Neuromodulation of emotion using functional electrical stimulation applied to facial muscles

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Abstract

Background and Objective: Major depressive disorder (MDD) is a common condition, for which available pharmaceutical treatments are not always effective and can have side-effects. Therefore, alternative and/or complementary MDD treatments are needed. Research on facial expressions has shown that facial movements can induce the corresponding emotions, particularly when specific attention is paid to voluntarily activating muscles that are typically only activated involuntarily while expressing emotions. We hypothesized that functional electrical stimulation (FES) applied to facial muscles may enhance this effect, due to its ability to modulate central nervous system plasticity. Thus, applying FES to the facial muscles associated with smiling (including the "Duchenne marker") may increase the activity of subcortical nuclei related to positive emotions and counteract symptoms of depression.

Methods: Twelve able-bodied subjects received FES and were compared to a group of 12 control subjects. Both groups underwent the same experimental procedures involving a cognitive task, and a deception was used such that subjects were unaware that the objective was to modulate mood. Assessments with the Positive and Negative Affect Schedule – Expanded Form (PANAS-X) were administered before and after the experiment.

Results: No significant between group differences were found in the change scores for our primary outcomes, the PANAS-X item “happy” and aggregate scores “Joviality” and “Positive Affect”. Significant differences were, however, detected for secondary outcomes “determined”, “daring”, “scared” and “concentrating”.

Conclusions: These results suggest that modulating emotion using FES may be possible, but is difficult to target accurately. Further work is warranted to explore FES applications to MDD.

Keywords: Functional electrical stimulation, depression, emotion, affect, facial muscles, Duchenne marker.

Introduction

Major depressive disorder (MDD) is a condition that affects an alarmingly high number of people at some point during their lives, with a prevalence varying between 3% and 16%, depending on the country [1]. Although a number of pharmaceutical interventions are available, some MDD sufferers are partially or completely resistant to these treatments, and it is estimated that up to 50% of patients do not achieve full remission [2]. In addition, anti-depressant drugs have a number of side-effects, including nausea, insomnia and weight gain. Alternative and/or complementary forms of treatment for MDD are therefore needed.

A substantial body of research has been devoted to the study of facial movements as they relate to particular emotions. Facial expressions for basic emotions (happiness, fear, surprise, etc.) have been found to be well-defined and universal across cultures [3]. Certain facial muscle movements can be easily controlled voluntarily, while others occur primarily during "genuine" emotions. For example, voluntary smiles (e.g. smiles for social purposes, without any particular emotional involvement) usually consist only of the upward curving of the lips, whereas spontaneous smiles due to positive emotions also involve the eyes. The specific pattern of eye movement associated with genuine smiling is known as the Duchenne marker, and is characterized by a raising of the cheeks and the appearance of crows-feet wrinkles next to the eyes [4, 5]. These two types of smiles are mediated by different neural pathways. Voluntary smiles are initiated in the motor cortex and routed via the pyramidal motor system. In contrast, involuntary smiles arise mainly from subcortical nuclei and are routed via the extrapyramidal motor system: clinical evidence from Parkinson's patients displaying the "masked face" syndrome suggests that the basal ganglia is involved in the production of emotional expression [6], while evidence from patients with brain lesions exhibiting emotional facial paresis suggests the possible involvement of various regions of the basal ganglia and thalamus [7]; neuroimaging studies have also substantiated the involvement of the basal ganglia [8]. A related observation has been that voluntarily producing and holding an expression can induce the corresponding emotion [9, 10]. This effect has been linked to afferent facial feedback received as a result of the facial movements [11, 12]. The induction of emotion is more effective when a person pays specific attention to voluntarily activating muscles that are usually only used involuntarily (e.g., the Duchenne marker) [13, 14], possibly because the voluntary facial expression is then closer to a genuine one.

Functional electrical stimulation (FES) is a technique in which muscles are electrically stimulated, causing them to contract. FES has been shown to have therapeutic applications: artificially stimulating paralyzed or weakened muscles after spinal cord injury or stroke while the individual attempts to voluntarily contract those same muscles can lead to significant functional improvements [15, 16]. Recent studies have shown that this process is accompanied by plasticity in the central nervous system (CNS), with regions affected by the injury and associated with the stimulated muscles displaying increased activity [17, 18]. We therefore hypothesized that applying FES to the facial muscles associated with smiling (including the Duchenne marker) may increase the activity of the CNS regions related to positive emotions (e.g. in the basal ganglia). This hypothesis is based on the existence of a close neural connection between these muscles and brain regions, as evidenced by the importance of the extrapyramidal pathway in the expression of genuine emotion, combined with the greater effectiveness

of the Duchenne marker for artificially inducing emotion using voluntary movements. In other words, we hypothesized that this neural connection will provide a pathway through which FES can be used to modulate mood. If this hypothesis proves correct, FES applied to facial muscles may lead to new methods to combat the symptoms of MDD. Here, we report the results of experiments aiming to validate our hypothesis in able-bodied subjects in order to pave the way for future clinical studies.

