Hybrid Brain Computer Interface and Functional Electrical Stimulation for Sensorimotor Training of Sub-acute Participants with Tetraplegia: A Case Series

ABSTRACT

Background and Purpose: Bilateral impairment of hand function in tetraplegia decreases quality of life. The purpose of the study was to test whether Functional Electrical Stimulation (FES) controlled by a hybrid Brain-Computer Interface (BCI) could be used for rehabilitation of the hand in participants with tetraplegia. This case series documents a concept of simultaneous training of efferent (motor) and afferent (sensory) pathways across the injury site.

Methods: Two participants with subacute tetraplegia took part in the study. Participant 1 with the rare Brown- Sequard syndrome at level C5 participated in 10 sessions while Participant 2, ASIA A at level C5 participated in 4 sessions. Their imagination ability and muscle strength was measured before and after the treatment. They received BCI-FES therapy 2-3 times a week in addition to the conventional therapy. A novel time-switch hybrid BCI was based on two spontaneously induced brain rhythms, the sensory-motor rhythm to activate a stimulator and the occipital alpha rhythms to deactivate the stimulator.

Results: Both participants learned to operate the BCI-FES system on the first session. Average classification accuracy was 83.5% (left hand) and 83.8% (right hand) for participant 1 and 83.8% for the right hand of participant 2. Visual feedback provided fourfold increase of brain response during imagination of movement in both participants. Participant 1had moderate improvement in functional outcome while there was no changes for participant 2.

Discussion and Conclusion: We demonstrated feasibility of BCI-FES for simultaneous sensori-motor training using two naturally induced brain rhythms. Studies on larger number of participants would be needed to separate the effect of training from the effect of the natural recovery.

BACKGROUND AND PURPOSE

Motor imagery (MI) activates similar brain areas as real movements and is a potentially powerful tool to promote motor rehabilitation.[1] There have been only a few studies on the effect of MI on recovery of participants with Spinal Cord Injury (SCI)[2,3] showing potential for improved hand trajectory after tendonesis.

The major problem with MI is how to assist participants to imagine moving their paralyzed limbs. With the advent of Brain Computer Interface (BCI) it has become possible to measure a person's brain activity while imagining movements. [4,5,6] However previous BCI studies performed on chronic SCI participants had a focus on developing assistive devices for a long term use, rather than on using BCI for rehabilitation of movements[4].

BCI studies with a focus on rehabilitation were mostly performed on stroke participants [5,6] as BCI promotes functional reorganization of the cortical structures. [7,8] So far the scientific community has been insufficiently exploring the potential of BCI for rehabilitation of SCI participants, although it is believed that only 10% of spared neuronal pathways is sufficient to provide a functional recovery. [9] In SCI participants reorganization occurs at the cortical and sub-cortical level, [10] causing spinal cord atrophy,[11] cortical atrophy[12,13] and cortical reorganization of sensory-motor cortex.[14-17] BCI targeting cortical structures may increase the volume of activation of the motor cortex controlling muscles affected by a SCI. At the same time it may also prevent secondary complications such as phantom limb sensation and neuropathic pain.[18-20]

In patients with SCI it is difficult to noninvasively record and modulate neuronal activity from the site of the injury, but it is believed that input from the brain and periphery may promote activity- dependent plasticity of the spinal cord.[21-22] From that reasoning a therapy based on combined simultaneous activation of the motor pathways (through MI) and the sensory pathways (through FES) of the corticospinal tract should have a bigger effect than

both therapies alone.[8,23] This is supported by the principle of Hebbian learning,[24] i.e. 'things that fire together wire together'. Studies on able-bodied people show that peripheral electrical stimulation enhances Motor evoked potential in people performing either real[25] or imagined movements.[26]

BCI studies on stroke participants were not concerned with the integrity of the afferent sensory pathways so brain response to FES were not measured. In SCI participants activation of sensory-motor cortex through FES would be a prerequisite for successful therapy.

To enable a fully participant-driven system, capable of controlling both activation and deactivation of FES on the participant's own pace, we proposed a hybrid on/off BCI switch which relies on two induced brain rhythms, the sensory-motor and the occipital alpha rhythm. The novelty of the proposed system is that, unlike hybrid systems in the literature which rely on a combination of evoked and externally induced rhythms, [27] this system is solely based on two participant-induced EEG rhythms and as such does not require any additional external device to initiate either an on or off command.

In this study we tested feasibility of using BCI-FES system on two sub-acute participants with tetraplegia in realistic clinical environment. We assessed simultaneous activation of sensory and motor pathways by observing muscular and cortical responses.

CASE DESCRIPTION

Participants

Two right handed participants with tetraplegia participated in the study. Participant 1, aged 45, was ASIA B 3 months post-injury with an incomplete hemi-section of the spinal cord, known as a *Brown-Sequard* syndrome. The injury was at level C5, living him with preserved sensation but no motor function in his left wrist, and preserved motor function but no sensation in his right arm and hand. Participant 2, age 32 was C5 complete (ASIA A,

complete injury defined as no sensation at S4/S5 level) but had weak sensation in his right forearm with no wrist and hand function. At the time of the study they were both hospitalized receiving their regular occupational therapy 5 times a week for one hour. The Oxford Manual Muscle test was used to asses the function of the upper limbs muscles before and after the experimental treatment. The study was conducted in accordance with the Declaration of Helsinki and was approved by the regional hospital Ethical Committee. Both participants provided informed consent.

INTERVENTION PROTOCOL

Recording and Testing Procedures:

The EEG was recorded using the gtec EEG amplifier (Guger Technologies, Austria). A ground electrode was connected to their left ear. EEG was recorded bipolarly from electrode location CF3-CP3 and CF4-CP3. The sampling frequency was 256 samples/s and the EEG signal was filtered between the 0.5 and 30 Hz. Impedance was kept under 5kΩ. Electrical stimulation (Rehastim, Hasomed, Switzerland) was applied using bipolar electrodes placed on the hand extensor muscles. Stimulation parameters were: pulse duration 300 μs, amplitude 15 mA, frequency 30 Hz. Pulse amplitude gradually increased during first 5s to minimize discomfort. Flexion of was not practiced to avoid hyper flexion. One bipolar channel, located over the contralateral cortex, was used to control FES applied to the extensor muscles of the right and left wrists.

The participants ability to generate imagined movements was tested using Kinaesthetic and Visual Imagery Questionnaire (KVIQ)[28] with a 5-point rating scale (1 no imagery, 5 excellent imagery), separated for kinaesthetic (KI) and visual imagery (VI). The experiment consisted of two phases. In the first phase, participants performed a cue-based motor imagination task. This task was used to produce Event-Related Synchronisation/ Desynchronisation maps (ERS/ERD)[29] to determine frequency bands that were most reactive

to motor imagery. These frequency bands were used in the second phase to control FES. In the second phase participants took a part in a longitudinal BCI-FES study. ERD/ERS were also calculated in the second phase to demonstrate activation of FES by self-paced MI. ERD/ERS presents relative change of power of the EEG signal across a range of frequency bands during motor imagination as compared to a reference period. Desynchronisation (ERD) shows a relative drop in energy and is related to the increased cortical activity during motor imagination task. In its simplified version, for a chosen frequency band, ERS/ERD is calculated as

$$ERS/ERD\% = \frac{(E-R)}{R} \cdot 100$$

Where E is 'an event', e.g. MI and R is ' a reference period' preceding the event.

ERS/ERD maps were created in EEGLab[30], under Matlab. Time-frequency analysis was performed using a sinusoidal wavelet with minimum 3 wavelet cycles per data window at lowest frequencies. To present statistically significant areas a t-percentile bootstrap method was used with a significance level α=0.05 (N=2000 trials). A False Discovery Rate[31] correction for multiple comparisons.

Cue based motor imagination task

The volunteers sit in front of a computer screen approximately 1.5m away. They were instructed to perform a kinaestehtic MI with their left and right hand, depending on the direction of the cue shown on the screen. An arrow symbol pointing right indicated motor imagery of the right hand while an arrow pointing to the left indicated motor imagery of the left hand. Experimental paradigm is shown in Fig. 1. A single trial consisted of the following: at t=0s a warning sign (a cross) appeared on the screen and stayed there till t=5s. At t=1s an arrow appeared on the screen and stayed there until t=2.25s. Participants were instructed to imagine/attempt repetitive movements of their hand from the moment the arrow

appeared on the screen till the moment a cross disappeared from the screen, i.e. from t=1s until t=5s. The arrows appeared in a random order. The time between the two trials was also random, between 5s and 8s. The whole session was divided into smaller sub-sessions, each sub-session lasting about 5min, presenting 20 arrows (10 arrows in each direction). The BCI paradigm was developed using the BioSig Open Source package[32]. Participants 1 had 6 sessions (60 trials of each hand) while participant 2 had 4 sessions (40 trials of each session) due to limited sitting time, resulting in reduced duration of the session. The ERD/ERS maps were calculated with respect to the reference period (R in Equation 1) before the warning sign, from t=-0.5s until t=-1.5s. The event (E in Equation 1) was the whole period of motor imagery, from t=1s until t=5s.

Figure 1 about here

BCI controlled Functional Electrical Stimulation

The experimental setup is shown in Fig 2. We asked participants to imagine the feeling in their muscles as if they were opening the hand to grasp the object (kinaesthetic imagery). A BCI detected the participants' intention to open their hand and used it as a control signal to activate the FES, thereby opening the participant's hand (FES ON Fig 2). To facilitate MI a Graphical User Interface in the form of a scale (GUI) was used to provide participants with visual feedback of their brain activity. To deactivate the stimulator (FES OFF Fig 2) participants closed their eyes and relaxed, thus generating OFF command signal for the FES device. Alternatively FES could be switched off automatically after 10s.

