Brain-Computer Interface and Functional Electrical Stimulation for Neurorehabilitation of Hand in Sub-acute Tetraplegic Patients

Functional and Neurological Outcomes

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Keywords: Brain Computer Interface, Functional Electrical Stimulation, Neurorehabilitation, Tetraplegia, Hand.

Abstract: The aim of this paper is to compare neurological and functional outcomes between two groups of subacute hospitalised patients with incomplete tetraplegia receiving two experimental therapies. Seven patients received 20 sessions of Brain Computer Interface (BCI) controlled Functional Electrical Stimulation (FES) while five patients received 20 sessions of passive FES. The treatment assessment measures were EEG during movement attempt, Somatosensory evoked potential (SSEP) of the ulnar and median nerve and the range of movement of both wrists. Patients in both groups initially had intense cortical activity during a movement attempt, which was wide-spread, not restricted to the sensory-motor cortex. Following the treatment, cortical activity restored towards the activity in able-bodied people in BCI-FES group only. SSEP also returned in 3 patients in BCI-FES group while in FES group no changes were noticed. The range of movement improved in both groups and results are inconclusive due to the small number of participants. This study confirms the feasibility of prolonged BCI-FES therapy in a hospital setting. The results indicate better neurological recovery in BCI-FES group. Larger and longer studies are required to assess the potential advantage of BCI-FES on functional recovery.

1 INTRODUCTION

Brain Computer Interfaces (BCI) controlled functional electrical stimulation (FES) has two main applications for neurologically injured patients: to restore the lost function as an assistive device for a long term use (Pfurtscheller et al. 2003) or to improve a partially preserved function. In the latter case, BCI-FES is used as a rehabilitative device on a short-term basis (Fei et al. 2008, Daly et al. 2009, Tan et al. 2011, Tam et al. 2011, Young et al. 2014, Mukaino et al. 2014, Li et al. 2014). The main advantage of rehabilitation based on BCI-FES over FES alone is that it is based on patient's active intention to move and it simultaneously activates sensory and motor pathways, thus promoting neuroplasticity based on associative, Hebbian learning (Hebb 1949). Experiments on able-bodied people showed that Motor Evoked Potential (MEP) is enhanced more when the grasp function was guided by BCI-FES than when it was guided by either BCI or FES alone (McGie et al.2014).

Most publications advocating BCI-FES for rehabilitation purposes are case studies on stroke patients (Fei et al. 2008, Daly et al. 2009, Tan et al. 2011, Tam et al. 2011, Young et al. 2014, Mukaino et al. 2014). Larger studies or studies including other groups of patients are rare. Only recently a BCI-FES study on stroke patients has been published including a control and a treatment group (Li et al. 2014). Li et al. showed that patients receiving BCI-FES achieved better functional and neurological recovery than patients receiving FES alone. Another randomised controlled trial on stroke patients (Kim et al. 2015) showed better functional improvement in patients receiving BCI-FES as compared to patients receiving FES only, but failed to present any result showing brain activity pre and post therapy. Also recently, our group showed the feasibility of BCI-FES therapy on spinal cord injured patients. In that study on two patients early after injury, we showed that BCI-FES could be therapeutically used in incomplete tetraplegic patients in a hospital setting (Vuckovic et al. 2015). In the current study, we further explore the potential of BCI-FES for rehabilitation of hand functions in people with tetraplegia (high level spinal

Osuagwu, B., Wallace, L., Fraser, M. and Vuckovic, A..
Brain-Computer Interface and Functional Electrical Stimulation for Neurorehabilitation of Hand in Sub-acute Tetraplegic Patients - Functional and Neurological Outcomes.
In *Proceedings of the 3rd International Congress on Neurotechnology, Electronics and Informatics (NEUROTECHNIX 2015)*, pages 15-23
ISBN: 978-989-758-161-8

cord injury SCI). We compare neurological and functional outcome between the group of patients receiving 20 sessions of BCI-FES hand therapy with a matched control group receiving the same number of therapy sessions with passive FES.

2 MATHERIALS AND METHODS

2.1 Patients

Twelve subacute patients with tetraplegia (12 male, 51.7±18.4 min 20, max 75) participated in the study. All patients were three months or less post-injury, were still at the hospital and had therefore received daily standard hand therapy in addition to the experimental therapy (Table 1). Their level of injury was cervical, C4-C7 affecting both hands. All patients had incomplete injury, ASIA B or C, meaning that they had partially preserved sensation by no preserved movement (ASIA B) or had partially preserved both sensation and movement (ASIA C) (Marino et al., 2003). Because of the small number of patients with SCI, a semi-random order of recruitment was created in advance assigning patients to the one or the other treatment group. Patients were assigned upon recruitment to a corresponding group (20 patients in total are planned for the whole study, that is still running).

The study has been approved by the National Healthcare Service Regional Ethical Committee. This study is a registered clinical trial NCT01852279.

