. Mostly, the anterior cingulate and insular cortex were targeted. The most frequently applied symptoms for programming from the "symptom checklist" were chronic pain, fibromyalgia, headache, anxiety, and depression. Neuropathic pain, musculoskeletal pain, and intrinsic connectivity network 4 were also used for the achieving the best results (Thatcher, 2010). Patient's sessions were frequently alternated between surface NFB and LORETA NFB, depending on the degree of elevated beta power or the degree of LORETA pain matrix dysregulation before a particular session.

A commercially available computerized neurocognitive testing battery was used for the initial assessment of two patients (NeuroTrax Corporation, Bellaire, TX). NeuroTrax Corporation cognitive testing is a computerized neuropsychological assessment where the patient is compared to age- and education-matched healthy controls; the mean score is 100 and the standard deviation is 15. QEEG analysis was completed using

commercially available NeuroGuide software (Applied Neuroscience, Inc.) and previously recorded 19-channel digital EEG.

Approximately 1 to 3 min of artifact-free, eyes-closed EEG segments were selected after previously recording EEG with the Deymed Truscan 32 (DEYMED Diagnostic, Payette, ID), and these EEG segments were then subjected to further QEEG analysis. NFB therapy consisted of 30-min sessions once or twice a week using auditory feedback.

## RESULTS

### Case 1

This case involves a 59-year-old physician who developed neuropathic pain in his groin after a surgical urologic procedure. The pain was reported to be "burning" in character and persisted all day. The patient was treated with multiple antipain medications, including narcotics. He was also treated with multiple nerve blocks with no significant improvement. Due to overlapping resistance to antidepressant medications, he was treated with electroconvulsive therapy, which subsequently may have contributed to his possible cognitive problems. Computerized neurocognitive testing was grossly unremarkable with only a mildly below-average memory score. Based on patient report, electroconvulsive therapy did not result in any mood improvement. This patient was referred by a local psychiatrist for NFB therapy to address pain and depression that was refractory to conventional medical treatment. His initial QEEG maps showed marked elevation of temporal beta power (Figure 1A). In this summary of QEEG data from comparisons to the NeuroGuide database, the color green represents areas where power deviations from the norm are in the range of 0 to 1 *SD* from the mean, light orange represents deviations in the range of 1 to 2 *SD*, and dark orange and red signify deviations over 2 *SD*.

The LORETA analyses showed an increase in the left insular cortex in theta (Figure 1B) and beta activity (Figure 1C).

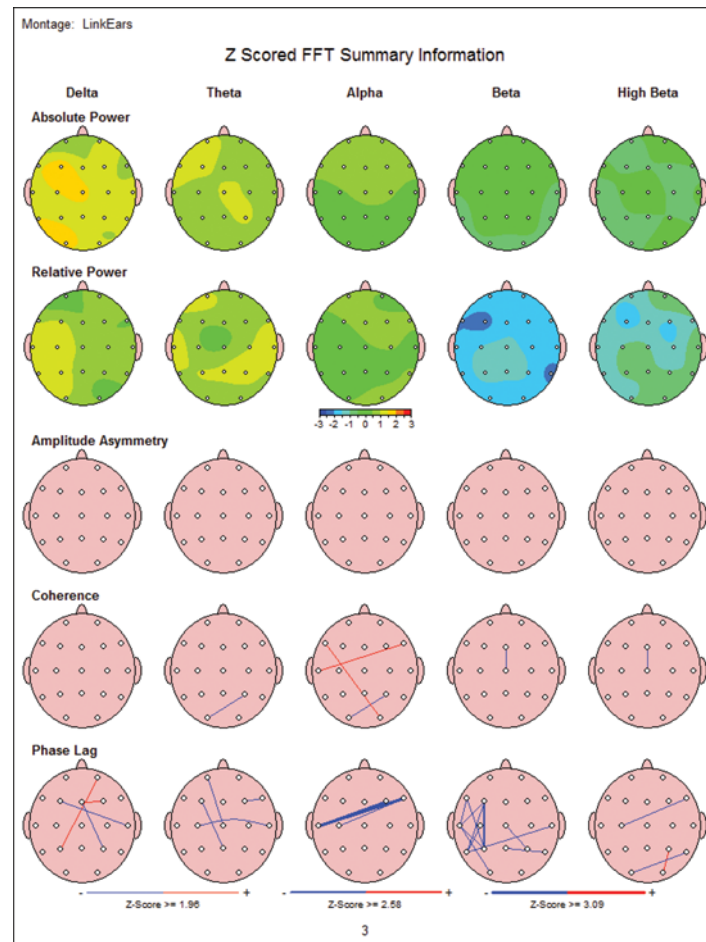
After just four sessions of Z-score LORETA NFB, the patient reported major improvement of his symptoms, with an 80% reduction of