Figure 2 about here

The on-line environment was developed in Simulink/Matlab (Mathworks 2009), which had representative modules of both the EEG device gtec.usbamp and of the electrical stimulator the Rehastim (Hasomed, Switzerland). A Graphical User Interface (GUI) was designed in LabView 9 (National Instruments), which communicated with Simulink via the

Simulation Interface Toolkit. The GUI had three screens: Screen 1 (Fig. 3) was used for participants' training to improve motor imagery and provide visual feedback of the Power spectral density (PSD). PSD value was used to activate FES through BCI. Screen 2 was used to setup parameters for the occipital alpha control for a hybrid BCI. Screen 3 provided a simultaneous overview of the PSD in all five frequency bands. Screens 2 and 3 were used by the experimenter only.

Figure 3 about here

On the left side of Screen 1 there was a scale with an indicator, providing the instantaneous value of the PSD in one of the following frequency bands: delta, theta, mu/alpha, beta 1 (12-16 Hz) and beta 2 (16-24 Hz). These five bands cover the main frequency range of interest. Alpha and beta 2 are called sensory-motor rhythms (SMR)[33]. During the imagination of movement PSD od SMR typically drops[29], shifting the scale to the left. Right from the scale there was a counter showing how many times FES was activated. A graph in the middle showed instantaneous PSD in the last 5s. Under the graph there were two write-in fields to set the value of 'the Threshold' and 'the Time'. Every time PSD was under 'the threshold' value for duration of 'the time' the counter increased by one and FES was activated. On the right side of the screen there was a drop down menu to select between the right and left hand and another drop-down menu to select between the five different frequency bands..

BCI-FES control strategy

The control was based on a time-controlled threshold switch. A controlled parameter was Power Spectral Density (PSD) of the EEG signal in a chosen frequency band, calculated using a 5^{th} order Hanning window, over a moving average window of 1s, in steps of 125 ms (giving 8 samples/s). To *activate* the FES, a PSD was measured over the contra-lateral cortex,

CF3-CP3 for the right hand and CF4-CP4 for the left hand. Before each training session participants were asked to briefly imagine moving their hand. MI activated the sensory-motor area, causing a decrease in the PSD of the (SMR). A minimum PSD value was taken as 'a Threshold'. Participants were then asked to relax with their eyes open for 60s. In case the PSD unintentionally dropped under 'The Threshold' within this period of time (as indicated by a counter on Screen 1), the threshold value was reduced and the whole procedure was repeated. Empirical iterative procedure is shown in Fig. 4. Compromise had to be made between system reliability and ease of use.

Figure 4 about here

Once control parameters were set participants had to apply MI to keep the PSD under the 'The Threshold' for 1s in order to activate the FES. A one second long time switch was introduced to avoid unintentional activation of FES by natural fluctuation of SMR. Following this, if sensory pathways were preserved, FES kept the Sensory-Motor Area (SMA) active. Thus a low PSD of SMR was initially achieved centrally by MI (activating motor pathways) and then maintained by FES. Once the FES was switched on, participants did not have to continue with the MI because the sensory-motor area was being kept active by FES through the afferent sensory pathways. Combined MI and FES action formed the basis of the sensory-motor training.

A disadvantage of this was that once the FES activated the sensory-motor area, it could not be switched off by using the SMR. To deactivate the FES participants used their natural alpha rhythm from the occipital area (O1 and O2).[33] Unlike the SMR, the occipital alpha rhythm was not affected by the electrical stimulation and could be independently controlled even in the presence of FES. The PSD of the alpha activity (8-12 Hz) in this area increased when participants closed their eyes and relaxed. Participants' PSD of the alpha rhythm on either O1 or O2 had to stay above 'The Threshold' for 1s in order to deactivate a FES.

For calculating ERS/ERD maps the 'event' period started at the moment the FES was activated (t=0s). Participants were asked to keep PSD under the 'threshold' from t=-1s until t=0s. 'Reference' period was chosen from t=-4s till t=-2s. ERS/ERD maps were shown for a period t=-5s until t=5s. Electrical stimulation lasted from t=0s until t=10s.

OUTCOMES

Figure 5 shows ERD/ERS maps in participants 1 and 2 over the contralateral side of the brain from the hand receiving the training. Both participants had the most reactive frequency band in the mu range (8-12 Hz) which was used to calculate PSD to control the FES. Participant 1 had a weaker response from the hand with lost proprioception, than from the hand with lost motor function. Participant 2 had weaker desynchronisation of the mu rhythm then participant 1.

Figure 5 about here

Before treatment, participant 1 had KI score 2.3 and VI score 3.5 (2=poor, 3=moderate) while participants 2 had KI score 2.0 and VI score 3.1. Participant 1 practiced one hand at time, motor imagery of his left hand and combined sensory-motor imagery of his right hand. Initially he had difficulties with MI of his right hand. We facilitated his object-oriented MI by providing sounds from various everyday objects and placing objects in front of the participants. Object-oriented motor imagery is a preferred MI strategy in people with low KI score.[34] Participant 2 practiced MI with his right hand only. Due to limited sitting time, duration of the experimental session was up to 1 hour.

Figure 6a shows average values of PSD over one training session of the left hand in Participant 1 in the mu, theta and beta 1 frequency band over the electrode location CF4-CP4. Theta (4-8 Hz) and beta 1 (12-16 Hz) were chosen as frequency bands adjacent to the mu frequency band (8-12 Hz). Stimulation started at t=0s (dashed vertical line). A sharp decrease

in mu PSD can be noticed prior to the stimulation, staying under 'The Threshold' value for 1s. During FES, PSD of mu rhythm increased slowly but stayed noticeably lower than in the period before stimulation. PSD in the other two rhythms did not drop, indicating voluntary control of mu rhythm. Fig. 6b show ERD/ERS map of the same period (reference period was from t=-4s to t=-2s) indicating a drop in the energy level of the mu rhythm about 2s prior to FES activation which was sustained during electrical stimulation. 'The threshold' value was much lower than the statistical significance used to calculate the ERD/ERS maps to prevent unintentional activation of the FES. Comparing range of ERS/ERD bars in Fig 5 and 6 one can notice four fold stronger ERD during FES control than during spontaneous motor imagery without feedback (600% compared to 150% in Fig 5).

Figure 6 about here

Fig 7 shows corresponding values from the electrode location CF3-CP3 when Participant 1 controlled FES over his right wrist muscles. Mu PSD (Fig 7b) dropped prior to stimulation but then reached higher levels during FES, indicating that the FES did not activate the sensory-motor cortex to the same level as during MI of the hand with preserved sensation. While ERD/ERS maps show much stronger ERD than during motor imagery without feedback, it is weaker and less sustained than for the left hand.

Figure 7 about here

Fig 8a shows the PSD of the mu and beta 1 band for electrode location CF3-CP3 in Participant 2 while controlling the FES applied over his right wrist muscles. His ERD with feedback was much stronger than the ERD without feedback (Fig 5).

Figure 8 about here

It could be noticed that although the percentage of ERD is much higher when visual feedback is provided, ERD seemed less sustained then during cue-based motor imagery task shown in Fig. 5. One possible explanation for this is that participants stopped the MI once the

FES was activated. Intensity of the FES activation was gradually increased over the first 5s but it might not have been strong enough to produce statically significant ERD. When FDR is used to compensate for multiple comparisons, weaker ERD were treated as 'non-significant'. Therefore the ERD which would be statistically significant in Fig 5, where max ERD was up to 150% would not be statistically significant in Fig 6-8 where maximum ERD was up to 600%.

Figure 9a shows the False Positive (FP) activation rate for using BCI training over different sessions for both participants. The FP measure was used to test the reliability of the BCI control. A False Positive activation rate shows, in percentage, how many times the FES was activated when a participant did not intend to activate it. The task was to activate the FES 20 times. The FES was deactivated automatically after 10s. The average FP rate for participant one's left hand was 16.5 ±7.5 %, and 16.2±6.3% for the right hand. The average FP for participant 2 was 16.2 ±6.3 %. The FP was in a range of the error rate of similar BCI systems[4-6]. Slight variation in the day-to-day FP rate was influenced by numerous external factors, such a poor sleep/tiredness, lack of concentration or pain. As previously mentioned, motor imagery of the right hand in patient 1 was additionally facilitated by auditory stimulus. Without that stimulus the patient would not be able to concentrate enough to keep PSD value under the threshold value. This however would not influence the FP rate as it was related to unintentional activation of the FES rather than inability to activate the FES.

There was no False Negative activation (no activation of FES when participants performed the required task) due to the simple design of the BCI protocol that depended only on the amplitude of the PSD and time. Thus classification accuracy was calculated as 100-FP%. Classification accuracy was 83.5% for patient one's left hand, 83.8% for patient one's right hand and 83.8% for patient two's right hand. Figure 9b shows the 'Threshold' values to activate the FES. It can be noticed that the 'Threshold' value was typically higher in the first

session than in the following one. We also notice that 'Threshold' values are proportional to the FP rate, with the higher threshold corresponding to the higher error rates.

Figure 9 about here

To measure the effect of the FES only, the experimenter activated the FES ten times on both the right and left hand in Participant 1. The number of trials was not large enough to produce the ERS/ERD , so only the average PSD values were calculated. Fig 10a shows the PSD in mu, beta 1 and beta 2 bands over the electrode location CF3-CP3 during MI of the right hand. FES starts at t=0s. PSD in the mu band (solid line) does not drop even in the last five seconds when the FES reached its maximum value. Beta 2 rhythm (dashed-dot line) was lower during the FES than in the reference period while beta 1 rhythm seemed unaffected by it.

Fig 10b shows PSD in mu, beta 1 and beta 2 bands over the electrode location CF4-CP4 during MI of the left hand. Both the sensory-motor rhythms dropped during the FES (t>0s) while PSD in beta1 remained unaffected.