2.2 Initial and Final Assessments

The study consisted of three phases: initial assessment, treatment and final assessment. Initial and final assessment consisted of identical tests. Test were divided into neurological and functional. The neurological tests comprised of electroencephalography (EEG) recording during left and right hand movement attempts (MA) and somato-sensory evoked potential (SSEP) of the median and ulnar nerves of both hands. The functional assessments consisted of measurement of the range of movement of the left and right wrist and Manual Oxford Scale muscle test MMT (Porter, 2013) of hand and arm muscles. MMT test has 6 grades (0=no contractions felt in the muscle, 5=hold test position against strong pressure). Due to the nature of the injury, initially patients had better preserved voluntary control of muscles in shoulders and upper arms (MMT=3 to 4) than of the forearm, wrist and hand. Initial MMT of the forearm/hand muscles was between 0 and 2 (MMT=2 moves through the range of motion through a horizontal plane, i.e. cannot resist gravity). Formarm/hand muscles involved *supinator*, *pronator*, *extensor digitorum communis*, *extensor carpi radialis brevis* and *longus*, *flexor carpi radialis* and *flexor digitorum profundis*. Due to the large number of assessed muscles, the MMT outcome will be presented elsewhere. Functional and neurological assessments were performed on different days, to minimise patients' discomfort.

2.2.1 Cue-based Movement Attempt

A standard cue-based paradigm was implemented with rtsBCI, a part of the open source Biosig toolbox (Vidaurre et al. 2011), implemented under Simulink, MATLAB (Mathworks, USA). Patients sited in their wheelchairs approximately 1.5 from a computer screen. A trial started at t=-3 s and ended at t=3 s. At t=-1s a warning cue (a cross) was presented at the screen. At t=0s an execution cue (an arrow) appeared on the screen. After t=3s the screen stayed blank for a random period of 1-3 s before the next trial. Total time between two trials was random, between 7s and 9s. There were two types of arrows, an arrow pointing to the right for MA of the right hand and to the left for the MA of the left hand. Patients were instructed to attempt waving their hand continuously from t=0s till t=3s. Note that unlike able-bodied persons, paralysed people can differentiate between imagination of movement and movement attempt, in the absence of overt movements. Because the aim of the study was the restoration of voluntary hand movement, we considered MA being more appropriate task than the imagination of movement. There were 120 trials (60 for each hand) divided in 4 runs each consisting of 30 trails (15 for each hand)

During this task patients' EEG was measured with 48 electrodes placed according to the 10/10 system (Jurcak et al, 2007) using usbamp device (Guger technologies, Austria). Electrodes covered the central region of the sensory-motor cortex, parietal cortex and sparsely covered the frontal and occipito-temporal cortices. Forty seven electrodes were used to record EEG while one electrode was placed at the lateral cantus of the *orbicularis oculi* of the right eye to record electrooculogram (EOG). EEG was recorded with respect to the linked-ear reference with the sampling frequency of 256 samples/s. Impedance was kept under 5 kΩ. A ground electrode was placed at the electrode location AFz. EEG signal was filtered on-line between 0.5 and 60 Hz and notch-filtered at

Table 1: Information about patients. First 7 patients received BCI-FES therapy, last five received FES therapy.

Patient	Injury level	ASIA	Age
1	C6	C	70
2	C4	B	25
3	C6	B	32
4	C5	C	20
5	C6	C	74
6	C5	B	51
7	C6/7	C	61
8	C5	C	36
9	C5/6	C	61
10	C6	C	75
11	C4	B	51
12	C6	C	64

50 Hz using the IIR digital Butterworth filter built into a modular amplifier.

2.2.2 Off-line Analysis of EEG during Movement Attempt

Continuous data were split into trials starting at t=-3 and ending at t=3s, with respect to the execution cue. Datasets of each patients were decomposed into independent components (IC) (Hyvarinen, and Oja, 2000) using Infomax algorithm implemented in EEGlab (Delorme and Makeig, 2004) under Matlab (Mathworks, USA). Components were visually inspected and components corresponding to noise (line noise, EOG, EMG and ECG) were removed and signal was back projected into EEG domain. A common average reference was computed for all channels.

Time-frequency analysis was performed in EEGlab based on event-related spectral perturbation, which is an extension of the event-related synchronisation/desynchronisation (ERD/ERS) (Pfurtscheller and da Sliva, 1999). A baseline period was from t=-2s till t=-1s. The Morlet wavelet transform was used to perform a time-frequency analysis in 3-60 Hz, with a Hanning-tapered window applied and the number of cycles set to 3 at the lowest frequency.

An average ERD/ERS across patients was created using Study structure in EEGlab. Average ERD/ERS scalp maps for a chosen frequency band and time window were created through Study structure. The statistical non-parametric method with Holm's correction for multiple comparisons (Holm, 1979) was used to test for statistically significant differences between ERD/ERS scalp maps before and after treatments of patients within a group, with a significance level set to p=0.05.