neuropathic pain as well as marked improvement of his depression. Subsequent QEEG analysis showed a major reduction of temporal beta power, and LORETA demonstrated resolution of the left insular cortex theta and beta dysregulation (see Figures 2A and 2B). Unfortunately, due to reoccurring symptoms, this patient frequently comes back for more NFB sessions. He has completed 65 sessions so far.

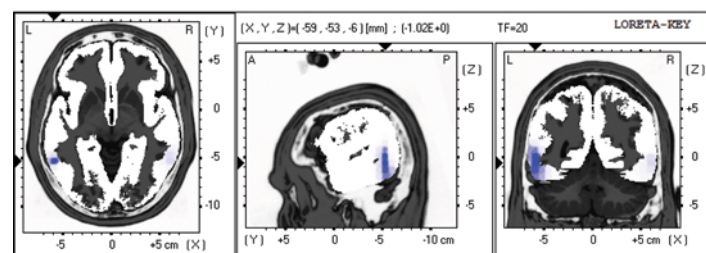
Overall, the patient reported around 50% improvement of both pain and depression.

### Case 2

A 58-year-old female also was referred by her psychiatrist and primary care physician for evaluation of chronic pain associated with depression. She reported a long-standing history of spinal pain (more than 20 years) with two



(A)



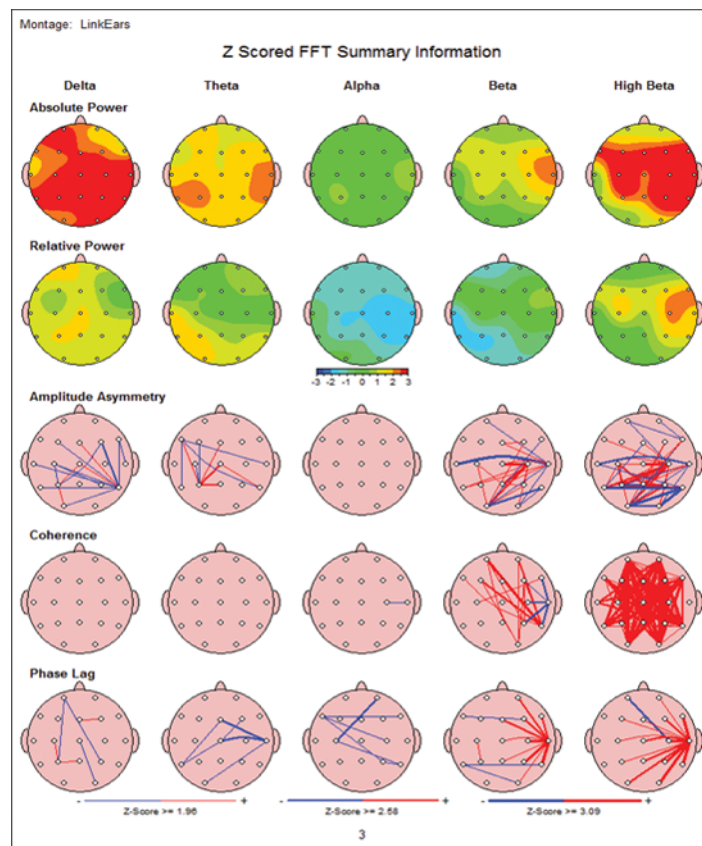
(B)

FIGURE 2. (A) Case 2: Posttreatment QEEG. (B) Case 1: Posttreatment LORETA analysis. (Color figure available online.)

