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Rehabilitating the motor circuits of the brain – Towards adaptive BCI-training after stroke

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REHABILITATING THE MOTOR CIRCUITS OF THE BRAIN – TOWARDS ADAPTIVE BCI-TRAINING AFTER STROKE

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Abstract

Loss of motor function after stroke substantially impacts the day-to-day life. In addition, the rehabilitation process is demanding and can require difficult physical exercises. Motor Imagery (MI), a technique where the user imagines the sensation of performing a movement, has been shown to activate similar brain activity as physically performing the movement. Brain Computer Interfaces (BCIs) with MI-based neurofeedback is a promising approach for rehabilitating loss of motor function without the use of physical exercise. For this technology to be used in rehabilitation, it is crucial that the neurofeedback reflects underlying neural activity that is functionally relevant for motor recovery. To this end, I believe personalisation is key. Therefore, in this thesis I have investigated important components for personalisation of a MI-BCI system for post-stroke rehabilitation. Specifically, I have 1) explored a distance-to-bound approach for adapting the BCI task difficulty, 2) investigated the impact of continual visual feedback on MI-related cortical activity, and 3) analysed the feasibility of extracting a novel motor-related feature.

I suggest that adjusting the difficulty of an MI-BCI, using distance-to-bound, targets stronger Event Related Desynchronisation (ERD) during neurofeedback training. However, strong ERD does not directly correlate with improved motor function, highlighting the importance for personalisation. I further provide evidence, in a group of stroke patients, that continual visual feedback does not interfere with the MI-related cortical activity, nor does it lead to stronger activity. Finally, I show that transient heterogenous features in the beta band, so called beta bursts can be extracted from both the lesioned and healthy hemispheres of stroke patients. These results contribute both methodologically and scientifically in building a stronger foundation of knowledge for the development of MI-BCI rehabilitation after stroke.

However, there is still need for more research to fully understand the complexity of neurofeedback stroke rehabilitation. I believe this thesis sheds light on important considerations when developing the different components of a BCI designed to promote motor recovery after stroke.

Sammanfattning

Förlust av motorisk funktion efter stroke påverkar i hög grad det dagliga livet. Dessutom är rehabiliteringsprocessen krävande och kan innebära svåra fysiska övningar. Motorisk föreställning (MI), en teknik där användaren föreställer sig känslan av att utföra en rörelse, har visat sig aktivera liknande hjärnaktivitet som vid fysisk rörelse. Hjärn-datorgränssnitt (BCI) med MI-baserad neurofeedback är en lovande metod för att rehabilitera förlust av motorisk funktion utan fysisk träning. För att denna teknik ska kunna användas i rehabilitering är det avgörande att neurofeedbacken speglar underliggande neural aktivitet som är funktionellt relevant för motorisk återhämtning. I detta syfte anser jag att personalisering är nyckeln. Därför har jag i denna avhandling undersökt viktiga komponenter för personalisering av ett MI-BCI-system för rehabilitering efter stroke. Specifikt har jag: 1) utforskat en "distance-to-bound"-metod för att anpassa svårighetsgraden i BCI-uppgiften, 2) undersökt effekten av kontinuerlig visuell feedback på MI-relaterad kortikal aktivitet, och 3) analyserat möjligheten att extrahera ett nytt motorikrelaterat signalmönster.

Jag föreslår att justering av svårighetsgraden i ett MI-BCI, med hjälp av "distance-to-bound", riktar in sig på starkare händelserelaterad desynkronisering (ERD) under neurofeedbackträning. Dock korrelerar inte ERD stark med förbättrad motorisk funktion, vilket understryker vikten av personalisering. Jag presenterar vidare bevis, i en grupp strokepatienter, att kontinuerlig visuell feedback inte stör MI-relaterad kortikal aktivitet, men inte heller leder till starkare aktivitet. Slutligen visar jag att korta heterogena signalmönster i frekvensbandet beta, såkallade betaburstar, kan extraheras från både den skadade och friska hemisfären hos strokepatienter. Dessa resultat bidrar både metodologiskt och vetenskapligt till att bygga en starkare kunskapsgrund för utvecklingen av MI-BCI-rehabilitering efter stroke.

Det finns dock fortfarande behov av mer forskning för att fullt ut förstå komplexiteten i neurofeedbackbaserad strokerehabilitering. Jag tror att denna avhandling belyser viktiga aspekter att beakta vid utvecklingen av de olika komponenterna i ett BCI-system som syftar till att främja motorisk återhämtning efter stroke.

I want to thank my friends and family
for their endless support

List of papers

This thesis is based on the following papers, which are referred to in the text as Papers A and B.