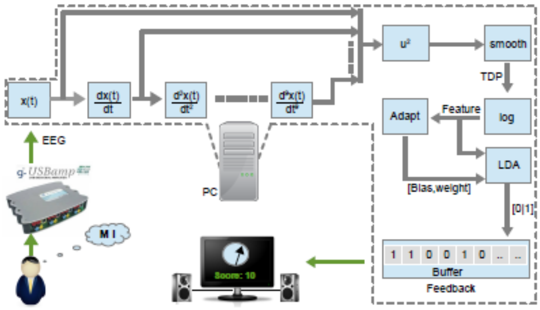


Figure 1: BCI setup showing computation of TDP.

2.2.3 Somato-sensory Evoked Potential

Somatosensory evoked potential is a response of the central nervous system to an electrical stimulation (Gugino and Chabot, 1990). The SSEP may infer motor functions on the assumption that an injury severe enough to a damage the sensory pathways may also affect motor pathways. The SSEP was analysed to detect the latency and the amplitude of the N20 peaks that occurs around 20ms following an electrical stimulus. In able-bodied people N20 latency is highly repeatable. The increased delay of N20 is an indicator of the damage of the neural pathways. The damage results in axon demyelination which causes reduced propagation velocity along the axon, manifested as the increased latency of N20 peak. In more severe cases, the amplitude of N20 is reduced or it is completely absent (Curt and Dietz 1999). The recovery of the neural pathways, followed by re-myelination, results in re-appearance of the N20 and in reduced N20 latency.

In the current study SSEP was measured for the left and right median and ulnar nerves, as these two nerves share innervation of the wrist and fingers. All the four nerves were stimulated separately, one at the time using a single pulse electrical stimulation (Model DS7, Digitimer,UK). Electrodes were attached on the surface of the skin above the corresponding nerves at the wrist. A stimulation intensity was set so that a small visible twitch could be observed at the thumb for the median nerve and at the little finger for the ulnar nerve. For each nerve, electrical stimulation was delivered 250 times with a frequency of 3 Hz. SSEP of the right hand median and ulnar nerve was measured at the electrode location CP3 and of the left hand nerves at the electrode location CP4. EEG was recorded with usbamp, with a sample rate of 4800 Hz, band passed between 2-2000 Hz and notch filtered at 50 Hz. Individual responses were averaged with respect to the onset of stimulation.

2.2.4 Measurement of the Range of Motion of the Wrist

In patients with incomplete tetraplegia who have partially preserved control of movement, the range of motion (ROM) is reduced, as compared to the able-bodied people. The ROM of the right and left hand wrist, during extension and flexion was measured using Zebris system (Zebris Medical GmbH, Germany). The measurement procedure is based on the travel time measurement of ultrasonic pulses. The pulses are emitted by three stationary transmitters and are recorded by small markers which are ultrasound microphones. The Zebris system markers were placed on bony landmarks on the subject's hand at the radius (marker 1), carpometacarpal joint (marker 2) and the carpometacarpal bone (of the index finger or the thumb, marker 3). The ROM was calculated as an angle between intersecting imaginary lines formed between markers 1-2 and markers 2-3.

2.3 Therapy Sessions

Treatment consisted of 20 sessions, each lasting approximately one hour, organised 3-5 times weekly, depending on patients' availability. One group of patients received active therapy; they attempted hand movement that was detected by BCI which then activated FES applied to their hand muscles (BCI-FES group). The other group of patients received passive on-off FES therapy (FES group). They got the same amount of FES stimulation as BCI-FES group but the stimulator was activated automatically. In both groups, therapy was applied on both hands, as spinal cord injury typically affects both hands, though not necessarily to the same extent.

2.3.1 Off-line Brain Computer Interface based on Movement Attempt

The BCI algorithm was based on time-domain parameters (TDP) (Vidaurre et al. 2009). On each day, a quick off-line session was recorded consisting of 20 trials for each hand, following the experimental protocol described in 2.2.1. In our previous study on able-bodied people (Osuagwu and Vuckovic 2014), we showed that such short recording session results in an initial classification accuracy between 75% and 100%. Note that off-line classifier parameters are further updated and refined during on-line BCI, as described later in the text. During therapy sessions, patients' EEG was recorded from three pairs of bipolar electrodes located over the sensory-motor cortex, CP3-CF3, CPz-CFz and CP4-CF4. EEG was recorded with usbamp, band-filtered online between 0.5 and 30 Hz (5^{th} order Butterworth filter), with sampling frequency 256 Hz. The ground electrode was attached to the ear. The impedance was kept under 5 kΩ.