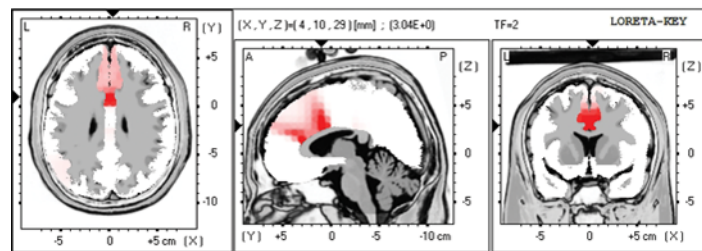
prior surgeries and multiple pain management visits. This patient has been on multiple medications including narcotics (MS Contin) and was treated with a spinal cord stimulator with little improvement in pain control. She reported associated headaches, depression, and memory problems, and she was taking two antidepressant medications. Before NFB initiation, QEEG analysis showed a major increase in frontal and central delta and beta power, as well an area of dysregulation in the anterior cingulate cortex on LORETA imaging (see Figures 3A

and 3B). Increased bilateral temporal theta power was noted, likely corresponding to her memory problems.

Computerized neurocognitive testing showed a low memory score of 53, which is more than 3 SD below the mean. After initiation of NFB, the patient reported marked improvement of all symptoms after just two sessions of Z-score LORETA NFB with continuous improvement in the following sessions. After LORETA NFB, the QEEG showed marked improvement in frontal delta and beta



(A)



(B)

FIGURE 3. (A) Case 2: Pretreatment QEEG. (B) Case 1: LORETA analysis. (Color figure available online.)

overexpression and resolution of cingulate cortex dysregulation (see Figures 4A and 4B). In addition, bilateral theta power overexpression improved with NFB therapy, which was associated with a subjective improvement of memory. She completed a total of 25 sessions. Unfortunately, the patient sustained another fall and injury to her spine and did not follow up with NFB thereafter due to her

inability to drive. No follow-up computerized neurocognitive testing was obtained.

### Case 3

A 59-year-old male developed shingles, leading to numbness and a burning sensation in both legs. He was subsequently diagnosed with postherpetic neuropathy and sensory-motor polyneuropathy. He was placed on multiple

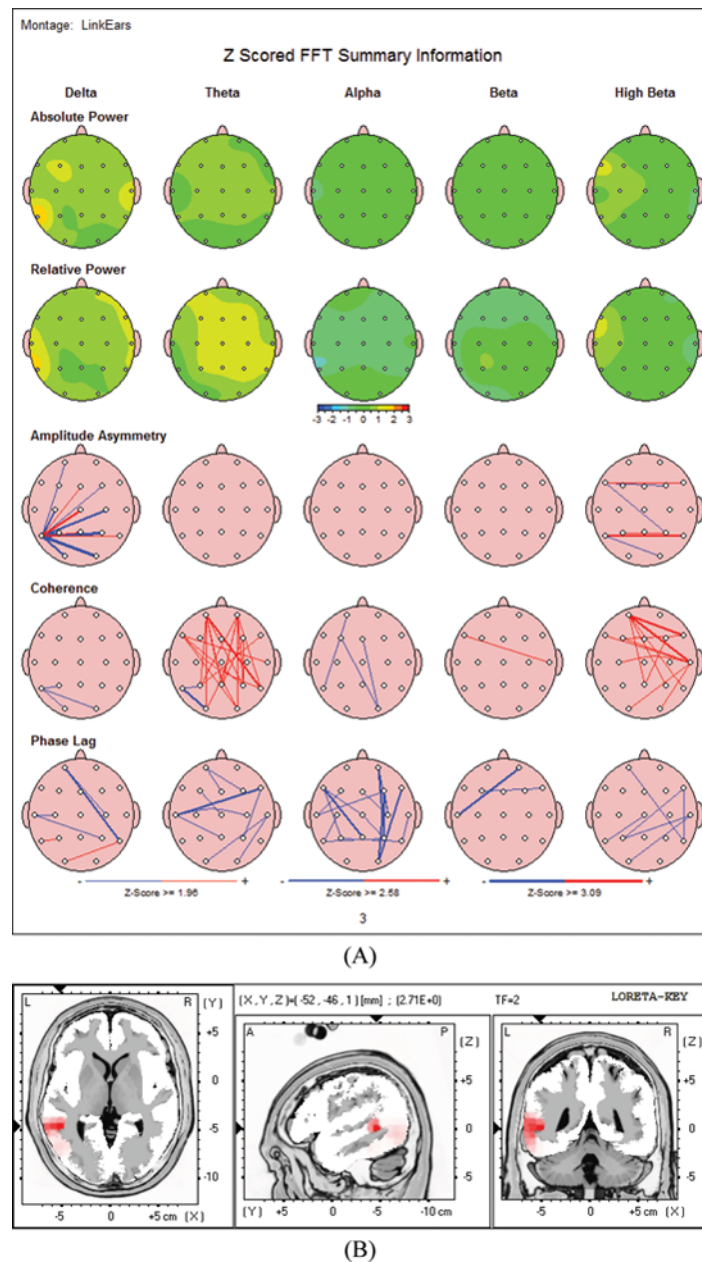


FIGURE 4. (A) Case 2: Posttreatment QEEG. (B) Case 2: Posttreatment LORETA analysis. (Color figure available online.)

