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BRIEF COMMUNICATION

Exploratory Study of Low Resolution Electromagnetic Tomography (LORETA) Real-Time Z-Score Feedback in the Treatment of Pain in Patients with Head and Neck Cancer

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Abstract

Acute pain from mucositis in patients with head and neck cancer (HNC) undergoing radiation therapy (RT) is common, and may not respond well to narcotics. We used low resolution electromagnetic tomography z-score neurofeedback (LFBz) to investigate whether patients could modify brain wave activity associated with acute pain and whether this would reduce the experience of pain. HNC patients scheduled for RT had baseline pre-pain onset measures (EEG and numeric rating scale) collected before RT and then at pain onset before using analgesics, after each LFBz session and at the end of RT. Up to six sessions of LFBz training were offered over the remaining RT. Up to six 20-min sessions of LFBz were offered over the remaining RT. Data were collected before and after each LFBz session and at the end of RT. Seventeen patients recruited; fourteen were treated and reported decreased pain perception. LFBz allowed patients to modify their brain activity in pre-designated areas of the pain matrix toward the direction of their baseline, pre-pain condition (including Brodmann areas (BAs) 3, 4, 5, 13, 24, and 33). LFBz can modify brain regions relevant for pain and these changes were associated with self-reported decreases in pain perception.

Keywords EEG · Neurofeedback · LORETA · Pain · Cancer

Introduction

At least 80% of patients undergoing radiation therapy (RT) for head and neck cancer (HNC), with or without chemotherapy, experience acute mucositis. Mucositis may cause substantial pain, interferes with a patient's ability to aliment orally leading to nutritional challenges and weight loss, and may lead to interruptions in planned cancer therapy, all of which may in turn affect treatment outcomes (Rosenthal 2007). Opiod analgesics do not control mucositis pain well (Ling and Larsson 2011), and other medical treatment options are limited (Clarkson et al. 2010).

The ability for humans to control their pain psychophysically has been studied extensively, and methods such as distraction (Valet et al. 2004) and conditioned pain modulation (Moont et al. 2010) have been associated with reduced subjective pain ratings and differences in neural activation (Piche et al. 2009). Electroencephalogram (EEG) neurofeedback, a brain-computer-interface, with auditory and visual rewards given for "learned" modification of EEG activity over a particular region of interest (ROI), provides real-time information to the participant about their own brain function

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and can be considered a means of gaining control over physiological processes, including the experience of pain (Congedo et al. 2004).

Our aims were: (1) determine whether it was feasible to provide this therapy in a head and neck radiation setting; (2) design an EEG neurofeedback training protocol using low resolution electromagnetic tomographic neurofeedback using a z-score approach (LFBz), and investigate whether patients could modify their brain function in targeted areas; (3) examine change in pain report; and (4) determine whether there was an association between subjective pain reports and EEG-assessed brain changes.

Results

Patients

Of the 17 patients recruited, 11 were male, 13 were Caucasian, average age of 56 years. Average worst pain at baseline was 0.9; worst pain reported before LFBz (T2) was 5.6. Each patient received 6 MV of radiation energy and 3 patients also received 12–16 MV.

Feasibility

Two patients withdrew due to lack of interest, and one did not experience pain. Fourteen patients completed at least one LFBz session, 12 completed at least three sessions, and five completed six sessions, fulfilling the feasibility criteria.

LFBz

LFBz1 resulted in a shift in current source density (CSD) from the "painful" EEG state towards the "baseline" state in every region that was targeted except BA 32, which continued to increase in CSD (Fig. 1). Group means of CSD shifts were also in the expected direction in every region that was not specifically targeted by LFBz, but which is involved in pain processing (Fig. 1).