Time domain parameters were calculated for 7-30 Hz EEG frequency band using equation 1

$$TDP = \left\langle \operatorname{var}\left(\frac{dX(t)^j}{dt^j} \right) \right\rangle \quad j = 0,...p \tag{1}$$

Where X(j) is a wide-band EEG, t is a current sample, j is a derivative (p=9), 'var' is a variance operator and $\langle . \rangle$ was used to present smoothing/averaging operator. Smoothing was a result of applying a one second long moving average filter. The variance operator in this equation acts as the band-power operator since the variance of the band-passed filtered signal is equal to the bandpower (Vidaurre et al. 2009). The BCI setup showing computation of TDP is shown in Fig. 1. The squaring and smoothing (Fig. 1), performed over 1s is a part of a band-power calculation. Following this, logarithmic transformation of TDP parameters was performed to enforce normal distribution required for classifier based on linear discriminant analysis (LDA) (Fukunaga, 1990).

2.3.2 On-line Brain Computer Interface based on Movement Attempt

During therapy a session, BCI was used on-line with classifiers to discriminate between a hand movement and no movement. To improve performance of BCI on-line LDA classifier, the mean values of both classes and the within class covariance matrix were updated during training. The on-line adaptation was necessary due to small number of off-line trials. Short off-line training was needed due to a limited time patients had for the study, which had to fit within their daily routine (typically 1 hour for BCI setup and for training of both hands).

The difficulty of activation of BCI was adjustable, so difficulty can be e.g. increased to reduce the false positive rate or decreased to make a task easier for a patients who is tired or has a low concentration. The difficulty was adjusted by setting the length of EEG sequence in which a desired class (left or right hand) had to be successfully detected. A classifier made a decision based on EEG sequence of length b (typically b=1.5-2s, while maximum allowed length B=3s or 768 samples). However, a classifier could make a decision based on a portion period called f.

So if a total sequence for a particular training day is b=2s, with maximum sequence B=3s and f=75% then difficulty d is 50%.

$$d = \frac{b \cdot f}{B} = \frac{2s \cdot 0.75}{3s} = 0.5 \qquad (2)$$

On each therapy session a patient performed 30-40 MA of each hand, separated in sub-sessions consisting of 20 trials. Each successfully detected movement attempt resulted in the activation of FES, as described below. During therapy sessions, patient sit in front of a computer screen. They were instructed to attempt a movement upon the appearance of a visual cue. A feedback in the form of a gauge was provided to patients. They were told that during MA, when the gauge indicator reaches 0, there will be activation of a set of electrodes attached to their hand muscles in a predefined order. After each 10 trial sub-session patients got visual information on the screen about their performance.

2.3.3 Functional Electrical Stimulation

Functional electrical stimulation was delivered using a multichannel FES device (Rehastim, Hasomed, Germany). Four bipolar electrodes were attached over the wrist and hand/thumb extensor and flexor muscles to assist patients to perform grasp by opening and closing their hand. The electrodes were attached to sequentially stimulate *the extensor digitorum*, *extensor pollicis longus*, *flexor digitorum superficialis* and *flexor policis brevis*. The first two muscles are extensors and the latter two are flexor muscles. Stimulation of the first two muscles resulted in opening of the hand and four fingers (index finger to pinkie), followed by thumb abduction; subsequent stimulation of two flexor muscles resulted in closing of the hand. The whole stimulation sequence lasted 10s. Frequency of stimulation was 26 Hz, pulse width was 200 µs and the current amplitude varied between 15 mA and 35 mA and was individually chosen for each patient to produce visible muscle contraction without discomfort. The same setup was used for both patient groups. The main difference was that BCI-FES group had to activate FES by attempting to open and close hand and for FES group stimulator was activated automatically in 10s on and 10 off sequence.

3 RESULTS

3.1 Attempted Movement ERD/ERS

Average ERD/ERS scalp maps during MA for both groups were created for θ, α, β1 (12-16 Hz) and β1 (16-24 Hz) bands. A difference in scalp maps before and after therapy was calculated for each group. Largest difference were found for BCI-FES group in β1 for both hands (Fig 2). Both groups had strong parietally shifted activity before the therapy. Only in patients, receiving BCI-FES, following the therapy, the activity 'restored', shifting back to the central cortical region. The lateralisation of ERD during MA of the left and right hand can also be noticed in Fig 2a,b, column 'BCI-FES', row 'After'. Red dots in bottom rows in Fig 2a and b show electrodes, located