medications including pregabalin (Lyrica) and nortriptyline. His QEEG before NFB showed markedly increased frontal delta power and bilateral temporal beta power (see Figure 5A). In addition, left insular dysregulation was identified on LORETA imaging (Figure 5B).

The patient reported mild improvement of pain after the fourth NFB Z-score LORETA session and major improvement after the fifth session. He reported that he could wear shoes again, whereas before NFB he was able to wear

only sandals due to neuropathic pain. The patient completed the initial 12 NFB sessions, after which he reported about a 60% reduction in pain from his baseline pain levels. Three months later, the patient came for additional NFB therapy, still reporting 50% less pain than at baseline. Subsequent NFB sessions have reduced pain by approximately 75% when compared to his pretreatment level of pain. A QEEG analysis completed during the period of pain improvement showed marked decrease

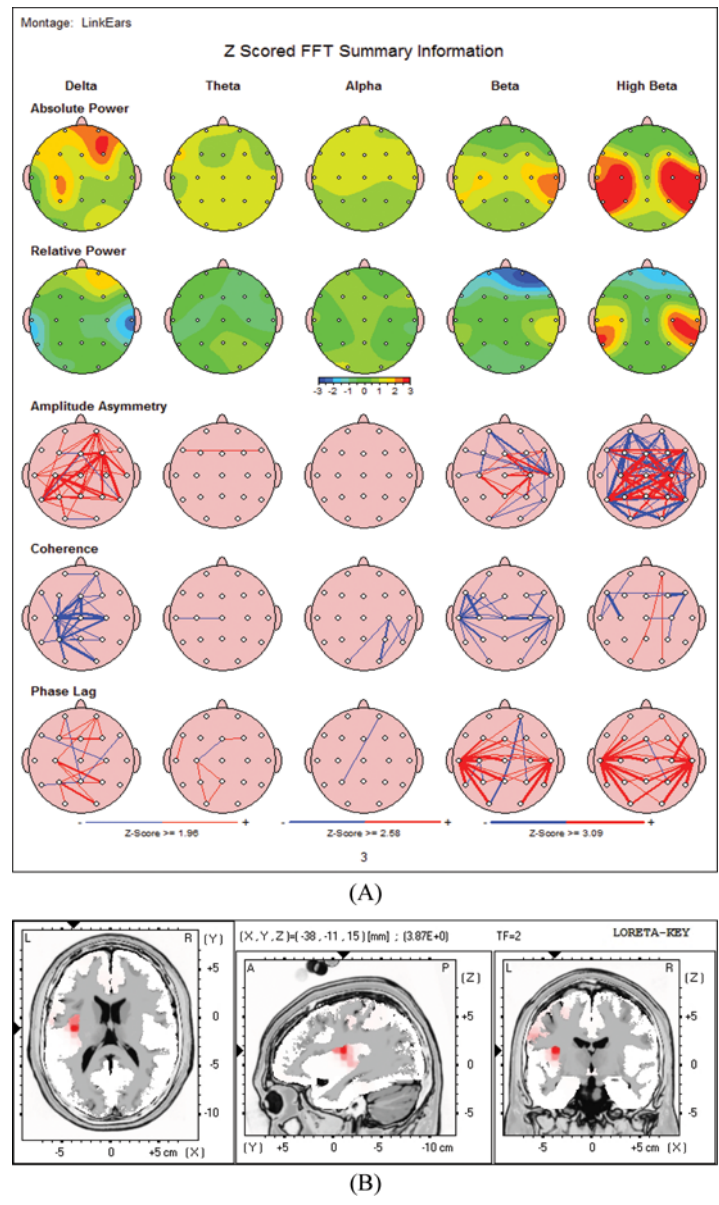


FIGURE 5. (A) Case 3: Pretreatment QEEG. (B) Case 2: Pretreatment LORETA analysis. (Color figure available online.)