Methods

Experimental design

We investigated the ability of a single session of FES to modulate positive aspects of mood and emotion. An important component of the effectiveness of FES in other applications appears to be that the subject voluntary attempt to move the target muscles at the same time as they are being stimulated. This phenomenon is hypothesized to be due to Hebbian plasticity, occurring at the synapses where the efferent voluntary commands meet the afferent antidromic action potentials produced by the FES [19]. The subjects receiving FES in our study were therefore instructed to attempt to voluntary activate the stimulated muscles (see stimulation details below). In order to discriminate between the effects of the FES and the effects of voluntary holding a facial expression, a control group was used, which performed the same experimental procedures as the FES group but without any stimulation.

Our study involved measures of affect through standardized questionnaires (see outcomes below), and these reports were likely to be skewed if subjects were aware of the true purpose of the experiment. For that reason, a deception was used in our experimental design. A mock experiment was designed that allowed us to collect the data required to validate our hypothesis, while presenting the subjects with a different rationale for the procedures. Subjects were told that the goal of the experiment was to investigate applications of FES in Bell's palsy (a form of facial paralysis). FES has previously been applied in this context [20, 21]. Although some applications of FES involve stimulating areas where sensation is impaired (e.g., below the level of spinal cord injury), this is usually not the case in Bell's palsy. We therefore told subjects that we were investigating whether distraction related to the sensations caused by FES during facial stimulation (mild to moderate pain) has any impact on cognitive function. Assessments related to affect were justified by citing links between emotional state and performance in cognitive tests. This study was approved by the Research Ethics Board of the Toronto Rehabilitation Institute, and all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed.

Experimental procedures

At the beginning of the session, subjects were given specific instructions on how to voluntarily perform the Duchenne smile ("raise your cheeks, then let your lip corners come up" [9]), and were allowed to practice with guidance from the investigator. Subjects then sat in front of a computer screen, and were required to perform 3 different tasks in the alternating order below. Each task lasted 30 seconds and the 2-minute block was repeated 25 times in the course of a one-hour session, with short breaks after 10 and 20 blocks. The cognitive component of the tasks was implemented using a visual n-back test, a common method to produce a cognitive load for experimental purposes. In this test, a sequence of symbols is presented, and the subject is required to press a button when a symbol appears that had previously appeared exactly n steps before in the sequence [22, 23]. In this study, n was set to 0, 1 or 2 in alternating blocks.

For the **intervention group**, the tasks were as follows:

1) Produce a continuous voluntary smile while receiving FES (no cognitive task).
2) Retain a neutral expression while performing the cognitive task.
3) Produce a continuous voluntary smile while performing the cognitive task and receiving FES.
4) Retain a neutral expression while performing the cognitive task.

Since 2 of the 4 tasks involve FES, the intervention group subjects received a total of 25 minutes of FES during the course of the 50-minute experiment. The goal of Task 1 (voluntary smile with no cognitive task) was to ensure that the FES group spent at least a portion of the session focusing entirely on assuming the correct expression, without the distraction of the cognitive test. To justify this procedure in the context of our deception (cognitive impact of FES for facial palsy), subjects were told that the goal was to give them breaks from the cognitive test while still replicating a clinically realistic amount of FES delivery. The neutral expression task was repeated to provide regular breaks from the FES and to ensure that the subjects remained comfortable.

For the **control group**, the same tasks were used, with the exception that FES was not applied during tasks 1 and 3. Subjects were still instructed to perform the voluntary smile.

FES was delivered using Compex Motion stimulators (Compex SA, Switzerland). Bipolar surface adhesive electrodes measuring 2.5 cm by 1.25 cm (Nikomed USA Inc., USA) were placed bilaterally on the zygomatic major and orbicularis oculi muscles, which were stimulated simultaneously. 150 μs biphasic pulses were delivered at 60 Hz, with amplitudes in the 3-9 mA range. The pulse duration and stimulation frequency were chosen based on preliminary stimulation attempts during the protocol development stage. Amplitudes were determined for each subject at the beginning of the session, with the objective of producing visible contractions in the target muscles while avoiding unnecessary pain or excessive movement (e.g. complete closing of the eye). Note that the zygomatic major and orbicularis oculi are the two muscles required to produce an expression of happiness according to the Facial Action Coding System (FACS,[24]), though only the orbicularis oculi is specific to genuine smiles [9, 13]. Electrode placement is illustrated in Figure 1. Activation of the correct facial muscles was monitored throughout the experiment by the investigator, for both the FES and control groups.

Subjects were interviewed at the end of the session in order to ascertain whether or not the deception was effective, and then informed of the true purpose of the experiment.

Assessments

The Positive and Negative Affect Schedule – Expanded Form (PANAS – X, [25]) was administered before and after the experimental session (before the deception was revealed). This assessment asks the subject to rate 60 words or expressions that describe feelings and emotions on a scale of 1 to 5, depending on how strongly the expression describes their current state ("not at all" to "extremely"). In addition, aggregate scores are defined by combining several of the 60 base items. Our primary outcomes for this study were the PANAS-X scores for "happy" (base item), "joviality" (aggregate score comprising "happy", "joyful", "delighted", "cheerful", "excited", "enthusiastic", and "lively"), and "positive affect" (aggregate score comprising "active", "alert", "attentive", "determined", "enthusiastic", "excited", "inspired", "interested", "proud", "strong"). All other components of the PANAS-X were considered secondary outcomes.