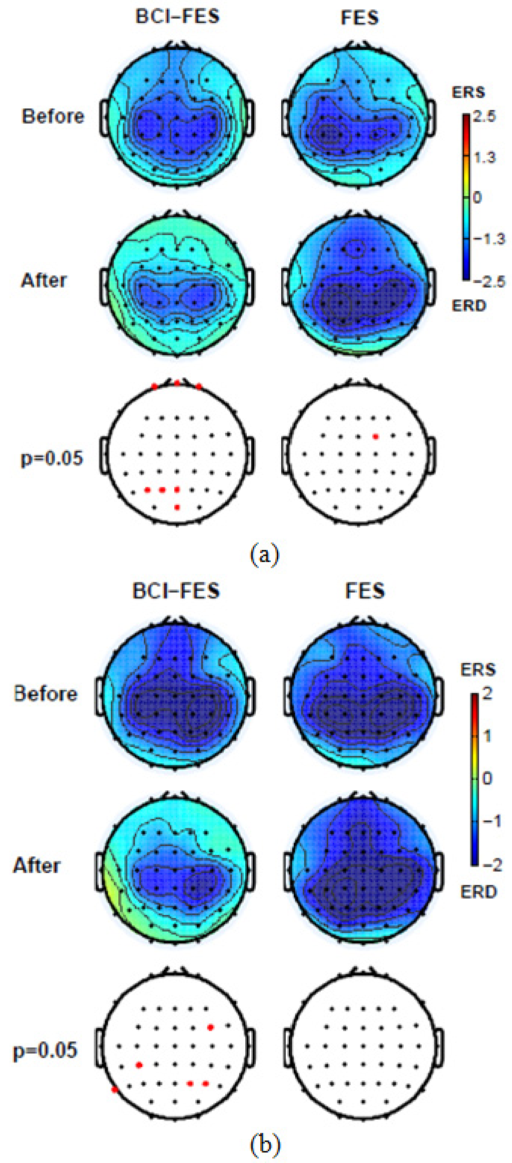


Figure 2: Event related synchronisation/ desynchronisation scalp maps for 12-16 Hz, averaged over t=0.5-2s, during movement attempt in two patient groups before and after 20 therapy sessions. (a) the right hand and (b) the left hand.

in the parietal cortex in BCI-FES group, in which ERD has significantly changed after the therapy. Previous studies indicate that parietal shift is due to an injury (Fig 2a.,b, both groups, row ‘Before’) and that in patients who functionally recover, cortical activity shifts back towards the central region (Green et al. 1998), as in able-bodied people. In BCI-FES group similar trend could be noticed in all other frequency bands, being also statistically significant for the left hand in the α band, and for the right hand in the θ band. No statistically significant changes (apart from one electrode showed in Fig 2a, bottom row) were noticed in FES group.

3.2 Somato-sensory Evoked Potential

Seven patients from BCI-FES and four from BCI were available for this test. Table 2 shows in how many patients N20 peak was visible in SSEP of the medial and ulnar nerve. Results in the table are presented as pre/post therapy.

Table 2: The number of patients who had visible N20 peak in their SSEP pre/post therapy in both patent groups.

	Median		Ulnar	
	left	right	left	right
BCI/FES	4/6	2/5	1/3	1/2
FES	2/2	1/0	1/1	0/0

In all patients in BCI-FES group, who initially had visible SSEP, the N20 latency was reduced post-therapy. The average N20 latency over 7 SSEP in total was 25.0±3.1 ms pre-therapy and 23.5±2.7ms post-therapy, being an indicator of neurological recovery. On the contrary, in FES group, N20 latency slightly increased from 23.5±1.6 ms to 23.9±1.9 ms. Figure 3 shows an example of N20 pre and post therapy in patient 1 who received BCI-FES therapy. Location of the N20 has shifted towards a lower latency post therapy and the amplitude (peak to peak) increased.

3.3 The Range of Motion

Five patients from BCI-FES group and three patients from FES were available for both initial and final assessment of ROM of the wrist. All patients in both groups, except patient 11 from FES group, had the increased range of motion of wrist following the therapy (Fig 4). Numerical values of ROM before and after the therapy, expressed as the degrees of an angle, are shown separately for flexion and extension of the right hand wrist. An increase in ROM indicates functional recovery. Due to the small number of participants it was not possible to perform a statistical analysis.

4 DISCUSSION

This study demonstrates the application of BCI-FES as a rehabilitative device for patients with incomplete tetraplegia. We used BCI based on time domain parameters with on-line adaptation (Vidaurre et al. 2009), which allowed short off-line training. Patients who are still in a hospital and receive standard treatment, have a very limited time for a BCI-FES therapy (Rupp 2014). BCI algorithms should therefore have quick electrode setup and should require minimum (if any) daily offline adjustment of parameters. We used 6 electrodes for 3 bipolar recording, that is much smaller than the number of electrodes used for algorithms based on common spatial patterns (16-63 electrodes, Fei et al. 2008, Li et al. 2014) and comparable with the number of electrodes for algorithms based on time-frequency parameters in a selected frequency band (2-12 electrodes, Tam et al. 2011, Mukaino et al. 2014, Young et al. 2014, Vuckovic et al. 2015).

