

# NEUROTHERAPY AS A CATALYST IN THE TREATMENT OF FATIGUE IN BREAST CANCER SURVIVORSHIP

David V. Nelson, PhD<sup>1#</sup> and Mary Lee Esty, PhD<sup>2</sup>

Pharmacologic and non-pharmacologic treatments for cancer-related fatigue (CRF) have produced mixed and often disappointing results. Treatment using the Flexyx Neurotherapy System (FNS), a novel variant of electroencephalograph biofeedback that involves minutely pulsed electromagnetic (EM) stimulation of brainwave functioning, was explored to determine utility for alleviating CRF in a 45-year-old woman who had debilitating fatigue with onset during chemotherapy for stage II infiltrating right breast cancer, who had been free of signs of disease for over five years, and who had been struggling to increase her activity level and engage in regular exercise without benefit. FNS was administered in 10 weekly sessions.

Alleviation of fatigue and other potentially interrelated symptoms (cognitive clouding, sleep disturbance, pain, and negative mood/emotions) and overall greater activity level was sustained at six-month follow-up. Very low energy EM brainwave stimulation therapies such as FNS may contribute to an enlivening of drive to engage in greater energized activity.

**Keywords:** fatigue, exercise, breast cancer, neurotherapy, neurofeedback, EEG biofeedback

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## INTRODUCTION

Breast cancer is the most common cancer in women worldwide.<sup>1,2</sup> A host of distressing symptoms often accompanies the experience of breast cancer and its treatment.<sup>3-5</sup> Among these, fatigue is the most prevalent, although it often occurs in clusters with other symptoms (e.g., cognitive dysfunction, depression, and sleep disturbance).<sup>6-9</sup> It is also frequently the most persistent and debilitating.<sup>10</sup>

The treatment of cancer-related fatigue (CRF) has been marked by only modest progress.<sup>7,8,10</sup> Results from pharmacological clinical trials have been mixed and often disappointing.<sup>11,12</sup> Similarly, non-pharmacological treatments have not garnered universal support, although current evidence suggests aerobic exercise may be beneficial both during and after cancer treatment.<sup>10,13-15</sup> However, most studies focus on one circumscribed intervention and ignore the potential interaction of multiple contributing factors and possible need to combine and/or sequence multiple treatments to maximize effectiveness.<sup>6</sup> This became apparent as we set out to investigate the potential of neurotherapy for the treatment of CRF.

Neurotherapy, sometimes also known as electroencephalograph (EEG) biofeedback or neurofeedback, involves changing brainwave patterns to change symptoms associated with central nervous system dysfunction. Typically, EEG biofeedback is performed within an operant conditioning framework in which subjects acquire skills to change EEG activity by learning voluntary control over the production/inhibition of brainwave patterns.<sup>16</sup> Previous work<sup>17,18</sup> applying EEG stimulation treatments for alleviation of fibromyalgia symptoms, which include fatigue as well as widespread pain, cognitive, mood, and sleep disturbances, suggested the possibility of adapting this approach for CRF. As a novel variant of EEG biofeedback, rather than relying on operant principles, the Flexyx Neurotherapy System (FNS)<sup>19</sup> involves off-setting stimulation of brainwave activity by means of an external energy source, specifically, the conduction of electromagnetic energy (EM) stimulation via the connecting EEG cables.

This article reports on the effects of FNS in the treatment of one patient with moderately severe CRF. In the course of treatment the patient became more enlivened and also began to engage in a regular exercise program. The evolution of this process and implications for multidimensional intervention and research are discussed.

## PATIENT

The patient gave written informed consent prior to study with institutional review board approval. She was a 45-year-old, married, Caucasian woman who had been diagnosed six years and one month prior with stage II infiltrating cancer involving the right breast. She underwent bilateral mastectomy with

1 Department of Psychology and Philosophy, Sam Houston State University, Box 2447, Huntsville, TX 77341

2 Brain Wellness and Biofeedback Center of Washington, Bethesda, MD

# Corresponding author.

e-mail: nelsondv@shsu.edu; nelsondvshsu@gmail.com

tissue flap reconstruction and five months of chemotherapy. Her last chemotherapy treatment had been five and half years before beginning participation in neurotherapy. She was presently free of signs of breast cancer disease. Her medical situation otherwise was stable. She reported experiencing fatigue on a “constant everyday” basis and being quite “worried about what is going to happen.” She clearly linked the onset of her debilitating fatigue to chemotherapy. A year after diagnosis she experienced a significant period of depression because she “didn’t know what was happening.” This depression was less severe at the time of presentation for neurotherapy. However, she had become generally more irritable. The quality of her sleep was poor. She also experienced cognitive interferences, including forgetfulness. She reported a good relationship with her husband. Prior to diagnosis of breast cancer she had been “feeling really good” and doing “really well” at her job. She had remained employed while struggling to cope with fatigue since undergoing chemotherapy. She was attempting to engage in regular exercise with the encouragement of her husband, but was struggling to follow through and experiencing the same persistent level of fatigue.