Paper A: Jonatan Tidare, Martin Johansson-Alvarez, Jeanette Plantin, Susanne Palmcrantz, Elaine Astrand. *"Exploration of using "distance-to-bound" to manipulate the difficulty during motor imagery BCI training after stroke – A clinical two-cases study"*. Preprint medXRiv.

Paper B: Martin Johansson-Alvarez, Jeanette Plantin, Susanne Palmcrantz, Elaine Astrand. *"Instantaneous neural effects of continual visual neurofeedback after stroke"*. Pending for submission to a journal.

The included papers have been reformatted to comply with the thesis layout. Reprints were made with permission from the publishers.

Contents

Part I

Thesis

1. Introduction

Stroke affects many people all over the world [36]. In Sweden alone, around 25 000 people suffer a stroke every year [1]. It can cause permanent damage to the brain that will give lasting disabilities [24]. If the stroke affects the primary motor cortex it often causes persistent motor impairments. Conventional rehabilitation methods for these cases require some sort of physical activity, which can be challenging for individuals with severe motor disabilities following a stroke [27]. Mental imagery or more specific Motor Imagery (MI) is a method where the subject mentally imagines a specific physical movement. There is a long line of studies showing that the neural substrates of MI and those of real physical movements are highly overlapping [23]. Following this, MI has shown great potential in stroke rehabilitation since it does not require the use of physical movements but still stimulates the same area of the brain [8], [31].

Neurofeedback training is used to guide the participant to self-regulate neural substrates in order to train and reorganise the brain [51]. Electrical activity from the brain is recorded and analysed in real time to provide feedback for the participant in the form of visual, auditory, or another representation of this activity. For motor rehabilitation purposes, visual feedback is particularly useful since it can be represented by the movement of the targeted motor function [4]. Utilising MI to form the base features for the feedback would allow the patient to self-regulate neural substrates associated with motor functions [23].

To apply neurofeedback training in a controlled manner, a Brain Computer Interface (BCI) is usually developed. The BCI involves both hardware and software that allows brain signals to be recorded, processed and digitally analysed in real time. Common signal acquisition systems include Electroencephalography (EEG), Magnetoencephalography (MEG), and Magnetic resonance imaging (MRI) [30]. EEG is widely used in BCIs due to its high temporal resolution [25]. This is an important factor when applying neurofeedback in real-time, to allow for a responsive system and promote direct neural self-regulation. While feedback is not always incorporated in BCI systems, it is a crucial component in neurofeedback, where it enables a closed-loop neural learning environment [51].

While MI-BCIs have shown promising outcomes, identifying EEG features that are functionally relevant for motor improvement remains an outstanding research challenge of this technology. This challenge is further complicated by the fact that the features identified might not be the same for different patients. In addition to the already high variability observed in the brain of the healthy population, the heterogeneity displayed in stroke patients caused by

differences in extension and location of the lesion [28], makes personalisation essential .

This thesis aims to investigate the key components for a successful personalised MI-BCI system with the goal of obtaining a better understanding of what is important in promoting learning and neural reorganisation for stroke patients. This includes: i) adapting the difficulty of the BCI for the user to help target activity relevant for learning, ii) investigating the effects of continual visual feedback and how it affects the neural activity during MI feedback training, and lastly, iii) this thesis investigates a novel method of extracting behaviourally relevant features in the EEG data that could be leveraged for neurofeedback training.

2. Background

Stroke is caused by cerebral ischemia or hemorrhage, which prevents oxygen and nutrients from reaching brain cells, potentially leading to significant neurological damage. Without the supply of oxygen, the neurons of the affected area die and can no longer transmit neurological information. The stroke can occur in any region of the brain and will affect the person differently depending on the size and area of the brain lesion. Memory loss, difficulty speaking, spasticity, and physical impairment are among the common symptoms following a stroke, not to mention the potential for a fatal outcome. Stroke survivors suffer lifelong disabilities that can hinder day to day activities substantially, both physical and mental. If the stroke affects the motor cortex, or areas around it, the ability to move and control the limbs is usually decreased. In severe cases, motor function in the affected limb may be entirely lost. Conventional rehabilitation for motor impairment after stroke is typically physical and require some form of motor activity to be efficient. This excludes patients with severe motor impairments and with minimal to no movement in the targeted limb [27]. This thesis investigates novel methods to include this demographic of stroke patients in the neurorehabilitation process.

2.1 Motor imagery

MI is a mental exercise in which you imagine the movement of a body part [11]. You can imagine either a visual representation of the movement (visual MI) or the sensation you feel when you move that body part (kinaesthetic MI). The latter have been shown to produce brain activity similar to that of performing the actual physical representation of the movement, e.g., motor execution (ME) [23]. Earlier studies show that even with a brain lesion, stroke patients are capable of performing MI [8]. However, exceptions have been documented for lesions in the parietal region. MI has shown promising results when applied as a rehabilitation method to promote brain plasticity and improve physical recovery after stroke [49]. MI would allow stroke patients with severe motor impairment to perform therapeutic exercises similar to physical rehabilitation without the need for difficult motor movements.