Due to the injury to the spinal cord rather than to the brain, most research groups consider BCI-FES to

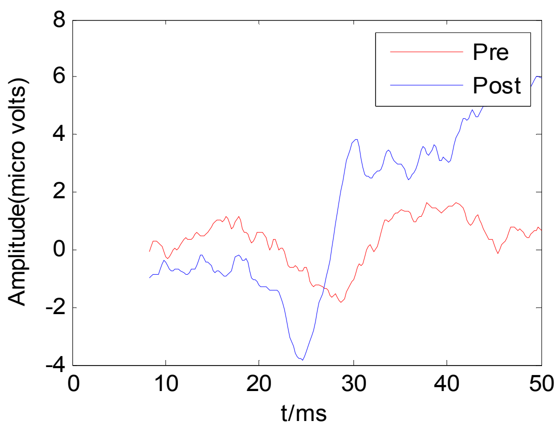


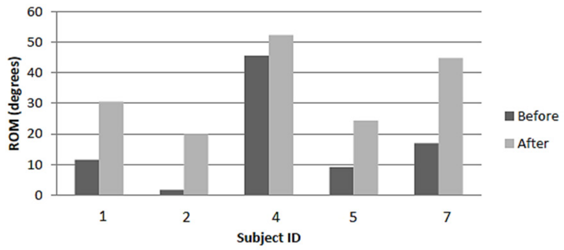
Figure 3: Somato-sensory evoked potential of the left ulnar nerve (note N20 peaks between 20 and 30 ms) in patient 1.

be an assistive rather than rehabilitative device for spinal cord injured patients. This paper, however, compares neurological and functional outcome of two hand therapies in incomplete sub-acute tetraplegic patients. A BCI-FES therapy involved active participation of patients, resulting in the combined activation of efferent and afferent pathways while FES therapy involved passive stimulation of muscles.

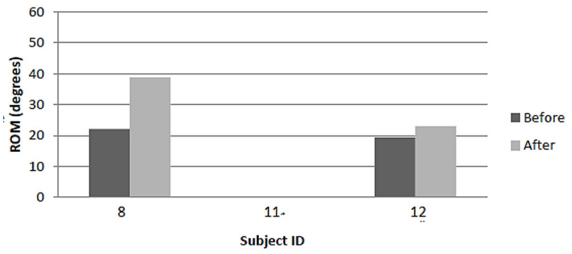
Previous BCI-FES rehabilitation studies on stroke patients reported increased ERD, from electrode located over the sensory-motor cortex, following a therapy (Li et al. 2014, Mukaino et al. 2014). In a subset of 4 patients included in this study we noticed the same phenomena (Osuagwu and Vuckovic 2014). However the novelty of the current study is that we looked at scalp maps rather than at isolated electrodes, which enabled us to notice the spatial restoration of cortical activity. Before the therapy, both groups had strong, parietal shift of cortical activity during MA. Following the therapy, only BCI-FES group, actively involved in the therapy, restored centrally located cortical activity during MA. This trend (parietal activity following injury, shifting towards central region upon recovery) has been previously reported in patients with spinal cord injury, where restoration of cortical activity was related to functional recovery (Green et al. 1998). This results is in-line with fMRI single case study (Mukaino et al. 2014) which showed initial diffuse blood oxygenation level and lateralisation of this activity following BCI-FES training.

SSEP was not used in BCI-FES studies in stroke patients because they had injury to the brain. In SCI patients however, this is a useful additional indicator of recovery. In BCI-FES patients group, SSEP following recovery showed re-appearance of N20 peak and reduced latency of the existing peaks. Though this was primarily noticed in BCI-FES group, due to the small number of patients, a statistical comparison between groups was not performed. Curt and Dietz (1999) showed a relation between the SSEP of the lower limbs and the recovery of walking which could be translated to recovery of the upper limbs.

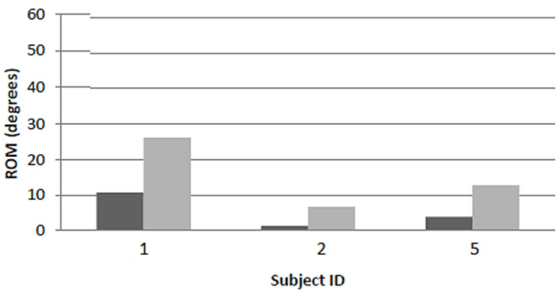
Improvement in ROM was noticed in both groups. In summary, while BCI-FES therapy results in a better neurological recovery, the results of functional recovery are inconclusive, partially due to the small number of patients being available for the ROM test. ROM is a functional assessment also used in studies on stroke patients (Kim et al. 2015). Studies on stroke patients additionally used Action Research Arm Test (ARAT) and Fugl Meyer Assessment of Motor Recovery to demonstrate better functional improvements in patients receiving BCI-FES (Li et al. 2014, Kim et al. 2015). SCI patients in the current study had more severe motor deficit than stroke patients and were not initially able to perform any of these task; therefore individual muscle strength was measured using MMT test. MMT is not a straightforward measure as each muscle should be observed individually, and unlike ARAT and FMA test, results of individual assessments should not be summed up over the muscles. This made MMT analysis complex, beyond the scope of this study.