In addition, we administered the Water-Level Task [26], a test of spatial reasoning. The Water-Level Task was not an outcome in our study, but was included to strengthen the deception: the presence of a cognitive assessment is to be expected given the study rationale that was provided to the subjects, and the presence of a second assessment made it less obvious that the PANAS-X was the crucial outcome. Furthermore, the Water-Level Task is a short pen-and-paper assessment that is unlikely to produce strong emotional reactions in the subjects (e.g., frustration) and skew other assessments. Similarly, the computerized n-back test was performed only as part of the deception, and the performance on this test was not used as an outcome in our study.

Lastly, subjects in the FES group were asked to rate the pleasantness/unpleasantness of the stimulation session on a 5-point Likert scale (Question: "Please rate the pleasantness or unpleasantness of the FES stimulation out of 5, with 1 being "very unpleasant" and 5 being "very pleasant"").

Subjects

Twenty-six able-bodied subjects were recruited for the study, and divided randomly into FES and control groups. These subjects were drawn from the community and self-reported not to be suffering from any mood disorders (i.e., the exclusion criteria that were presented and emphasized to the subjects included "Individuals currently suffering from a diagnosed mood disorder or brain disorder"). One subject in each group had to be excluded, in one case because the deception was not effective (i.e., the subject guessed the true purpose of the experiment), and in the other case because the subject was not able to reliably and voluntary active the orbicularis oculi to form a Duchenne smile. Thus, 12 subjects per group remained for analysis. The total sample contained 12 males and 12 females, with a mean age of 31.2 +/- 9.1 years; the intervention group contained 7 males and 5 females with a mean age of 26.7 +/- 5.6, and the control group contained 5 males and 7 females with a mean age of 35.3 +/- 9.7.

Statistical Methods

For each comparison, a Lilliefors test for normality was applied to each of the groups being compared. In within-group comparisons, if both sets of values were found to have a normal distribution, a paired t-test was applied, otherwise a Wilcoxon test was used. In between-group comparisons, if both groups were found to have a normal distribution, an unpaired t-test was applied, otherwise a Kruskal-Wallis test was used. Statistical significance was defined as $p < 0.05$.

Results

The PANAS-X scores (base items and aggregate scores) were used to perform three comparisons: initial vs. final scores in the control group, initial vs. final scores in the intervention group, and change in scores (final minus initial) in the intervention group vs. the control group. In case of missing values due to accidentally incomplete forms (2 instances out of 2,880 base item scores), initial and final values of the missing items were assumed to be equal.

Comparison of Initial and Final Assessments

A list of the PANAS-X items that were significantly different before and after the experiment is provided in Table 1, for both the control and intervention groups. These results reflect changes that occurred as a result of the experimental procedures, and are therefore a combination of the effects of the voluntary facial expressions, cognitive task, and FES (for the intervention group). Both groups showed significant differences in several of the PANAS-X base items and aggregate scores. The scores decreased in all cases except for “tired” and “fatigue”, which increased.

Comparison of Intervention and Control Groups

It is evident from Table 1 that the experimental procedures themselves had a substantial effect on the moods of the participants, whether or not FES was used. In order to better isolate the effects of the FES, Table 2 shows the results of the change score comparisons between the control and intervention groups, for all base items and aggregate scores in the PANAS-X. Significant differences were found for “daring” (increase), “scared” (decrease), “determined” (increase), and “concentrating” (decrease). The change score distributions of these outcomes for both groups are provided in Figure 2. A decrease in the “fear” aggregate score also very narrowly missed statistical significance ($p = 0.0535$, with a median change of -1 and a range of -3 to 0 in the FES group, compared to a median change of -0.5 and a range of -2 to 2 in the control group). The change score distributions for our primary outcomes of “happy”, “joviality”, and “positive affect” are provided in Figure 3. Although some qualitative differences can be observed, particularly in “happy”, for which the FES group showed a much broader distribution, none of the comparisons in Figure 3 reached statistical significance.

FES Sensation

When asked to rate the pleasantness or unpleasantness of the FES sensation, the FES group reported a mean score of 3.08 ± 0.76. In other words, the subjects on average reported finding the sensation “neither pleasant nor unpleasant”.

Discussion

We investigated the use of FES to modulate activity in neural pathways responsible for regulating emotion. Although the experimental procedures themselves had an impact on the reported mood of the subjects (with or without FES), significant differences were nonetheless found between the FES group and the control group in several of the secondary outcomes. No significant differences were found for the primary outcomes.