2.2 Brain computer interface

When applying MI as a rehabilitation method, it can be hard to know if the mental activity is targeting the relevant areas in the brain. There are no ex-

ternal indicators for the patient or physician to make good judgement on the exercise. When comparing MI training with lifting weights, the weights give immediate sensory feedback, such as feeling the resistance, seeing the movement, or sensing muscle fatigue. BCIs can assist both the patient and physician in obtaining similar perceivable representations of the MI task. A BCI is a direct link between the brain and a computer. It records the neural activity, makes necessary processing and provides the user with feedback. Common signal acquisition methods are EEG, MEG, and MRI. The signal is then digitised and saved as a data, representing the brain activity. This data can then be used to give a visual representation of the activity, or be decoded using signal processing and intelligent multivariate classification algorithms to control external devices or provide feedback. Figure 2.1 represents an example of a BCA setup where the feedback is given as a moving hand on a screen.

2.2.1 Feedback

The feedback mechanism in BCI systems plays a critical role in facilitating user learning, system adaptation, and overall performance. Feedback can be categorized into several types based on modality, timing, and continuity. Feedback may be visual, auditory, haptic, or multimodal, where multiple sensory channels are combined to enhance user engagement and data transfer.

In terms of temporal characteristics, feedback can be continuous, providing real-time updates on the streamed neural activity, or discrete, where feedback is given at specific intervals or upon task completion. Another important distinction is between direct (immediate) and delayed feedback. Direct feedback allows users to instantly perceive the consequences of their neural activity, which is essential for controlling external devices. In contrast, delayed feedback does not require the system to be real-time and can operate with limiting computational power, though it can reduce the intuitiveness and responsiveness of the system [33].

Feedback enables a neural learning environment that stimulates neural plasticity and promotes learning [20]. This neurofeedback driven BCI technology has shown promising results for neural reorganisation and rehabilitation [51]. Together with MI, a neurofeedback BCI can give the user direct response of their intended motor movement. Hence, providing indications on how well the MI is performed.

2.3 Electroencephalography

EEG is a neurophysiological method used to record electrical activity generated by neuronal synchronisation in the brain. It captures voltage fluctuations resulting from ionic current flows within neurons, offering high temporal resolution that makes it particularly suitable for studying dynamic brain processes

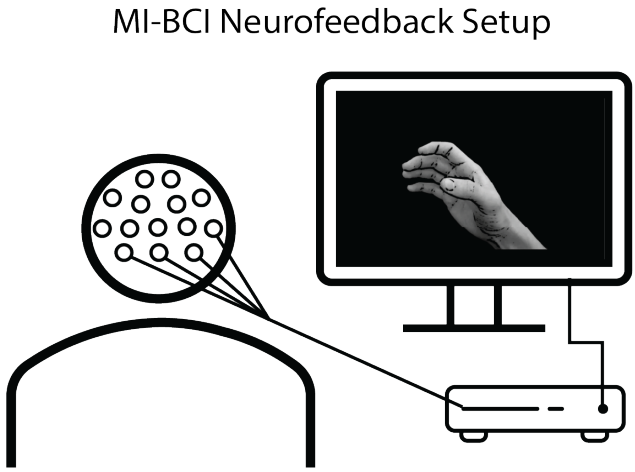

Figure 2.1. A BCI participant (left in the figure) has an EEG cap mounted on the scalp (64 Ag/AgCl active electrodes positioned according to the international 10/10 standard). The EEG is connected to a BCI that excecutes signal-processing and prediction in real-time. The feedback, based on the neurological activity, is presented in the form of a moving hand on the screen (seen to the right in the figure).

such as perception, attention, and motor control [13]. EEG can be applied either invasively, with electrodes placed directly on the cortical surface, or non-invasively, using surface-mounted electrodes positioned on the scalp. The latter approach does not require surgically implanted electrodes, but typically yields noisier signals due to the attenuation and interference introduced by the scalp and skull. The spatial resolution of an EEG is also limited to the amount of electrodes applied. A standard EEG systems typically utilise electrode arrays with 32, 64, or 128 channels, depending on the spatial resolution required. However, with its high temporal resolution and continuously streamed data it is particularly well-suited for online BCIs [5]. Despite its limited spatial resolution compared to imaging techniques like MRI, EEG remains a valuable tool due to its portability, cost-effectiveness, and ability to monitor brain activity in real time [5].