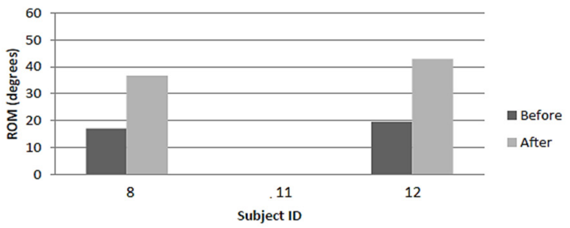
(a) BCI-FES - right wrist ext.



(b) FES - right wrist ext.



(c) BCI-FES - right wrist flex.



(d) FES - right wrist flex.

Figure 4: The range of motion during flexion and extension of the right hand wrist before and after therapy for each single patient in both groups.

A neurological recovery normally precedes a functional recovery. Patients in this study received 20 therapy sessions and had the last assessment shortly after the last therapy session. It is possible that FES patients would reach the same level of neurological recovery as BCI-FES patients but after a prolonged period of time. Alternatively, BCI-FES group might have shown long-term larger functional recovery than FES group due to better neurological recovery. It would be necessary to follow up patients for a prolonged period of time (e.g. up to 6 months) to establish whether those who showed better neurological recovery would achieve better functional recovery. Studies on the larger number of patients are required to establish a clear correlation between neurological recovery, as measured by the cortical activity, and functional recovery.

Neurological recovery might potentially prevent secondary consequences of SCI, such as spasticity and central neuropathic pain (Pikov, 2002). These complications are caused by disuse plasticity in the spinal cord but reflect themselves in the cortical activity (Wrigley et al. 2009, Vuckovic et al. 2014). In our recent study, we trained 5 chronic paraplegic patients with long-standing central neuropathic pain to voluntary modulate their brain activity over the sensory-motor cortex (neurofeedback), which resulted in reduced pain and in some patients in self-reported reduction of spasticity (Hassan et al. 2015). In the current study we demonstrated the restoration of the activity of the sensory-motor cortex as a result of BCI-FES training. In a long term, this might prevent secondary consequences of SCI. In the future, it would be useful having BCI-FES studies with follow up measures of spasticity and central neuropathic pain.

5 CONCLUSIONS

The study indicates that BCI-FES therapy of the hand in sub-acute incomplete tetraplegic patients provides better neurological recovery than passive FES therapy. Larger and longer studies are required to compare functional outcomes of these two therapies and explore the potential of preventing secondary complications by early BCI-FES interventions.

ACKNOWLEDGEMENTS

This work has been partially funded by EPSRC PhD scholarship EP/P505534/1. We would like to thank Dr Purcell and Dr McLane for their help with recruiting patients and to all patients for participating in the study.

REFERENCES

Curt, A., Dietz, V. (1999) Electrophysiological recordings in patients with spinal cord injury: significance for predicting outcome. *Spinal Cord*, 37(3). p.157–165.

Daly, J.J., Cheng, R., Rogers, J., Litinas, K., Hrovat, K., Dohring, M. (2009) Feasibility of a new application of noninvasive brain computer interface (BCI): a case study of training for recovery of volitional motor control after stroke. *J Neurol Phys Ther*, 33(3).p.203–211

Delorme, A., Makeig, S. (2004) EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *J Neurosci Meth*, 134(1). p.9 – 21.

Fei, M., Kai-yu, T., Suk-tak, C., Wan-wa, W., Ka-him, L., Kwok-wing, T., Xiaorong, G., Shangkai, G. (2008) BCI-FES training system design and implementation for rehabilitation of stroke patients. In *Proc IEEE Int Joint Conf. Neur Net and World Cong Comp Int*. p. 4103-4106.

Fukunaga, K. (1990) *Introduction to statistical pattern recognition*. Academic Press, London.

Green, J., Sora, E., Bialy, Y., Ricamato, A., Thatcher, R. (1998) Cortical sensorimotor reorganization after spinal cord injury an electroencephalographic study. *Neurology*, 50(4),p.1115–1121.

Gugino, V., Chabot, R.J. (1990) Somatosensory evoked potentials. *Int. Anesth. Clin*. 28(3).p.154–164.

Hassan, M.A., Fraser, M., Conway, B.A., Allan, D.B., Vuckovic, A. (2015) The Mechanism of Neuro-feedback Training for Treatment of Central Neuropathic Pain in Paraplegia: A Pilot Study. *BMC Neurology*. Accepted DOI:10.1186/s12883-015-0445-7.

Hebb, D. O. (1949) *Organisation of behaviour*. Wiley, New York.

Holm, S. (1979) A simple sequentially rejective multiple test procedure. *Scand J Stat*, 6(2).p.65–70.

Hyvarinen, A., Oja, E. (2000) Independent component analysis: algorithms and applications. *Neural Networks*, 13(4).p.411 – 430.

Jurcak, V., Tsuzuki, D., Dan, I. (2007) 10/20, 10/10, and 10/5 systems revisited: Their validity as relative head-surface-based positioning systems. *NeuroImage*, 34(4).p.1600 – 1611.