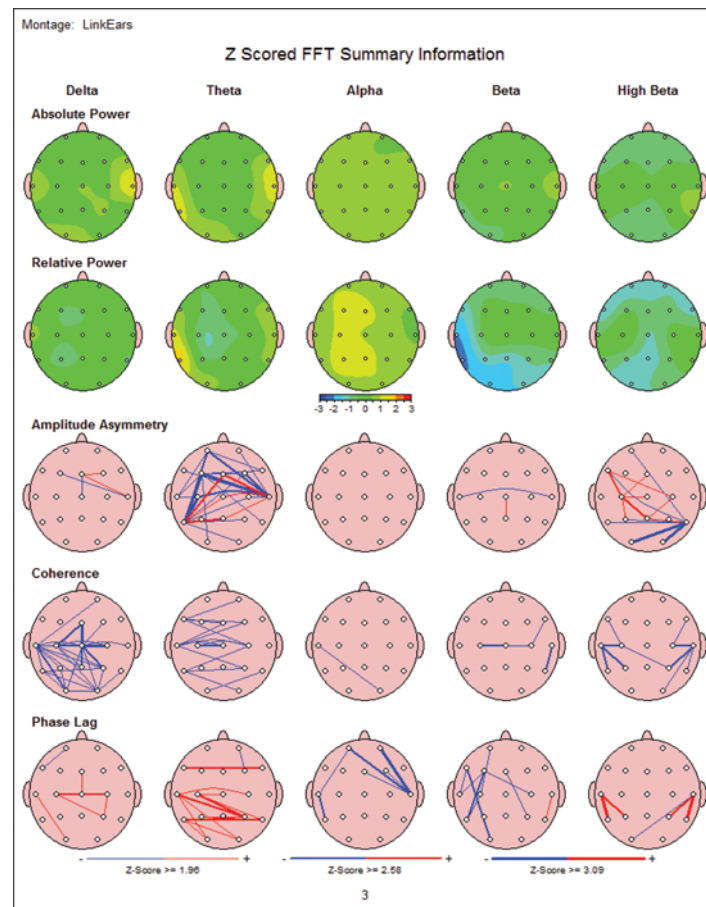


of delta and beta overexpression as well as resolution of insular dysregulation (see Figures 6A and 6B). The patient still continues to receive NFB, with total of 45 sessions completed so far.

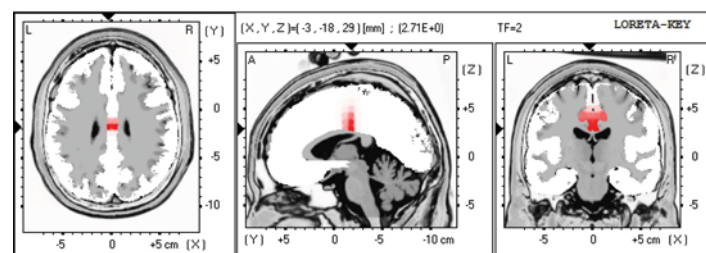
#### Case 4

This case involves a 46-year-old female with an 18-month history of trigeminal neuralgia on the right side of her face. The patient had been

taking pregabalin (Lyrica; 100 mg b.i.d.) for neuralgic pain and duloxetine (Cymbalta) for depression and pain. The patient reported that despite taking increasing doses of Lyrica (she previously was on 50 mg b.i.d.), the pain had not improved and she gained a lot of weight (her weight exceeded 300 lb). The patient was interested in trying an alternative modality of therapy, exhibiting interest in Z-score LORETA



(A)