Most of the changes occurring between the initial and final assessments in both groups are consistent with the nature of the experiment, which required the subjects to concentrate continuously on a repetitive cognitive task. Decreases in PANAS-X items such as "lively", "attentiveness", "serenity", "concentrating" and increases in “fatigue” and “tired” are therefore not surprising. Differences between the two groups, on the other hand, can be attributed specifically to the FES rather than the experimental procedures. The effects of the FES on mood may be mediated through the neural pathways relating emotion to facial expression, as per our hypothesis, or through a reaction to the sensory signals produced by the stimulation. The decrease in “concentrating” as a result of the FES does not have an obvious link with the specific facial expressions used in the experiments, but is consistent with the additional distraction caused by the FES sensation. The increases in “daring” and “determined” and the decreases in “scared”, on the other hand, could possibly be linked to short-term plasticity in the neural pathways of emotion. Although these were not the emotions that we were aiming to elicit, the orbicularis oculi motion that the subjects performed (slight narrowing of the eyes) is consistent not only with the Duchenne smile but is also closely related to the stereotypical expression of determination. It is also worth noting that “daring”, “determined”, and “scared” are all related emotions, making it unlikely that our results are due simply to type 1 errors in our sample. The decrease in “fear”, which was very close to statistical significance, is also in line with this analysis. Our results are therefore consistent with the hypothesis that FES can modulate brain regions involved in the facial expression of emotion. An alternative interpretation for the "scared" and "fear" results is that the subjects in the intervention (FES) group were more initially apprehensive about the experiment than the control group, because they knew that they were about to receive stimulation. Thus, after the experiment was over, the intervention group experienced a greater decrease in "scared" and "fear" than the control group. This interpretation is also supported by Table 1, which shows an initial vs. final decrease in "fear" in the intervention group but not the control group. Nonetheless, this explanation cannot account for the between-group differences in "determined" and "daring", which are still therefore most likely a result of the FES. Indeed, if the intervention group subjects had been more determined initially because of the anticipated challenge of the FES, their determination scores would have decreased more than that control group's by the end of the experiment, whereas in fact the opposite trend was observed.

Our primary outcomes did not show any significant differences between the two groups, although some qualitative differences are visible in Figure 3, in particular a wider range of effects on the "happy" item in the FES group than in the control group. On the other hand, the secondary outcomes that showed a significant difference are highly relevant to MDD. The increase in "determination" in particular, and to a lesser extent the increase in "daring" and decrease in "scared", contrast strongly with the feelings of helplessness and lethargy that can accompany MDD [27]. A reduced ability to concentrate is also a symptom of depression, so an increase in the "concentrating" item would have been desirable rather than the observed decrease, but as stated in the previous paragraph it is likely that this effect was due to the FES sensation rather than a neuromodulatory effect.

Numerous previous studies have demonstrated the close link between emotion and facial expression [10, 12-14, 28-30]. Our work relied more specifically on the existence of two separate neural pathways, mediating on one hand voluntary facial movements and on the other one hand spontaneous facial expressions resulting from emotions. This distinction is well supported by neuroimaging studies [8, 9] and clinical evidence [6,7]. The novelty of our work lies in our use of FES, which to the best of our knowledge has not previously been used to modulate the neural pathways underlying emotion. Deep-brain stimulation (DBS) and transcranial magnetic stimulation (TMS) are other electrical modalities that are being explored for the treatment of psychiatric disorders [31, 32]. The application of FES to facial muscles is appealing because it is simultaneously non-invasive (unlike DBS) and precisely targeted (unlike TMS). Rather than alter the activity of the neural circuits directly responsible for MDD, which are widespread and not fully understood, our approach aims to directly modulate the mood of the subject. Thus, it would not treat the underlying cause of the disease, but rather compensate for its symptoms. It is also for this reason that we were able to conduct our pilot study in able-bodied subjects rather than subjects with psychiatric disorders. Another recent study used surface stimulation of the trigeminal nerve in a pilot study for the treatment of depression [33]. Although related to the work presented here, the underlying mechanisms are different, first because the locations of stimulation are different, and second because the trigeminal nerve stimulation was not accompanied by any voluntary movement and was thus conceptually distinct from the FES intervention presented in this article. Our study also differs from previous work in that we observed the modulation of emotions that have not been examined before in this context. Whereas other studies linking emotion and facial expression have focussed narrowly on happiness and sadness, our results found greater effects in items of the PANAS-X that have not been closely investigated before, especially determination. This highlights the complexity and difficulty of "targeting" specific emotional effects, and suggests that further work will be necessary to better refine this type of intervention.

Limitations

The effects of the FES may have been partly obscured by the experimental procedures (cognitive task), which themselves had a negative impact on the primary outcomes (Table 1). Nonetheless, these procedures were judged to be necessary to present a plausible deception that would justify the use of facial FES in able-bodied subjects and minimize the likelihood of the participants guessing the true purpose of the study. The FES stimulation itself can also arguably be unpleasant, and the sensation of the FES may therefore have counteracted any positive neuromodulatory impact on positive affect.

When asked to report the pleasantness or unpleasantness of the FES, however, participant responses were neutral, suggesting that this potential confounding factor was not a major issue. In addition, during the assessments the Water-Level Task was always administered first, ensuring that a few minutes had elapsed between the end of the FES sensation and the final PANAS-X and allowing the subjects to somewhat "forget" the sensation before rating their affect.

Another consequence of the need for a deception was that the cognitive task reduced the ability of the subjects to focus entirely on their facial movements while receiving the FES. This was mitigated to an extent by the inclusion of Task 1, which involved only receiving FES and performing the voluntary movements, without the addition of the cognitive task. Nonetheless, this task represented half of the FES time and thus only a quarter of the total experiment time (12.5 minutes), whereas the other half of the FES time included the distraction of the cognitive task. The voluntary component is thought to be crucial to the effectiveness of FES therapy [15, 19], and therefore it is possible that the stimulation periods in which there was a distraction may have been less effective. Higher doses of FES therapy with no distractions may yield stronger effects. On the other hand, the fact that we obtained several significant results even with the limited dose of FES argues in favour of the viability of our method.