Kim, T., Kim, S., Lee, B. (2015) Effects of action observational training plus bran-computer interface-based functional electrical stimulation of paretic arm motor recovery in patient with stroke: a randomised controlled trial. [online] *Occup Ther Int*, Wiley Online Library, [Epub ahead of print] DOI:10.1002/oti.1403.

Li,M., Liu, Y., Wu, Y., Liu, S., Jia J., and Zhang, L. (2014) Neurophysiological substrates of stroke patients with motor imagery-based brain-computer interface training. *Int J Neurosci*, 124(6).p. 403–415.

Marino, R.J., Barros, T., Biering-Sorensen, F., Burns, S.P., Donovan, W.H., Graves, D.E., Haak, M., Hudson, L.M., Priebe, M.M. (2003) ASIA Neurological Standards Committee 2002. International standards for neurological classification of spinal cord injury. *The journal of spinal cord medicine*. 26 Suppl 1.p. S50–6.

McGie, S.C., Zariffa, J., Popovic, M.R., and Nagai, M.K. (2015) Short-term neuroplastic effects of brain-controlled and muscle-controlled electrical stimulation. *Neuromodulation*: 18(3).p.233-40.

Mukaino,M., Ono, T., Shindo, K., Fujiwara, T., Ota, T., Kimura, A., Liu, M., Ushiba, J. (2014) Efficacy of brain-computer interface-driven neuromuscular Electrical stimulation for chronic paresis after stroke. *J Rehab Med*, 46(4).p. 378–382,

Osuagwu, A.B., Vuckovic, A. (2014) Feasibility of using time domain parameters as online therapeutic BCI features. [online] In *Proc 6th Int Brain-Computer Interface Conf,* Graz, Austria. DOI:10.3217/978-3-85125-378-8-58.

Pikov, A. (2002) Spinal Plasticity. In Horch, K.W., Dhillon, G.S. (Eds) *Neuroprosthetics, theory and practice*. World Scientific Publishing, Singapoore.

Pfurtscheller, G., Lopes da Silva, F.H. (1999) Event-related EEG/MEG synchronization and desynchronization: Basic principles. *Clin Neurophisol*. 110(11).p.1842–1857.

Pfurtscheller, G., Müller, G.R., Pfurtscheller, J., Gerner, H.J., Rupp, R. (2003) 'Thought'--control of functional electrical stimulation to restore hand grasp in a patient with tetraplegia. *Neurosci Lett*. 351(1).p.33-6.

Porter, S. (2013) *Tidy's Physiotherapy*. Churchill Livingstone, Edinburgh.

Rupp, R. (2014) Challenges in clinical applications of brain computer interfaces in individuals with spinal cord injury.*Front Neuroeng*. 24.p.7:38.

Tam, W., Tong, K., Fei, M., Gao, S. (2011) A Minimal Set of Electrodes for Motor Imagery BCI to Control an Assistive Device in Chronic Stroke Subjects: A Multi-Session Study. *IEEE Trans Neural Syst Rehabil Eng*. 19.p.617-627.

Tan, H.G., Shee, C.Y., Kong, K.H., Guan, C., Ang, W.T. (2011) EEG controlled neuromuscular electrical stimulation of the upper limb for stroke patients," *Front Mech Eng*, 6(1).p.71–81.

Vidaurre, C., Kraemer, N., Blankertz, B., Schloegl, A. (2009) Time domain parameters as a feature for eeg-based brain-computer interfaces. *Neural Networks*, 22(9).p.1313–1319.

Vidaurre, C., Sander, T.H., Schlögl, A. **(**2011) BioSig: the free and open source software library for biomedical signal processing. *Comput Intell Neurosci.* 2011.p.935364.

Vučković, A., Hasan, M.A., Fraser, M., Conway, B.A., Nasseroleslami, B., Allan, D.B. (2014) Dynamic oscillatory signatures of central neuropathic pain in spinal cord injury. J Pain. 15(6). p. 645-55.

Vučković, A., Wallace, L., Allan, D.B. (2015) Hybrid brain-computer interface and functional electrical stimulation for sensorimotor training in participants with tetraplegia: a proof-of-concept study. *J Neurol Phys Ther*. 39(1).p.3-14.

Wrigley, P. J., Press, S.R., Gustin, S.M., Macefield, V.G., Gandevia, S. C., Cousins, M.J., Middleton, J.W., Henderson, L.A. (2009) Neuropathic pain and primary somatosensory cortex reorganization following spinal cord injury. *Pain*. 141.p.52-9.

Young, B. M., Nigogosyan, Z., Nair, V.A, Walton, L.M., Song, J., Tyler, M.E., Edwards, D.F., Caldera, K., Sattin, J.A, Williams, J.C., Prabhakaran, V. (2014) Case report: post-stroke interventional BCI rehabilitation in an individual with preexisting sensorineural disability. Front Neuroeng. 24.p.7-18.