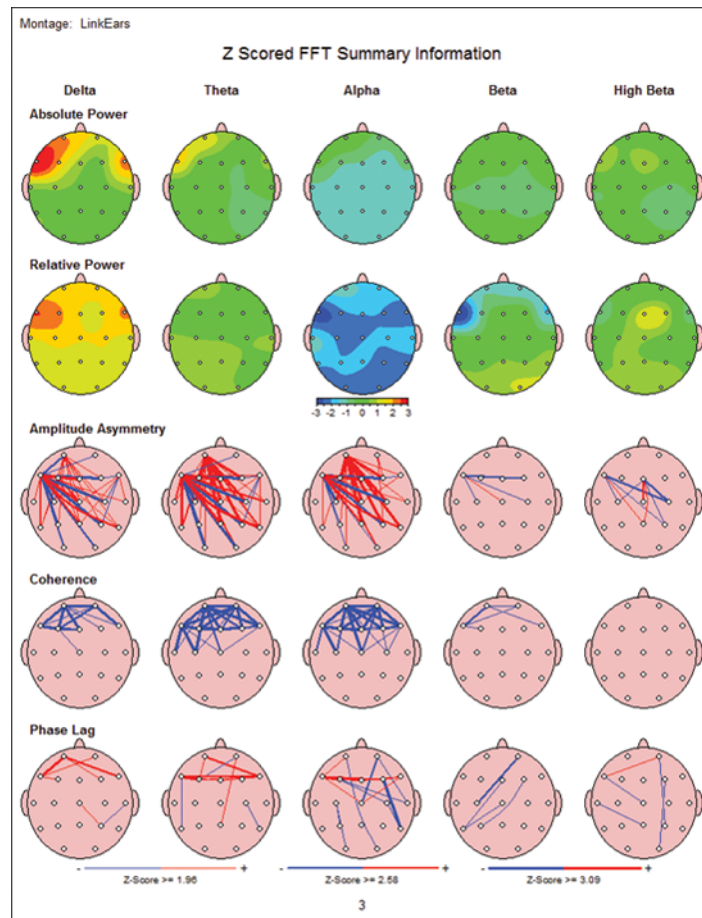


(B)

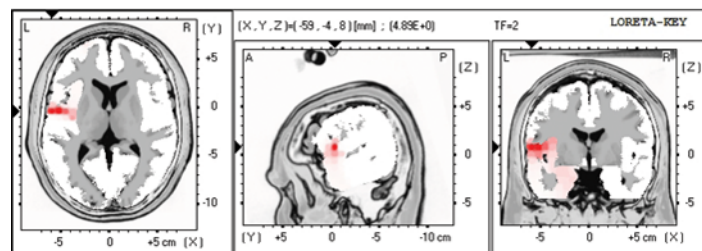
FIGURE 6. (A) Case 3: Posttreatment QEEG. (B) Case 3: Posttreatment LORETA analysis. (Color figure available online.)

NFB. Her initial QEEG showed elevation of fronto-temporal delta and theta power, as well as frontal beta power (see Figure 7A). In addition, LORETA analysis showed an area of dysregulation in the left insular cortex (see Figure 7B). She reported marked pain improvement after the first session of NFB, was able to reduce the dose of Lyrica after the second

session, and discontinued Lyrica completely after the fourth session. The patient completed 10 sessions of NFB and has been in remission for more than 4 months. The QEEG, completed after total pain resolution, showed an improvement in frontal delta, theta, and beta power, as well as a resolution of insular cortex dysregulation (see Figures 8A and 8B).



(A)



(B)

FIGURE 7. (A) Case 4: Pretreatment QEEG. (B) Case 4: Pretreatment LORETA analysis. (Color figure available online.)