The number of subjects used in our experiments is fairly small given the low dose of FES and thus modest expected effect, but this sample size was judged appropriate for an exploratory study, and still allowed us to detect a variety of effects (Tables 1 and 2).

Lastly, subjects voluntarily activated their orbicularis oculi muscles. Although this is not a typical component of voluntary smiling and instead is part of the "genuine" Duchenne smile, it would be worthwhile to investigate the effects of the FES in combination with periods of genuine rather than voluntary smiling. This approach would also minimize any concerns relating to the quality of the voluntary movements produced. In addition to the experimental difficulty of achieving this, however, such a paradigm does not lend itself well to any plausible deception involving the use of FES on facial muscles in able-bodied subjects without revealing the link to emotion. For that reason, we relied instead on the evidence showing that voluntary production of a Duchenne smile is effective at enhancing positive mood [13, 14], which in turn suggests a close link between the orbicularis oculi and the subcortical nuclei regulating emotion.

Conclusions

We investigated whether FES might enhance the mood-related effects of voluntarily activating facial muscles with close neural connections to the subcortical nuclei regulating emotions. Although the primary outcomes in our intervention group were not significantly different from those in our control group, several secondary outcomes with potential relevance to MDD did show significant differences. This provides some initial evidence that FES may indeed be able to modulate mood, even with small doses, but the specific effects are not easily controlled: in our case, effects were found in the PANAS-X items "determined", "daring", "scared" and "concentrating", rather than in our primary outcomes of

"happy", "joviality", and "positive affect". Further work is warranted to more precisely target the effects of this approach and to explore clinical applications in MDD.

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References

[1] L. Andrade, J. J. Caraveo-Anduaga, P. Berglund, R. V. Bijl, R. De Graaf, W. Vollebergh, E. Dragomirecka, R. Kohn, M. Keller, R. C. Kessler, N. Kawakami, C. Kilic, D. Offord, T. B. Ustun and H. U. Wittchen, "The epidemiology of major depressive episodes: results from the International Consortium of Psychiatric Epidemiology (ICPE) Surveys," *Int. J. Methods Psychiatr. Res.,* vol. 12, pp. 3-21, 2003.

[2] D. Souery, G. I. Papakostas and M. H. Trivedi, "Treatment-resistant depression," *J. Clin. Psychiatry,* vol. 67 Suppl 6, pp. 16-22, 2006.

[3] P. Ekman and W. V. Friesen, *Unmasking the Face.* Cambridge, MA, USA: Malor Books, 2003.

[4] P. Ekman, R. J. Davidson and W. V. Friesen, "The Duchenne smile: emotional expression and brain physiology. II," *J. Pers. Soc. Psychol.,* vol. 58, pp. 342-353, Feb, 1990.

[5] B. M. Waller, S. J. Vick, L. A. Parr, K. A. Bard, M. C. Pasqualini, K. M. Gothard and A. J. Fuglevand, "Intramuscular electrical stimulation of facial muscles in humans and chimpanzees: Duchenne revisited and extended," *Emotion,* vol. 6, pp. 367-382, Aug, 2006.

[6] W. E. Rinn, "The neuropsychology of facial expression: a review of the neurological and psychological mechanisms for producing facial expressions," *Psychol. Bull.,* vol. 95, pp. 52-77, Jan, 1984.

[7] H. C. Hopf, W. Muller-Forell and N. J. Hopf, "Localization of emotional and volitional facial paresis," *Neurology,* vol. 42, pp. 1918-1923, Oct, 1992.

[8] M. Iwase, Y. Ouchi, H. Okada, C. Yokoyama, S. Nobezawa, E. Yoshikawa, H. Tsukada, M. Takeda, K. Yamashita, M. Takeda, K. Yamaguti, H. Kuratsune, A. Shimizu and Y. Watanabe, "Neural substrates of human facial expression of pleasant emotion induced by comic films: a PET Study," *Neuroimage,* vol. 17, pp. 758-768, Oct, 2002.

[9] P. Ekman and R. J. Davidson, "Voluntary smiling changes regional brain activity." *Psch. Sci.,* vol. 4, pp. 342-345, 1993.

[10] D. Wiswede, T. F. Munte, U. M. Kramer and J. Russeler, "Embodied emotion modulates neural signature of performance monitoring," *PLoS One,* vol. 4, pp. e5754, Jun 1, 2009.

[11] M. B. Lewis, "Exploring the positive and negative implications of facial feedback." *Emotion,* vol. 12, pp. 852, 2012.

[12] A. Hennenlotter, C. Dresel, F. Castrop, A. O. Ceballos-Baumann, A. M. Wohlschlager and B. Haslinger, "The link between facial feedback and neural activity within central circuitries of emotion--new insights from botulinum toxin-induced denervation of frown muscles," *Cereb. Cortex,* vol. 19, pp. 537-542, Mar, 2009.

[13] M. G. Frank and P. Ekman, "Physiologic effects of the smile." *Directions in Psychiatry,* vol. 16, pp. 1-8, 1996.