Figure 10 about here

Hybrid BCI

A hybrid BCI was tested in one session. Participants were asked to activate and deactivate the stimulator at their own pace ten times. Fig. 11a and 12a show the PSD of the SMR while Fig 11b and 12b show the PSD of the occipital alpha. Because of the relatively high amplitude of the alpha rhythm in the occipital and central locations, we showed each individual stimulus rather than the average values, to demonstrate the dynamics of this process, i.e. time required to activate and deactivate the FES and the time between the two activations. The occipital alpha was unaffected by the electrical stimulation that affected the PSD in the sensory-motor area only. The participants' occipital alpha increased when they closed their eyes, even when the stimulator was switched on. This mu rhythm was however

clearly blocked with the FES, and only increased once the FES was switched off. The same phenomena could be noticed on both participants. Within the first 150s, participant 1 activated and deactivated the FES five times while participant 2 activated and deactivated it four times. None of participants had false positive activation of the FES using MI and both had one out of ten false positive of the deactivation using the occipital alpha.

Figures 11 and 12 about here

In the Oxford manual muscle test Participant 1showed moderate improvement in *Brachioradialis* from 1 to 3 and in *Extensor CarpiUlnaris* from 0 to 1, but that improvement might be also attributed to conventional therapy or to natural recovery (Table 1). Participant 2 had no improvement in the muscle strength score during the therapy.

Table 1

DISCUSSION

This paper demonstrates the feasibility of using a hybrid on/off BCI time-switch for rehabilitation purposes in sub-acute participants with tetraplegia. BCI had a dual function: to support MI practice and to control FES. Both FES[34] and MI[1-6] alone could activate the SMA but preserved proprioception provided stronger activation of SMR during electrical stimulation, thus enabling a combined activation of the sensory and motor pathways. Although both participants had low initial scores for kinesthetic imagery, which is associated with low BCI performance,[35] both were able to use BCI from the first session, thanks to both visual and proprioceptive feedback through the computer GUI, FES and object-oriented imagery.

To our best knowledge this is the first BCI study on sub-acute hospitalized BCI users, which explores the feasibility of BCI as a rehabilitation tool in a realistic environment. BCI treatment had to fit in an existing daily rehabilitation schedule without presenting a significant burden to participants with fragile health.

Although there is evidence that SCI may cause almost immediate changes in the large cortical networks within 1h[36], it is believed that major disuse plasticity occurs in the chronic phase.[10] Unlike chronic SCI participants in which disuse cortical reorganisation [14-17] affects motor imagery, [4] sub-acute participants can quickly learn to use MI to control the BCI. For simultaneous activation of the efferent and afferent pathways it was important that BCI control in the present study was based on the brain wave features present during the MI task, rather than on a post-imagery phenomena (beta synchronization), often used in BCI with participants with chronic SCI.

A participant with a relatively rare Brown-Sequard syndrome initially more easily performed the MI with the hand that had no motor function, rather than with the hand which had no sensation. Imagery of sensation was enhanced by visual and auditory stimuli. The other participants with minimum preserved proprioception reported no difficulty in performing the MI. A typical candidate for the BCI-FES therapy should be a person with an incomplete injury, with a mixture of preserved motor and sensory functions. Sensory training, in which tactile stimuli was augmented by sound, has been used for sensory training of patients with peripheral nerve injury.[37] To the best of our knowledge sensory training was not explored within the BCI paradigm and would require more research in the future.

The empirical time switch allowed quick setting of parameters immediately before the training with a reasonably low error rate. The time switch is also a very suitable method for rehabilitation, having the right timing between BCI classification and FES. The time switch relies on the low level of PSD that indicates active motor imagery (i.e. motor execution). In a recent study[20] it was shown that FES maximizes the motor evoked potential response if delivered during the MI, rather than immediately after. This is unlike the BCI systems used for communication and control, which often uses a post imagery phenomena[4].

A hybrid BCI allowed participants to determine the duration of the FES activation. Although this is less relevant for simple tasks, in the future it might allow more flexibility in performing complex tasks, such as combined reaching and grasping. Unlike the hybrid BCIs proposed in the literature, our hybrid BCI relied on two naturally induced brain rhythms and did not require additional equipment to induce the brain activity. [27] Occipital eyes-closed alpha is probably one of the rare brain rhythms that would be easier to control in sub-acute SCI than in able-bodied participant because SCI participants often receive medication which help them to relax.

The current study reflects some practical issues related to experiments in hospitalized sub-acute participants: variation in the participants level of concentration from one day to another affected BCI parameters and BCI reliability; limited sitting time (to prevent pressure ulcers) dictated simple experimental setup based in 2 bipolar channels and simple, threshold based algorithm. Most of previous BCI studies involved participants in the chronic phase, when the process of natural recovery is reduced and their general health condition is more stable. [2-6] However that also minimized the chances of a positive outcome of the experimental treatment and could lead to improper conclusions.

There are two limitations of this study, one being that participants took part for a relatively short period of time over a limited number of sessions; this was sufficient to demonstrate the feasibility of the system for a long-term use but was insufficient to demonstrate functional and neurological improvement. The second limitation is that the number of participants was small and the effect of treatment was mixed with the effect of the natural recovery. Further controlled studies with the larger number of participants are required to determine the functional relevance of a BCI-FES therapy and to differentiate between the effect of the therapy and the effect of a natural recovery. [38]

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Table 1 . Oxford manual muscle test, Participant 1, left hand.

Muscle	BR	EDC	ECU	ECR	FPL	EPL	FDP
Before	1+	1	0	1	1	1	1
After	3	1+	1	1+	1+	1	1+

FIGURE LEGENDS

FIGURE 1. Timeline of a cue-based experimental paradigm. Warning sign (a cross) appears at t=0s and stays on the screen untill t=5s. A cue (an arrow) indicating whether to imagine left or right hand movements appears at t=1.25s and stays until t=5s. Motor imagery lasts from t=1s until t=5s.

FIGURE 2. A participant controlling a hybrid BCI-FES system. GUI: Graphical User Interface, FES: Functional Electrical Stimulation, BCI: Brain Computer Interface. Participants obtain visual information about their brain activity through GUI. Imagination of opening/closing hand activates FES. Relaxation with closed eyes deactivates FES.

FIGURE 3. Graphical Unser Interface used to facilitate imagination of movements. Scale on the left shows instantaneous value of PSD in a chosen frequency band. A graph in the middle shows PSD during last 5s. Drop-down bars to the right are used to set frequency band and electrode location. Write-in fields are used to set values of parameters 'Time' and 'Threshold'.

FIGURE 4. Flow chart diagram showing the process of setting parameter 'Threshold' for (a) Motor Imagery BCI; (b) for the Occipital alpha BCI.

FIGURE 5. Event related synchronization/desynchronisation maps for imagination of movement (a) Participant's 1 left hand (contralateral side, CF4-CP4) (b) Participant's 1 right hand (contralateral side, CF3-CP3), (c) Participant's 2 right hand (contralateral side, CF3-CP3). Dashed vertical line at t=0s corresponds to the appearance of the warning sign; solid vertical line at t=1s corresponds to the appearance of a cue.

FIGURE 6. Averaged brain response over CF4-CP4 during imagination of the left hand movement in Participant 1. Electrical stimulation (FES) started at t=0s. (a) PSD graphs of mu band (solid line), theta band (dashed line) and beta 1 band (dashed-dot line). Horizontal line

between t=-1s and t=0s shows Threshold value for alpha PSD. (b) Event Related Synchronisation/Desynchronisation.

FIGURE 7. Averaged brain response over CF3-CP3 during imagination of the right hand movement in Participant 1. Electrical stimulation started at t=0s. (a) PSD graphs of mu band (solid line), theta band (dashed line) and beta 1 band (dashed-dot line). Horizontal line between t=-1s and t=0s shows Threshold value for mu PSD. (b) Event Related Synchronisation/Desynchronisation.

FIGURE 8. Averaged brain response over CF3-CP3 during imagination of the right hand movement in Participant 2. Electrical stimulation started at t=0s. (a) PSD graphs of mu band (solid line), and beta 1 band (dashed line). Horizontal line between t=-1s and t=0s shows Threshold value for mu PSD. (b) Event Related Synchronisation/Desynchronisation.

FIGURE 9. PSD graphs of brain response during externally triggered FES for participant 11: mu band (solid line), and beta 1 band (dashed line) and beta 2 band (dashed-dot line). FES starts at t=0s. (a) CF3-CP3 for stimulation of the right hand (b) CF4-CP4 for stimulation of the left hand.

FIGURE 10. Longitudinal BCI control (a) False positive rate across sessions for Participants 1 and 2 (b) FES activation threshold across sessions for Participants 1 and 2

FIGURE 11. Hybrid BCI, participant 1. (a) PSD of the mu rhythm, dashed line trapezoids represent FES. 'The Threshold' value was $0.2\mu V^2$ (not shown in the figure due to a small value) (b) PSD of the occipital alpha rhythms O1, dashed line trapezoids represent enlarged FES, (same as in (a)). A dashed-dot line shows 'the Threshold 'value of the occipital alpha.

FIGURE 12. Hybrid BCI, participant 2, (a) PSD of the mu rhythm, dashed line trapezoids represent FES. 'The Threshold' value was $0.3\mu V^2$ (not shown in the figure due to a small value) (b) PSD of the occipital alpha rhythms O1, dashed line trapezoids represent enlarged FES, (same as in (a)). A dashed-dot line shows 'the Threshold 'value of the occipital alpha.