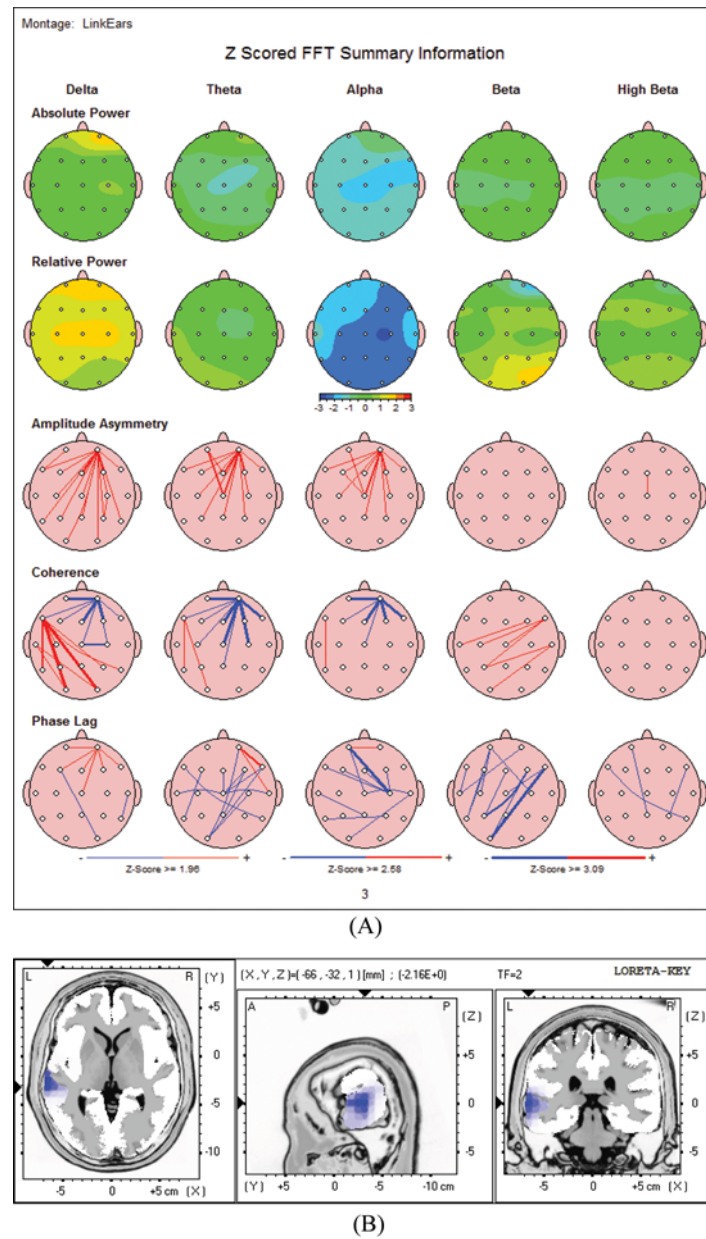


FIGURE 8. (A) Case 4: Posttreatment QEEG. (B) Case 4: Posttreatment LORETA findings. (Color figure available online.)

## DISCUSSION

The discussed cases indicate an encouraging potential for chronic pain reduction by direct cortical regulation using Z-score LORETA NFB. Regardless of the origin of the injury evoking the neuropathic pain (e.g., trigeminal or postherpetic neuralgia, peripheral neuropathy or chronic spinal pain), some similar findings in cortical dysregulation were identified. Very similar therapeutic approaches were used to ameliorate the

symptoms of the aforementioned pain disorders. Previously, other researchers described the efficiency of NFB in reducing pain due to headaches, fibromyalgia, and other pain syndromes (Caro & Winter, 2011; Kayiran, Dursun, Ermutlu, Dursun, & Karamürsel, 2007; Kayiran, Dursun, Dursun, Ermutlu, & Karamürsel, 2010; Stokes & Lappin, 2010; Walker, 2011). Stokes reported that 70% of migraine patients experienced at least a 50% reduction in pain. An even

better response was reported by Walker (2011), who found that 54% of patients with recurrent migraines experienced complete headache cessation after completion of NFB, with additional 39% of patients experiencing a greater than 50% reduction in migraine frequency. NFB was also reported to effectively treat burning mouth syndrome, complex regional pain syndrome, and trigeminal neuralgia (Jensen, Greirson, Tracy-Smith, Bacigalupi, & Othmer, 2007; Kenchadze, Iverieli, Okribelashvili, Geladze, & Khachapuridze, 2011; Sime, 2004). Ibric and Dragomirescu (2009) found that of 74 patients who had been unsuccessfully treated for pain from chronic disease, injury, surgery, or other sources, 68 (92%) reported a clinically significant improvement in their pain following at least 19 sessions of neurofeedback. However, prior reports usually employed one- or two-channel electrode neurofeedback systems that were frequently aimed at reducing excessive cortical beta activity. Penfield's sensory homunculus-cortical areas were also described as potential initial NFB target sites (Ibric & Dragomirescu, 2009).

Recently, Prinsloo et al. (2013) proposed a brain-computer interface as a learning paradigm to augment neuroplasticity for cancer pain management. By harnessing quantified electrical neurophysiological patterns and the brain's neuroplastic ability to learn and change, these researchers used neurofeedback to affect many factors, particularly those related to mental and physical pain, which are particularly problematic for oncology patients.

The case reports presented here illustrate marked improvement in pain control after a relatively short course of 19-electrode Z-score LORETA NFB treatments, although many of our patients have required an extended number of NFB sessions. A larger study may be needed to explore the full potential of 19-electrode, Z-score NFB for pain modulation and other medical conditions.

## CONCLUSIONS

Z-score LORETA neurofeedback represents a potentially significant advancement in the field of EEG biofeedback allowing direct targeting of

deeper dysregulated brain structures through the application of LORETA imaging. The pain cases described in this paper indicate that Z-score LORETA NFB is another treatment modality offering hope for chronic pain management.

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