[14] R. Soussignan, "Duchenne smile, emotional experience, and autonomic reactivity: a test of the facial feedback hypothesis," *Emotion,* vol. 2, pp. 52-74, Mar, 2002.

[15] M. R. Popovic, N. Kapadia, V. Zivanovic, J. C. Furlan, B. C. Craven and C. McGillivray, "Functional electrical stimulation therapy of voluntary grasping versus only conventional rehabilitation for patients with subacute incomplete tetraplegia: a randomized clinical trial," *Neurorehabil. Neural Repair,* vol. 25, pp. 433-442, Jun, 2011.

[16] T. A. Thrasher, V. Zivanovic, W. McIlroy and M. R. Popovic, "Rehabilitation of reaching and grasping function in severe hemiplegic patients using functional electrical stimulation therapy," *Neurorehabil. Neural Repair,* vol. 22, pp. 706-714, Nov-Dec, 2008.

[17] E. Beaumont, E. G. Codina, S. Dubeau, F. Lesage, M. Nagai and M. R. Popovic, "Restoring locomotion after spinal cord injury by optimizing the afferent neuronal circuitry with functional electrical stimulation," *Submitted for Review to the Journal of Spinal Cord Medicine, 2012,* .

[18] N. Kawashima, M. Popovic and V. Zivanovic, "Effect of intensive functional electrical stimulation therapy on the upper limb motor recovery after stroke: Single case study of a chronic stroke patient," *Physiotherapy Canada,* vol. in press, 2012.

[19] D. N. Rushton, "Functional electrical stimulation and rehabilitation--an hypothesis," *Med. Eng. Phys.,* vol. 25, pp. 75-78, Jan, 2003.

[20] D. McDonnall, K. S. Guillory and M. D. Gossman, "Restoration of blink in facial paralysis patients using FES," in *Proceedings of the 4th International IEEE EMBS Conference on Neural Engineering,* Antalya, Turkey, 2009, .

[21] P. J. Ohtake, M. L. Zafron, L. G. Poranki and D. R. Fish, "Does electrical stimulation improve motor recovery in patients with idiopathic facial (Bell) palsy?" *Phys. Ther.,* vol. 86, pp. 1558-1564, Nov, 2006.

[22] J. D. Cohen, W. M. Perlstein, T. S. Braver, L. E. Nystrom, D. C. Noll, J. Jonides and E. E. Smith, "Temporal dynamics of brain activation during a working memory task," *Nature,* vol. 386, pp. 604-608, Apr 10, 1997.

[23] L. E. Nystrom, T. S. Braver, F. W. Sabb, M. R. Delgado, D. C. Noll and J. D. Cohen, "Working memory for letters, shapes, and locations: fMRI evidence against stimulus-based regional organization in human prefrontal cortex," *Neuroimage,* vol. 11, pp. 424-446, May, 2000.

[24] P. Ekman and W. V. Friesen, *Facial Action Coding System: A Technique for the Measurement of Facial Movement.* Palo Alto, CA, USA.: Consulting Psychologists Press, 1978.

[25] D. Watson and L. A. Clark, *PANAS-X: Manual for the Positive and Negative Affect Schedule-Expanded Form.* University of Iowa: Iowa, 1994.

[26] J. Pascual-Leone and S. Morra, "Horizontality of water level: A neo-piagetian developmental review," in *Advances in Child Development and Behaviour, Vol. 23*, H. W. Reese, Ed. New York: Academic Press., 1991, pp. 231-276.

[27] A. T. Beck, R. A. Steer and G. K. Brown, *Manual for the Beck Depression Inventory-II.* San Antonio, TX: Psychological Corporation, 1996.

[28] F. Schneider, R. C. Gur, R. E. Gur and L. R. Muenz, "Standardized mood induction with happy and sad facial expressions," *Psychiatry Res.,* vol. 51, pp. 19-31, Jan, 1994.

[29] C. L. Kleinke, T. R. Peterson and T. R. Rutledge, "Effects of self-generated facial expressions on mood." *J Pers Soc Psych,* vol. 74, pp. 272-279, 1998.

[30] J. I. Davis, A. Senghas, F. Brandt and K. N. Ochsner, "The effects of BOTOX injections on emotional experience," *Emotion,* vol. 10, pp. 433-440, Jun, 2010.

[31] C. L. Allan, L. L. Herrmann and K. P. Ebmeier, "Transcranial magnetic stimulation in the management of mood disorders," *Neuropsychobiology,* vol. 64, pp. 163-169, 2011.

[32] W. K. Goodman and R. L. Alterman, "Deep brain stimulation for intractable psychiatric disorders," *Annu. Rev. Med.,* vol. 63, pp. 511-524, 2012.

[33] L. M. Schrader, I. A. Cook, P. R. Miller, E. R. Maremont and C. M. DeGiorgio, "Trigeminal nerve stimulation in major depressive disorder: first proof of concept in an open pilot trial," *Epilepsy Behav.,* vol. 22, pp. 475-478, Nov, 2011.

Table 1: PANAS-X Items showing a statistically significant difference between the initial and final assessments, for each subject group. Values provided are mean ± standard deviation. NP indicates that non-parametric statistics were used, and P indicates that parametric statistics were used (see Methods section of the text).