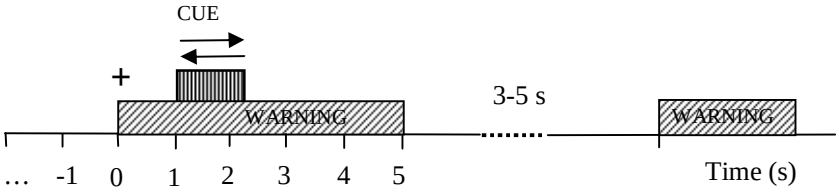


Figure 1

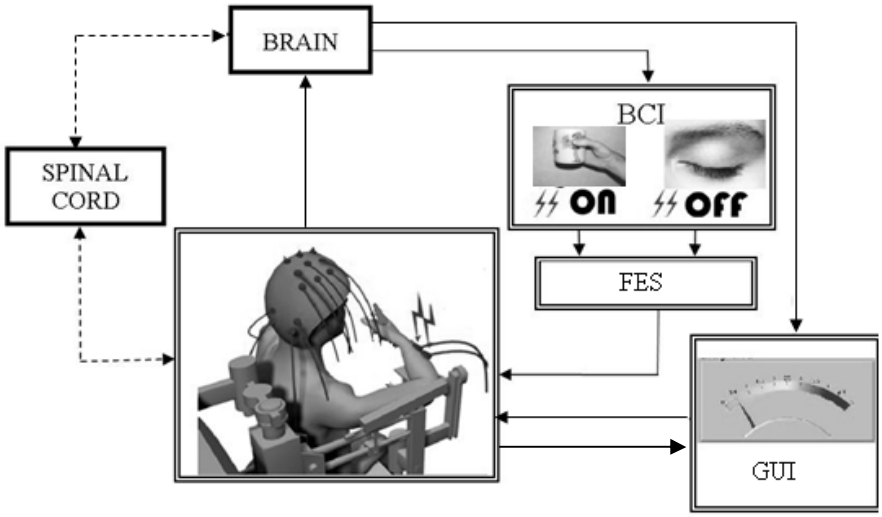


Figure 2.

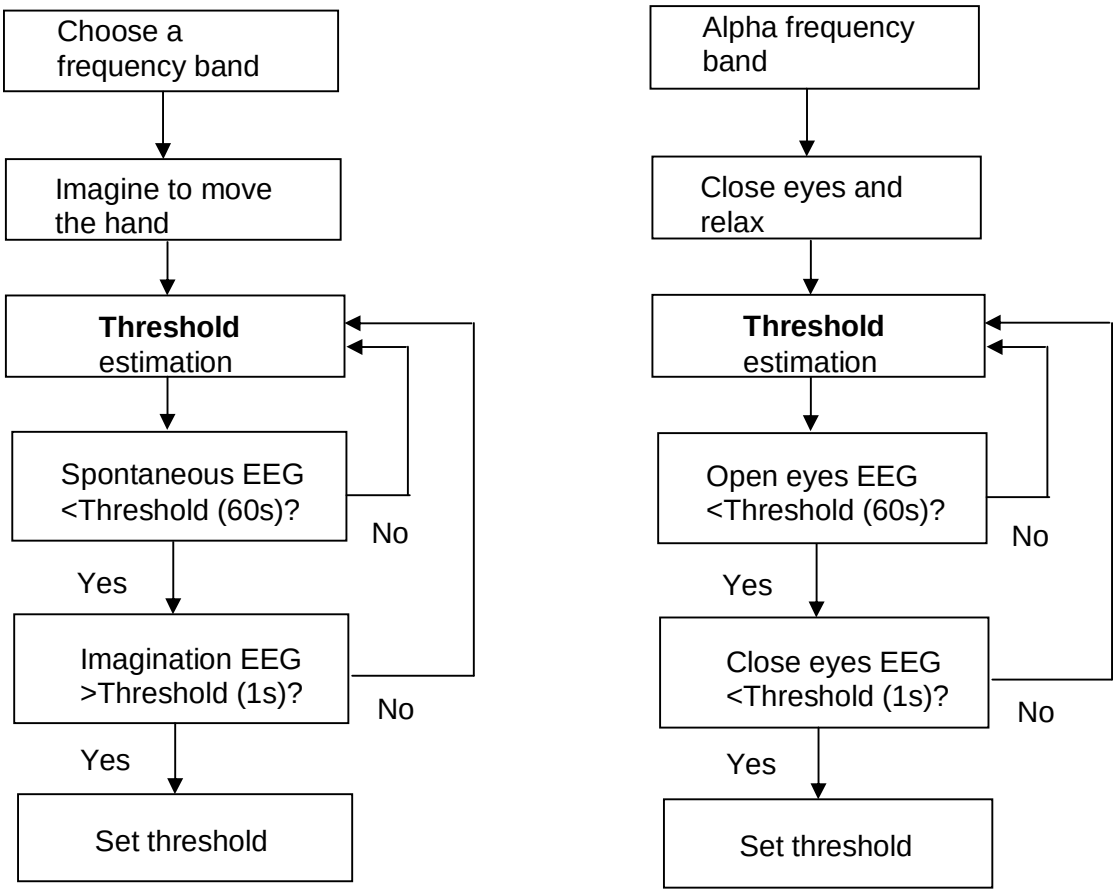
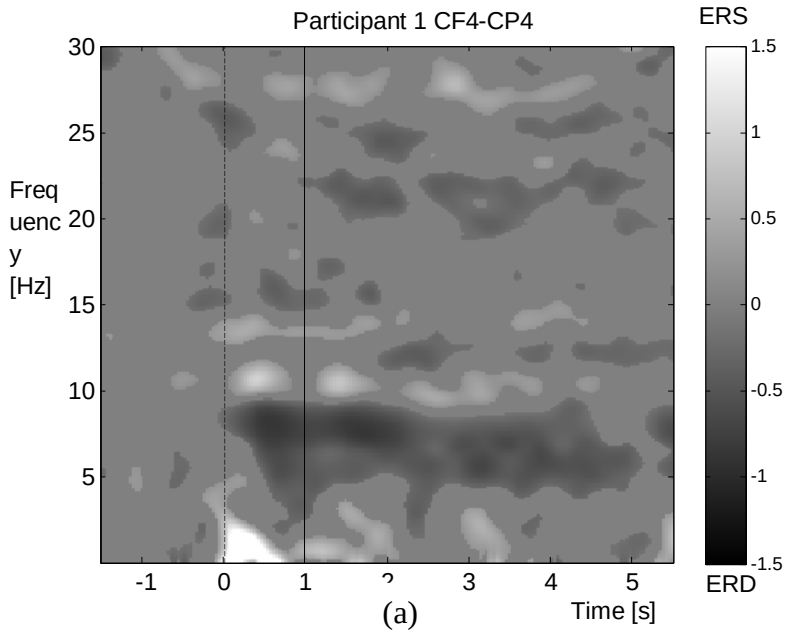
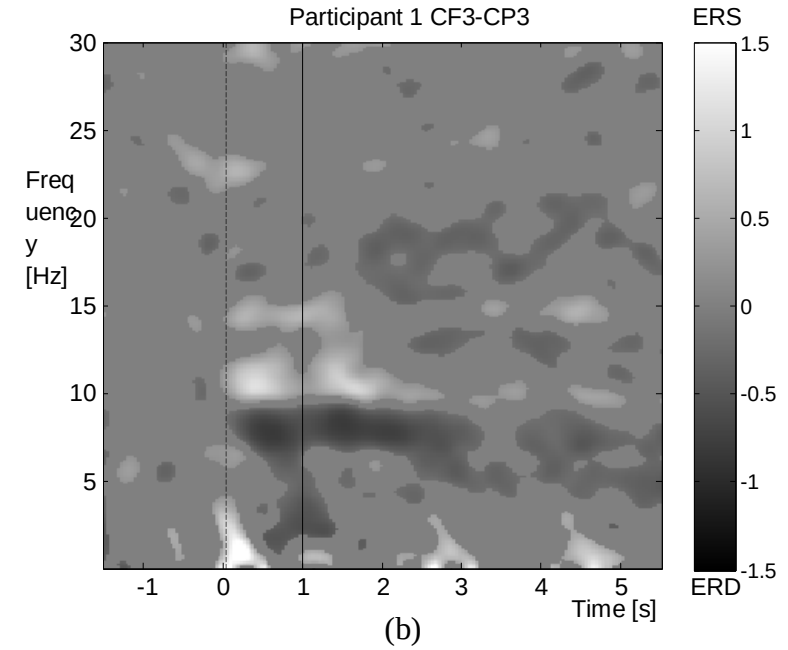

Choose a frequency band
Imagine to move the hand
Threshold estimation
Spontaneous EEG <Threshold (60s)?
No
Yes
Imagination EEG >Threshold (1s)?
No
Yes
Set threshold
Alpha frequency band
Close eyes and relax
Threshold estimation
Open eyes EEG <Threshold (60s)?
No
Yes
Close eyes EEG <Threshold (1s)?
No
Yes
Set threshold