## MATERIALS AND METHODS

### FNS Assessment and Treatment

FNS consists of a laptop computer and compact 2 Channel EEG (C-2) module with on-board feedback generating power, utilizing proprietary software to link the digital brainwave recording module through the computer to set parameters for the C-2 to emit pulsed EM stimulation. The system returns a signal to the subject via conduction from the C-2 module, varying as a function of the detectable peak EEG frequency (but offset from it), thereby permitting strategic distortion of the EEG.

**FNS assessment.** Initial recording of EEG activity without any stimulation was conducted with serial (not simultaneous) sampling done at each of 19 scalp electrode sites, based on the International 10/20 system, in a recommended<sup>19</sup> predetermined order. This did not allow for a quantitative EEG map, but did produce a rank ordering of sites according to total amplitude at each site. This sequence was utilized as the order in which to target treatment, beginning with the site with the lowest amplitude and continuing through to the highest. After completion of the entire sequence, it was begun again in the same order. During both assessment and treatment, the patient sat with eyes closed and engaged in no specific activity. A referential monopolar montage was used, with initial impedances kept below 5 k $\Omega$ .

**FNS treatment.** At a time pre-set in the software the dominant (peak) EEG frequency had added +20 Hz of EM stimulation for a maximum one-second burst of alternating on/off pulsing. For example, if the momentary dominant frequency was 10 Hz, the EM stimulation frequency for a maximum of one second pulsing was 30 Hz. Hence, the dose of EM stimulation was directly dependent on the momentary peak frequency in the EEG at the time the system was pre-set

to administer the stimulation. The intent was to capitalize on high frequency stimulation, given that higher EEG frequencies are generally associated with lower amplitudes, thereby being more likely to result in gentler low energy stimulation.

The first intervention session included one second of stimulation for each of three sites. The number of sites stimulated in each session then varied from two to three depending on the effects and any side effects, proceeding through the sequence of sites determined by the initial assessment. If bothersome discomfort within or between sessions was reported, the therapist had the option to vary the number of sites, including holding off entirely.

### Measures

**Revised Piper Fatigue Scale (RPFS).**<sup>20</sup> The 22-item RPFS yields a total and four subscale scores, which assess the following dimensions—behavioral/severity, affective meaning, sensory, and cognitive/mood. Higher scores reflect greater difficulty.

**Center for Epidemiologic Studies-Depression Scale (CES-D).**<sup>21</sup> The 20-item CES-D measures depression severity. Higher scores indicate presence of more symptomatology; a score  $\geq 16$  signifies the likelihood of clinical depression.

**Individual Symptom and Overall Activity Rating Scales.** At the beginning of each active treatment session, the patient completed eight separate current symptom and overall activity level 0–10 numerical rating scales with appropriate anchors, including fatigue (e.g., 0 = no fatigue at all, 10 = worst imaginable fatigue), cognitive clouding, overall body pain, quality of sleep, anxiety, depression, irritability/anger, and overall activity. For all, higher scores indicate greater difficulty. She completed the RPFS and CES-D at pre-treatment and immediate post-treatment and six-month follow-up.

## RESULTS

Following completion of the initial non-stimulation EEG assessment the patient subsequently attended 10 weekly sessions in which stimulation was administered and an 11th session one month afterwards. The first three sessions, during each of which three sites were treated, proceeded unremarkably. At Session 4 she reported a mix of positive changes (“I just want to go ... do things ... don’t want to stop ... more interested in what’s happening”) and some unusual symptoms. FNS was the “only thing different” she could identify to attribute these changes. However, she also reported brief sharp pains on the right side of her head that she likened to a “pin poking in a tender spot,” and always at the same spot. These were not activity or position dependent, and were highly variable in time of occurrence. She thought they were perhaps part of “things coming alive again.” Since she was not overly bothered by them, and given the experience of one of the investigators with similar rare reports of unusual head pain sensations during FNS treatment, a decision was made to continue with stimulation, but to cut back to treat only two sites. Thereafter, she continued to report a sense of wanting to be active. By Session 6 the brief pricking sensations subsided completely. She had continued with a heightened drive to “do things” to the extent of “over-doing.” Treatment of three

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