PANAS-X Item	Initial	Final	p-value
Control Group			
Base scores			
Daring	2.83 ± 1.19	1.58 ± 0.67	0.00 (NP)
Lively	2.92 ± 1.16	2.00 ± 0.85	0.00 (P)
Determined	3.58 ± 1.38	2.67 ± 1.07	0.02 (NP)
Aggregate scores			
Positive affect	30.83 ± 8.84	26.17 ± 8.83	0.01 (P)
Joviality	23.33 ± 6.57	20.17 ± 7.46	0.00 (P)
Self-Assurance	16.75 ± 4.14	13.75 ± 3.98	0.00 (P)
Attentiveness	13.83 ± 3.88	11.25 ± 3.86	0.00 (P)
Fatigue	8.08 ± 4.03	9.83 ± 4.49	0.04 (P)
Serenity	9.42 ± 2.43	6.67 ± 1.61	0.00 (P)
Intervention Group			
Base scores			
Attentive	4.08 ± 0.67	2.75 ± 1.14	0.00 (NP)
Tired	2.58 ± 1.31	3.25 ± 0.97	0.02 (P)
Nervous	2.00 ± 0.60	1.33 ± 0.49	0.04 (NP)
Concentrating	3.75 ± 0.87	2.67 ± 1.23	0.01 (NP)
Aggregate scores			
Negative affect	12.92 ± 1.93	11.67 ± 1.50	0.01 (P)
Fear	8.83 ± 1.70	7.42 ± 1.16	0.00 (NP)
Joviality	22.42 ± 6.46	19.75 ± 6.65	0.02 (P)
Self-Assurance	14.17 ± 3.10	12.08 ± 3.87	0.00 (P)
Attentiveness	13.67 ± 2.71	10.67 ± 3.92	0.00 (P)
Serenity	10.25 ± 1.76	7.25 ± 1.22	0.00 (NP)

Table 2: Significance of change score comparisons between the FES and control groups, for all items in the PANAS-X. A direction of change of ↑ indicates that the FES scores were higher than the control scores, whereas ↓ indicates that the FES scores were lower than the control scores. NP indicates that non-parametric statistics were used, and P indicates that parametric statistics were used (see Methods section of the text).

	p-value	Direction		p-value	Direction
PANAS-X Base Items					
cheerful	0.93 (NP)		active	0.16 (NP)	
disgusted	0.32 (NP)		guilty	0.15 (NP)	
attentive	0.11 (P)		joyful	0.47 (NP)	
bashful	0.42 (NP)		nervous	0.13 (NP)	
sluggish	1.00 (P)		lonely	0.93 (NP)	
daring	***0.04*** (P)	↑	sleepy	0.84 (P)	
surprised	0.19 (NP)		excited	0.53 (NP)	
strong	0.66 (NP)		hostile	0.32 (NP)	
scornful	0.12 (NP)		proud	0.45 (NP)	
relaxed	0.54 (NP)		jittery	0.17 (NP)	
irritable	0.51 (NP)		lively	0.26 (NP)	
delighted	0.98 (NP)		ashamed	1.00 (NP)	
inspired	0.34 (NP)		at ease	0.92 (NP)	
fearless	0.95 (NP)		***scared***	***0.03*** (NP)	↓
disgusted w/ self	0.32 (NP)		drowsy	1.00 (P)	
sad	0.33 (NP)		angry at self	0.32 (NP)	
calm	0.28 (NP)		enthusiastic	0.90 (NP)	
afraid	0.40 (NP)		downhearted	1.00 (NP)	
tired	0.71 (NP)		sheepish	0.17 (NP)	
amazed	0.17 (NP)		distressed	0.45 (NP)	
shaky	0.44 (NP)		blameworthy	1.00 (NP)	
happy	0.34 (NP)		***determined***	***0.03*** (NP)	↑
timid	0.30 (NP)		frightened	0.32 (NP)	
alone	0.55 (NP)		astonished	0.52 (NP)	
alert	0.35 (NP)		interested	0.78 (NP)	
upset	1.00 (NP)		loathing	0.32 (NP)	
angry	0.32 (NP)		confident	0.79 (NP)	
bold	0.52 (NP)		energetic	0.09 (NP)	
blue	0.93 (NP)		***concentrating***	***0.04*** (NP)	↓
shy	0.62 (NP)		dissatisfied w/ self	0.17 (NP)	
PANAS-X Aggregate Scores					
Negative affect	0.45 (P)		Self-Assurance	0.40 (NP)	
Positive affect	0.34 (P)		Attentiveness	0.72 (NP)	
Fear	0.05 (NP)		Shyness	0.92 (NP)	
Hostility	0.24 (NP)		Fatigue	0.84 (P)	
Guilt	0.79 (NP)		Serenity	0.75 (P)	
Sadness	0.92 (NP)		Surprise	0.43 (P)	
Joviality	0.81 (NP)				

Figure Captions

Figure 1: Trace of a photograph showing the locations of the bipolar stimulating electrodes, placed bilaterally on the muscles orbicularis oculi (electrodes labeled 1) and zygomatic major (electrodes labeled 2).

Figure 2: Boxplots comparing the change score distributions for the FES and control groups on the outcomes that showed statistical significance.

Figure 3: Boxplots comparing the change score distributions for the FES and control groups on the three primary outcomes.