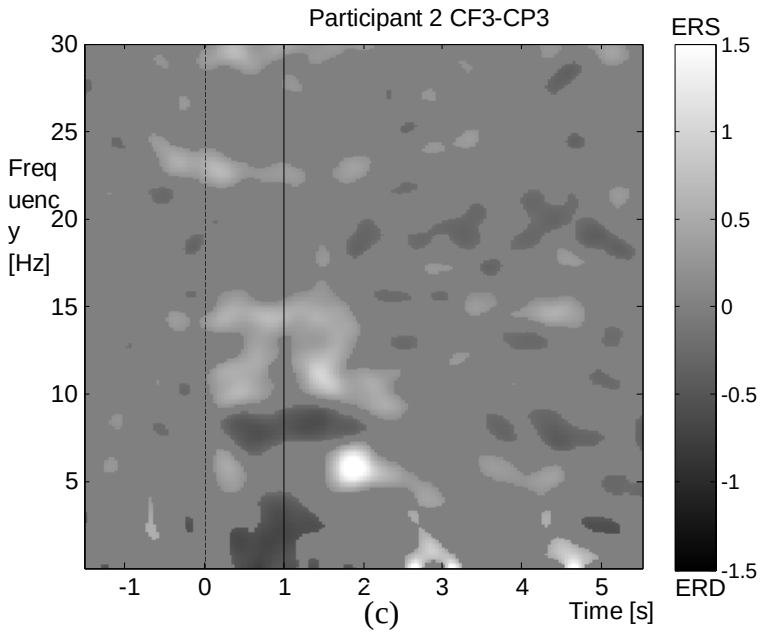
Figure 4


Participant 1 CF4-CP4
ERS
ERD
Frequency [Hz]
Time [s]
30
25
20
15
10
5
-1
0
1
2
3
4
5
1.5
1
0.5
0
-0.5
-1
-1.5

(a)

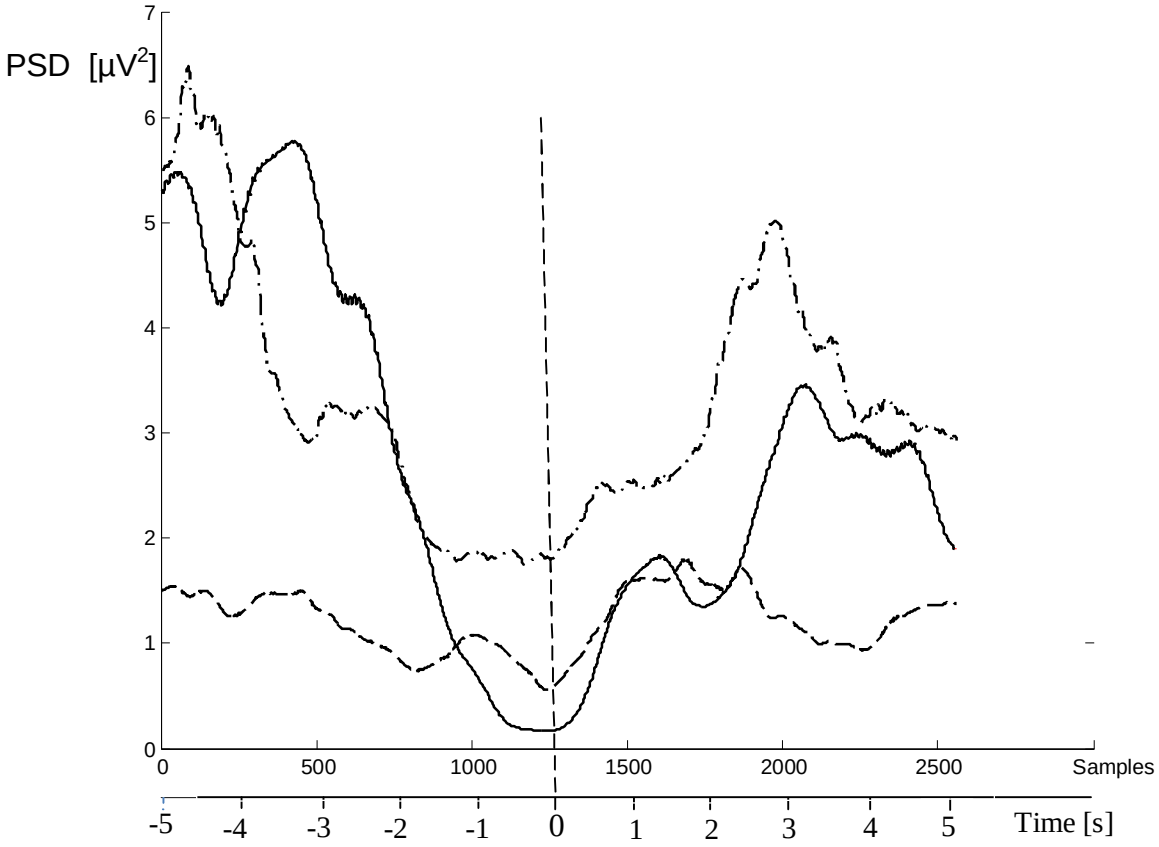

Participant 1 CF3-CP3
ERS
ERD
Frequency [Hz]
Time [s]
30
25
20
15
10
5
-1
0
1
2
3
4
5
1.5
1
0.5
0
-0.5
-1
-1.5

(b)


Participant 2 CF3-CP3
ERS
ERD
Frequency [Hz]
Time [s]
30
25
20
15
10
5
-1
0
1
2
3
4
5
1.5
1
0.5
0
-0.5
-1
-1.5

(c)

Figure 5


PSD [μV²]
7
6
5
4
3
2
1
0
0
500
1000
1500
2000
2500
Samples
-5
-4
-3
-2
-1
0
1
2
3
4
5
Time [s]

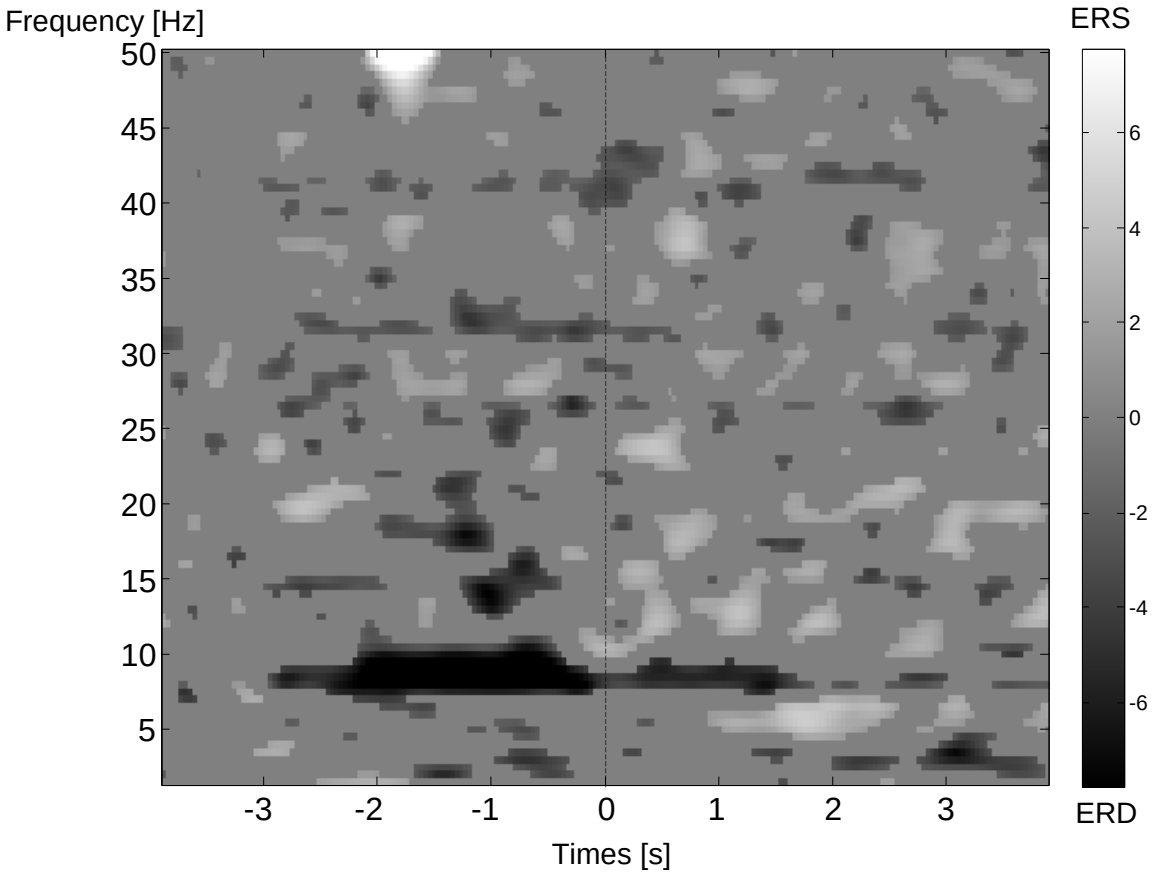
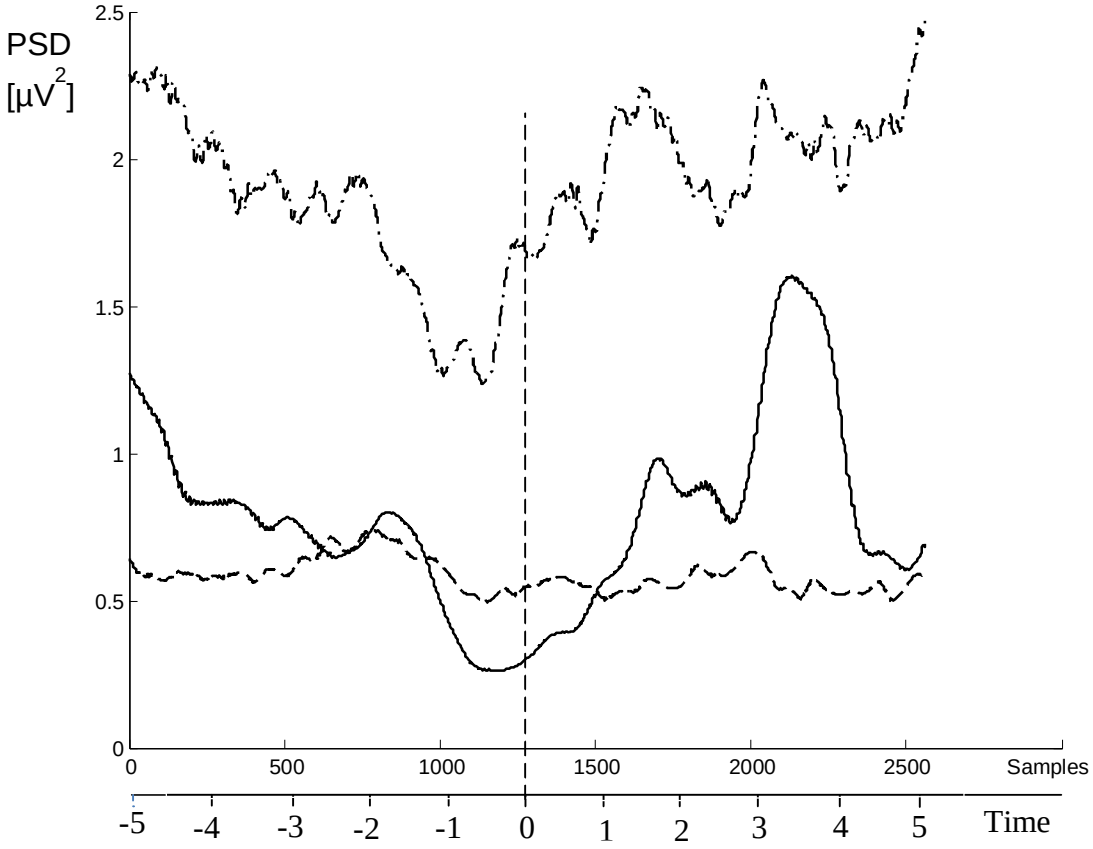
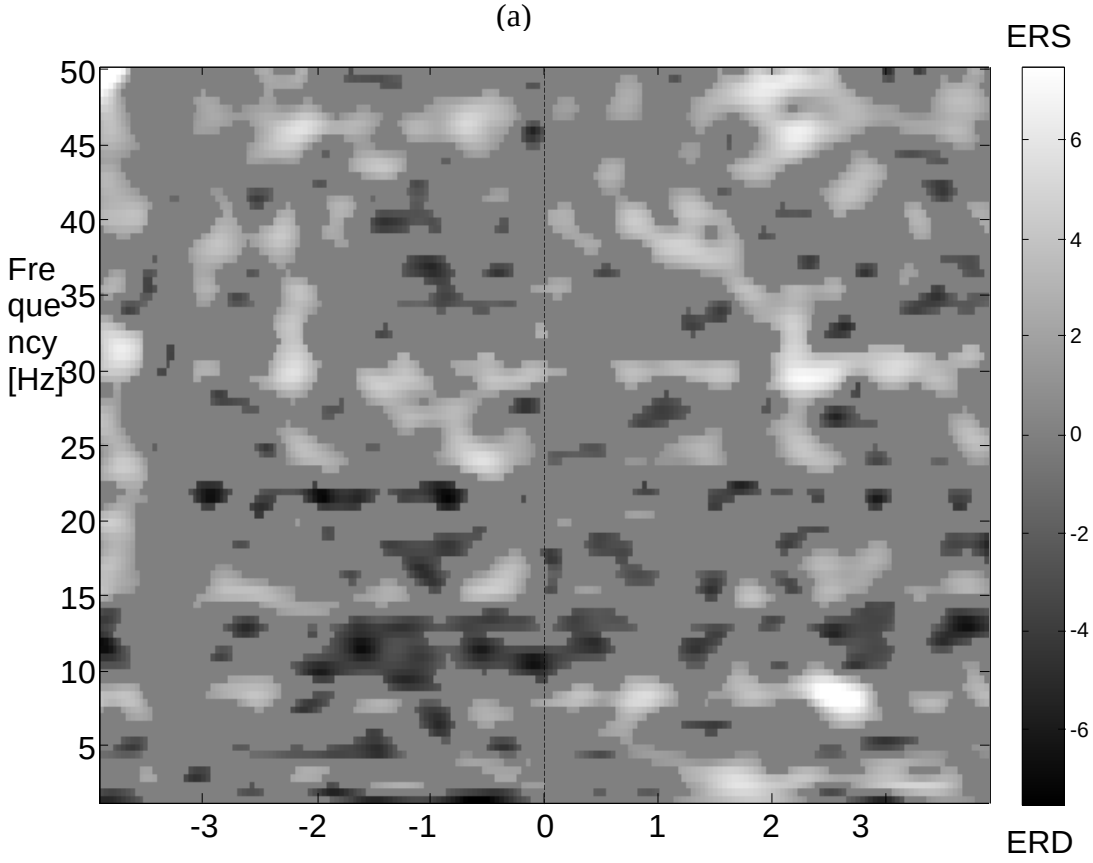