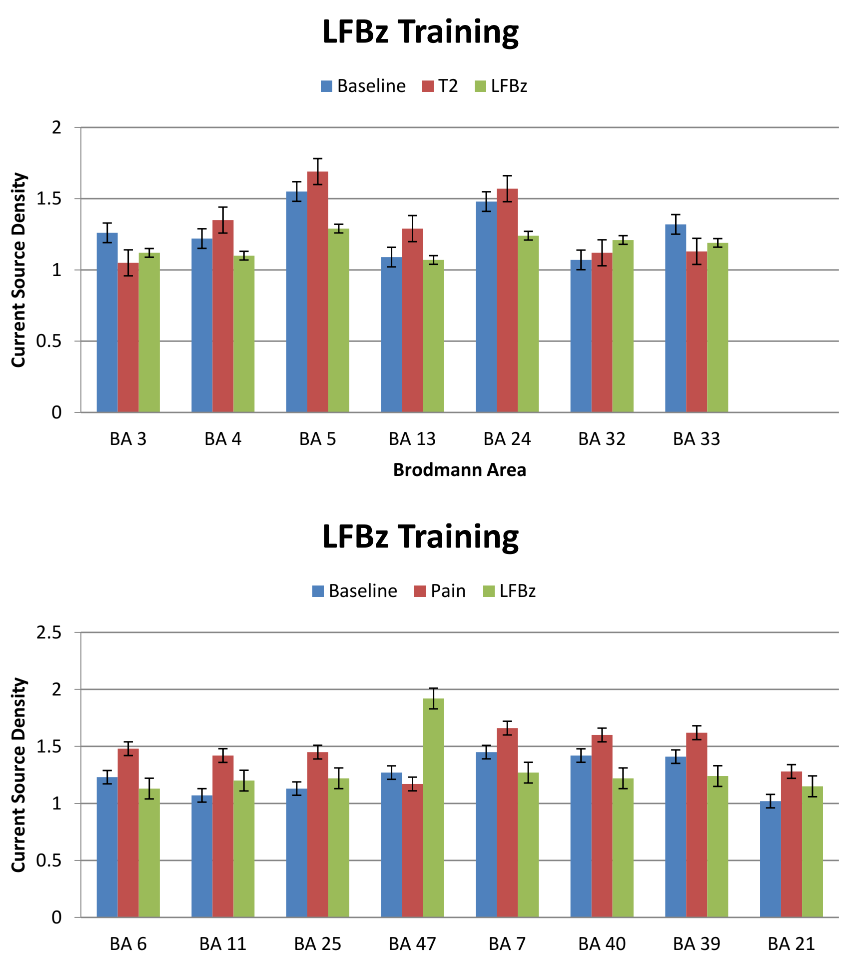

Fig. 1 Top: EEG CSD at baseline, pain onset, and post-neurofeedback training by Brodmann area. Bottom: EEG CSD at the same time-points by areas *not* specifically targeted by LFBz, T2 = pain onset. Error bars represent standard error (SE)

Subjective Report of Pain

For patients who changed after either session 1 or 3, but not both, there was an average drop in pain rating of 2.11 points (SD = 1.54, $p < .03$) after session 1, and an average decrease of 4 points, (SD = 0) after session 3.

EEG-Assessed Brain Changes and Pain Current Source Density

Regression results for LFBz1 show that of seven regions targeted for feedback, two of the regions produced an adjusted R^2 of 1.00 $F(1,3) = 3575$, $p = .012$. At step 1 of the analysis, BA 24 was entered into the regression and was significantly related to pain, $B = -8.047$, $t(4) = -6.36$, $p = .024$. The multiple correlation co-efficient at BA 24 was 0.929, indicating approximately 92.9% of the variance in the pain scores could be accounted for by BA 24. BA 33 entered into the equation at step 2 and was significantly related to pain, $B = 1.124$, $t(4) = 18.34$, $p = .035$. Pain was predicted by lower levels of CSD in BA 24 and to a lesser extent by higher levels of CSD in BA 33.

Alpha rhythms, thought to coordinate brain communication, showed the most activity in our analyses. Alpha decreased in key regions of pain processing (somatosensory and premotor areas) at pain onset but increased normalized with LFBz (particularly in the parietal and occipital regions) which was associated with a decrease in pain report. In other words, alpha activity seems necessary for patients to process pain, even if the activity exceeds the range considered “normal” ($z = 0$). Along the somatosensory cortex, we found increased alpha at T2 that diminished with LFBz training. Because attention and emotion influence pain differently, increased alpha activity in the pain condition specifically along this region could be the result of shifting attention toward the location of the pain in order to, for example, determine intensity. Additionally, a simultaneous increase in alpha in key areas of cognitive processing (BAs 6 and 10) could be a result of task demand secondary to gaming aspect of neurofeedback.

Discussion

This is the first study to observe brain activity reflecting subjective perception of pain during radiation therapy and as patients undergo a brain-computer interface to modify their experience of pain. LFBz resulted in a shift in CSD from the “painful” EEG state towards the pre-pain “baseline” state in every region except BA 32. Considering that neurofeedback is an active task requiring detection of error, reward anticipation, and monitoring of emotional or somatic states, it is not surprising that CSD increased in BA 32 in both the pain condition and after neurofeedback, as resources are allocated to perform tasks required in the session. BA 32 is the dorsal anterior cingulate and is intricately involved in pain processing. It is also probable that with increasing pain there is increasing CSD within BA 32.

We demonstrated that patients can voluntarily shift their brainwaves in pre-designated regions and that those shifts are associated with a shift in symptom report. To keep up with demand for non-addictive ways to moderate pain, clinicians may consider techniques that capitalize on innate healing abilities, both as stand-alone and adjunct therapies.

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Compliance with Ethical Standards

Conflict of interest The authors have no financial interest and nothing to disclose.

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