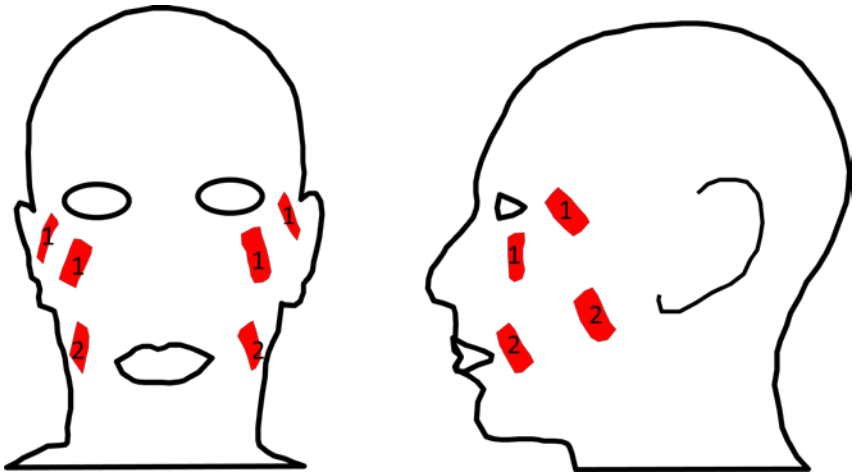

Figure 1

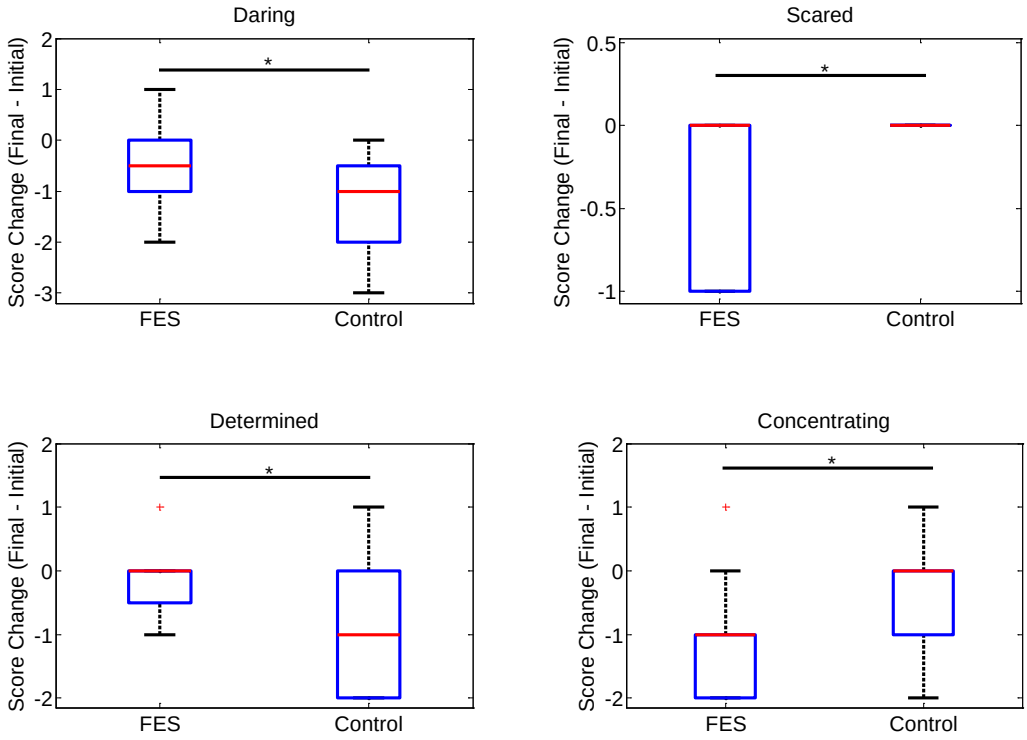

Figure 2

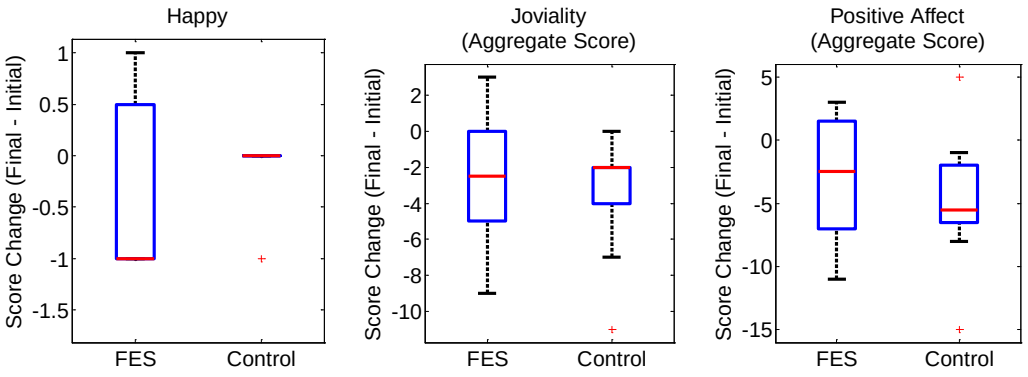

Figure 3