Frequency [Hz]
50
45
40
35
30
25
20
15
10
5
-3
-2
-1
0
1
2
3
Times [s]
ERS
6
4
2
0
-2
-4
-6
ERD

Figure 6

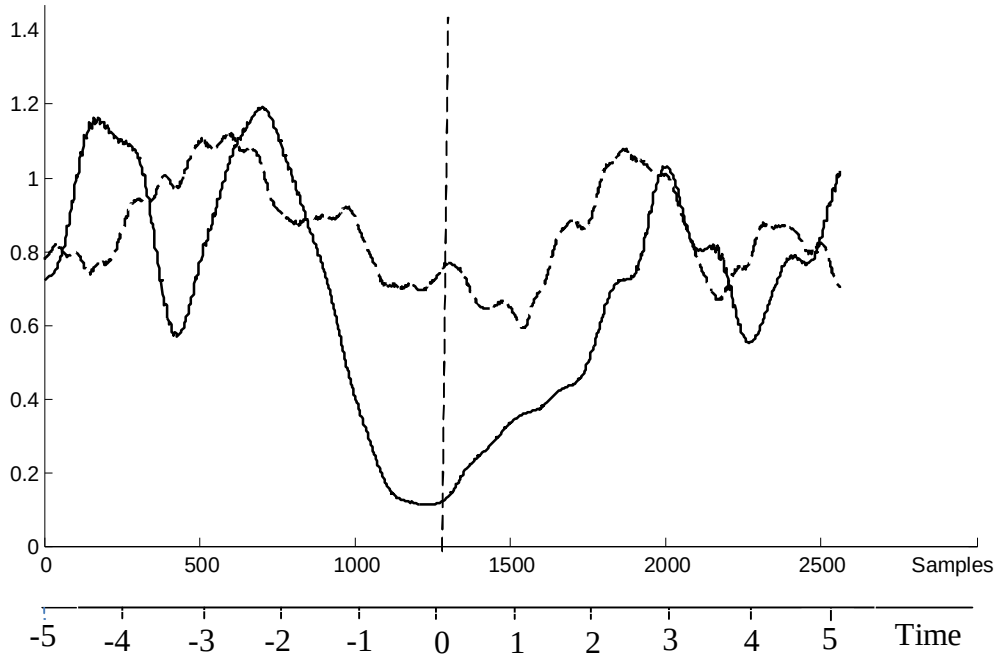

PSD
[µV2]
2.5
2
1.5
1
0.5
0
0
500
1000
1500
2000
2500
Samples
-5
-4
-3
-2
-1
0
1
2
3
4
5
Time

(a)

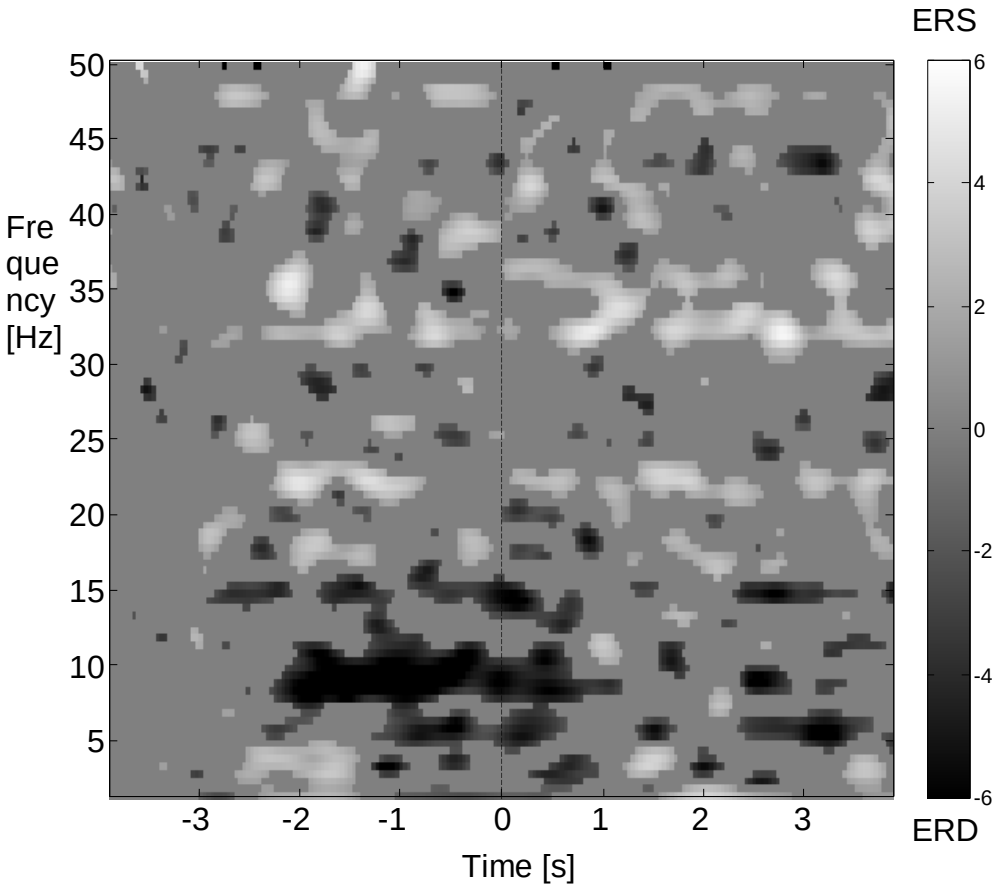

ERS
50
45
40
35
30
25
20
15
10
5
Frequency [Hz]
-3
-2
-1
0
1
2
3
6
4
2
0
-2
-4
-6
ERD

(b)

Figure 7

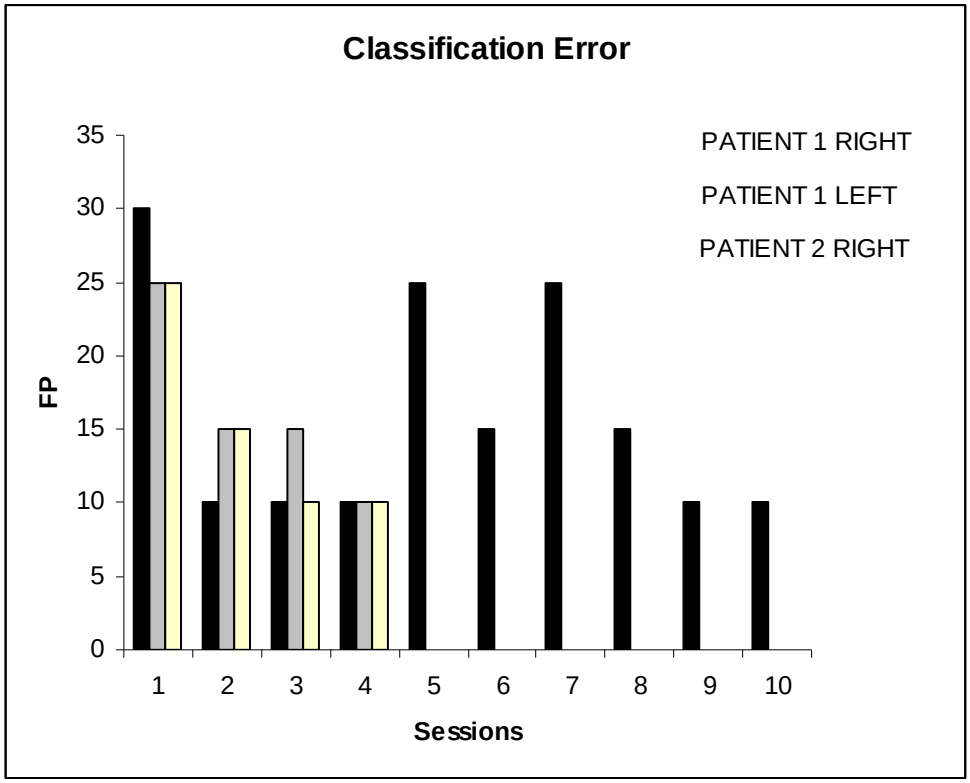

1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
500
1000
1500
2000
2500
Samples
-5
-4
-3
-2
-1
0
1
2
3
4
5
Time

(a)

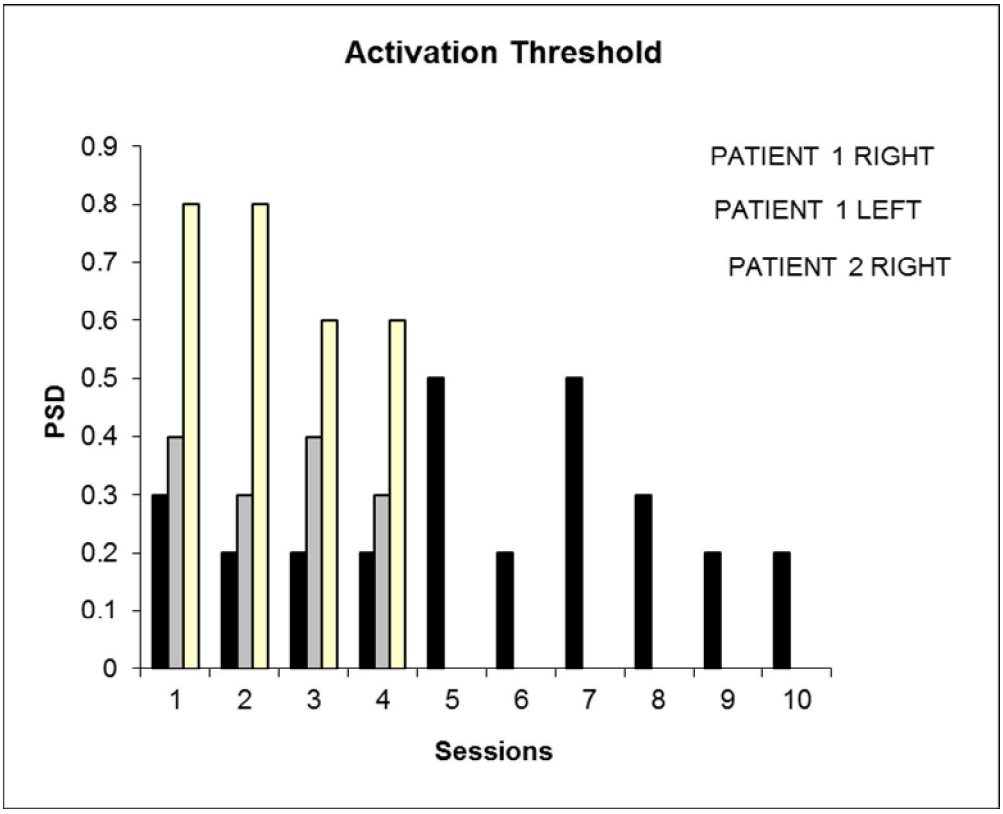

ERS
50
45
40
35
30
25
20
15
10
5
Frequency [Hz]
-3
-2
-1
0
1
2
3
Time [s]
6
4
2
0
-2
-4
-6
ERD

(b)

Figure 8

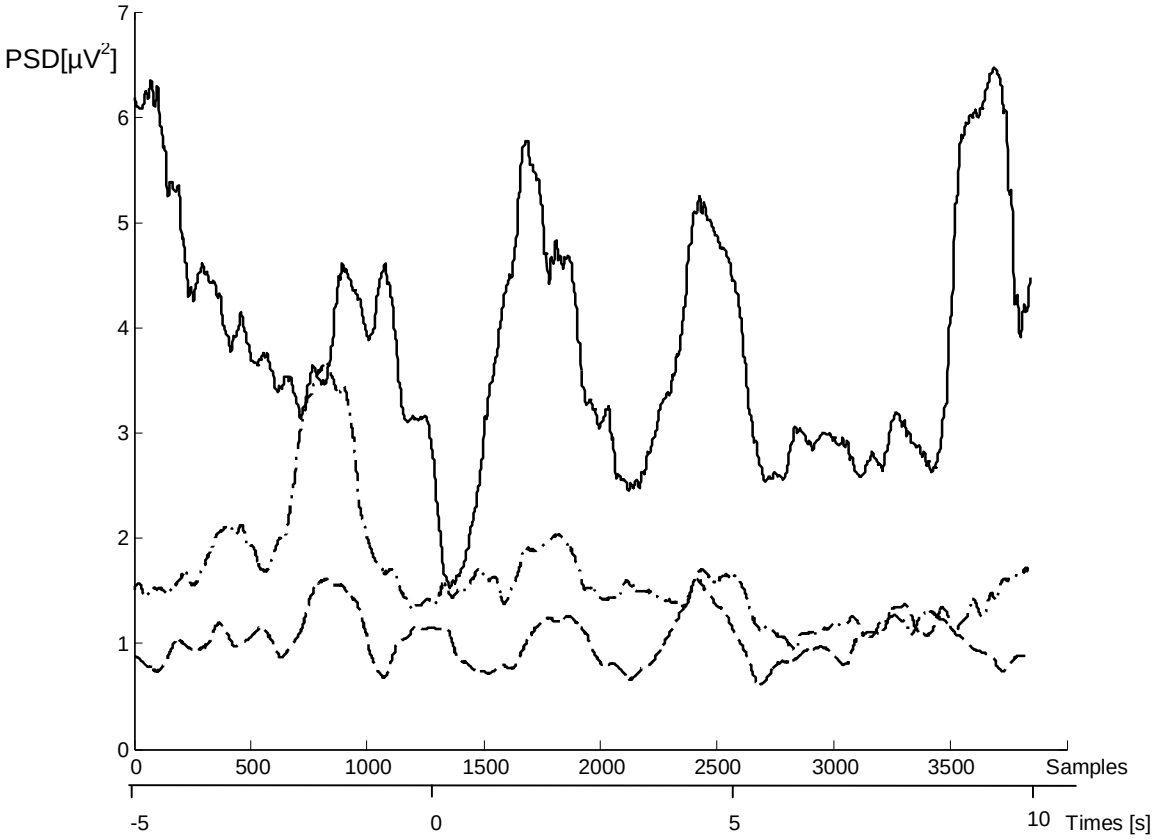

Classification Error
PATIENT 1 RIGHT
PATIENT 1 LEFT
PATIENT 2 RIGHT
FP
35
30
25
20
15
10
5
0
1
2
3
4
5
6
7
8
9
10
Sessions

(a)

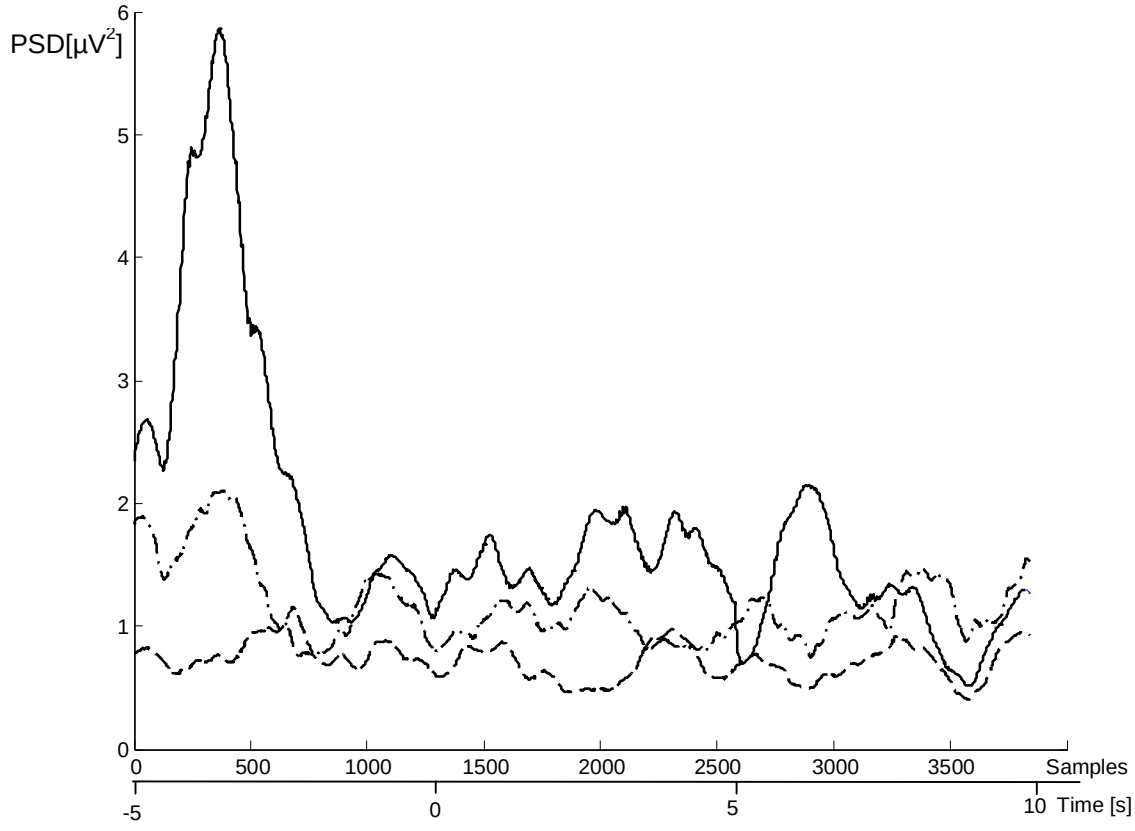

Activation Threshold
PATIENT 1 RIGHT
PATIENT 1 LEFT
PATIENT 2 RIGHT
PSD
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1
2
3
4
5
6
7
8
9
10
Sessions

(b)

Figure 9


PSD[μV²]
7
6
5
4
3
2
1
0
0
500
1000
1500
2000
2500
3000
3500
Samples
-5
0
5
10
Times [s]

(a)


PSD[μV²]
6
5
4
3
2
1
0
0
500
1000
1500
2000
2500
3000
3500
Samples
-5
0
5
10
Time [s]

(b)

Figure 10

(b)

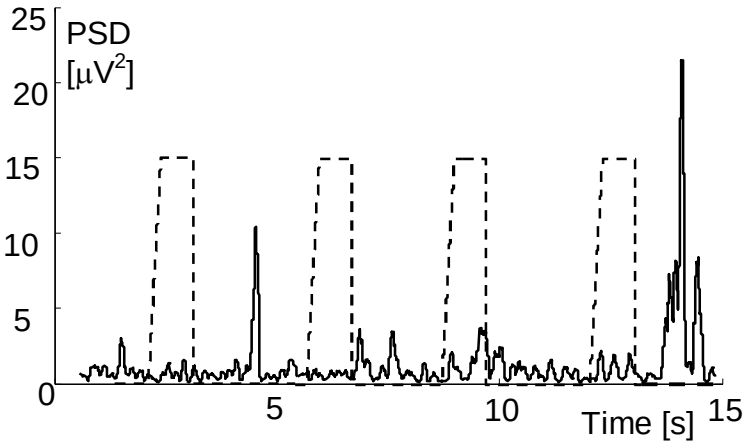
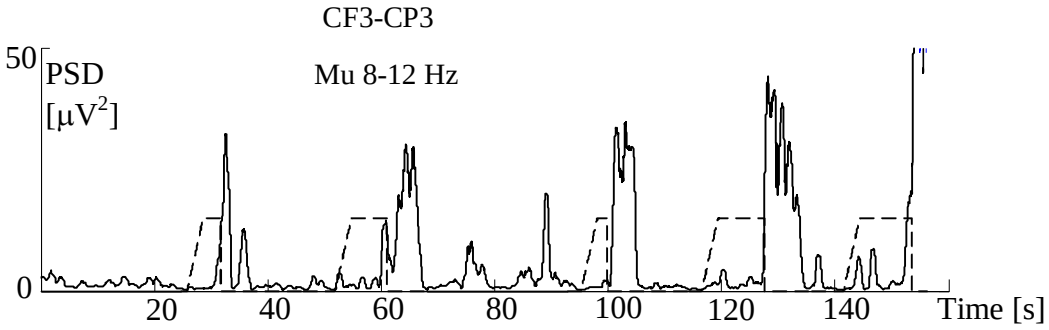
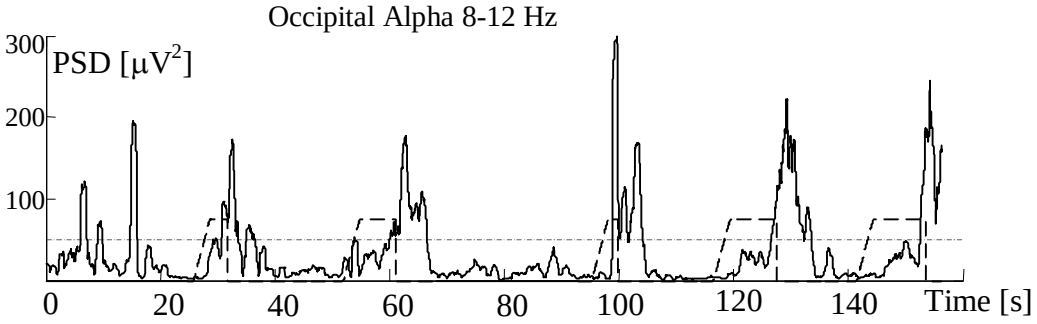


Figure 3

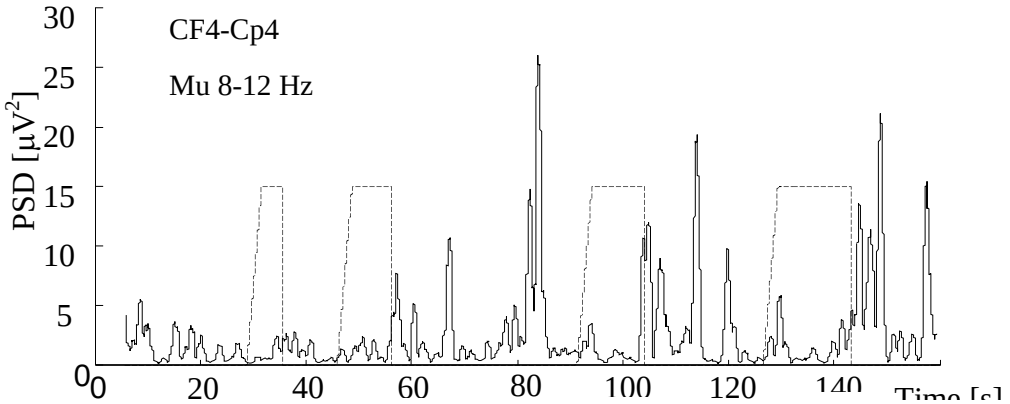

CF3-CP3
Mu 8-12 Hz
PSD
[μV²]
50
0
20
40
60
80
100
120
140
Time [s]

(a)

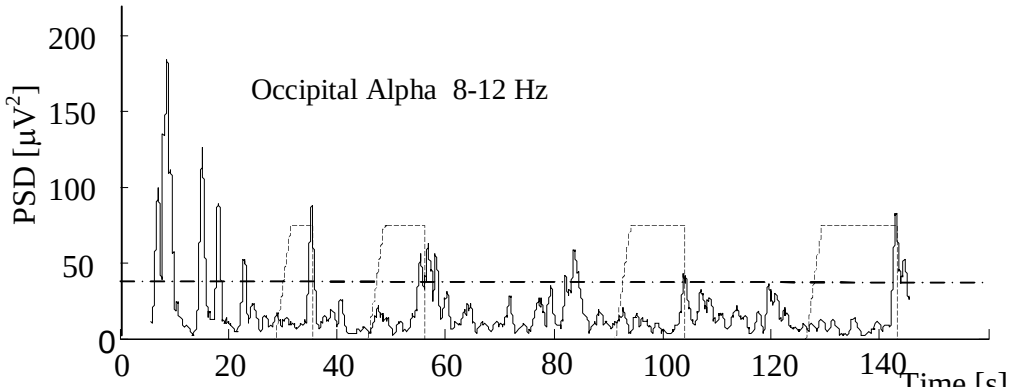

Occipital Alpha 8-12 Hz
PSD [μV²]
300
200
100
0
20
40
60
80
100
120
140
Time [s]

(b)

Figure 11


CF4-Cp4
Mu 8-12 Hz
PSD [μV²]
30
25
20
15
10
5
0
0
20
40
60
80
100
120
140
Time [s]

(a)


Occipital Alpha 8-12 Hz
PSD [μV²]
200
150
100
50
0
0
20
40
60
80
100
120
140
Time [s]

(b)

Figure 12