2.3.1 Signal processing

As previously mentioned, EEG signals are inherently susceptible to noise. They are often contaminated by physiological artifacts originating from muscle activity (electromyographic artifacts), eye movements and blinks (electrooculographic artifacts), as well as cardiac activity (electrocardiographic artifacts). Cardiac activity and eye movements typically produce low-frequency

artifacts, generally within the 1-4 Hz range, while muscle activity generates higher frequency artifacts, often exceeding 30 Hz. Sensorimotor activity from the brain tends to oscillate in the alpha and beta frequency bands (8-30 Hz) [32]. Artifacts can be attenuated using frequency band-pass filters, which isolate relevant neural oscillations while suppressing noise. Additionally, time-frequency decomposition techniques, such as wavelet transforms or short-time Fourier transforms, enable the representation of EEG data across both temporal and frequency domains, facilitating the extraction of features that are specific to particular time intervals and frequency bands. Selecting electrode channels over targeted neural substrates allows for additional spatial isolation. Finally, averaging the data across frequency bands and electrode channels yields a time-resolved representation of the neural activity, which can be quantified and expressed as power in decibels (dB).

2.4 Motor-related features

For a neurofeedback BCI system to produce feedback based on functionally relevant activity, we need to find features in the data that represent the desired activity. A reduction in EEG power over the sensorimotor cortex is commonly observed during motor planning and activation, reflecting task-related cortical desynchronisation of neurons involved in preparatory and execution-related processes [42], followed by an increase in power when the motor execution is completed. This phenomenon is referred to as Event-Related Desynchronisation/Synchronisation (ERD/ERS), with ERD specifically indicating decreased power in the alpha and beta bands over sensorimotor regions during motor-related activity. Since the features are observable during motor-related activity, it can also be seen during MI. Figure 2.2 shows the mean power over multiple trials and ipsilesional channels in the alpha band during an MI task. A distinct dip in power (increased ERD) is observable around the task onset, indicating imagined motor planning and execution. This ERD is sustained through the task and subsides when the task is completed. These features in the signals can be used to predict MI tasks by utilising, for example, threshold techniques or machine learning algorithms like Support Vector Machine (SVM).

2.4.1 Transient rhythms

ERD is limited in the sense that power is required to be sustained over a period of time and averaged over multiple trials to give reliable features. Instead of sustained rhythms over time, activity in the beta frequency band has lately been characterised as short transient and heterogenous events with high-amplitude power spikes during single trials [7], [17]. These beta bursts, as they are termed by the community, can be characterised by their peak amplitude,

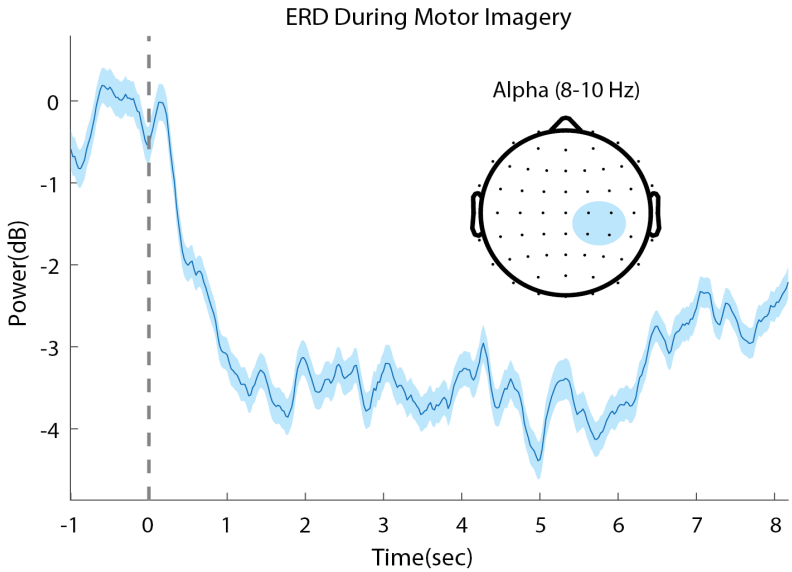

Figure 2.2. ERD represented in power(dB) over time(sec) for one patient during an MI task. The shadowed area is standard error over all trials. Power is calculated from the average over all trials, channels on the ipsilesional hemisphere (inserted topographical plot), and alpha frequencies (8-10 Hz). Dashed vertical line indicates task onset.

timing and duration, peak frequency and frequency span, or the overall waveform of the signal within a limited time window around the burst, as well as the amount of bursts and its rate [35], [22], The burst rate of high-amplitude bursts generally follows the temporal dynamics of ERD observed during sensorimotor activity [53]. Additionally, by analysing burst activity instead of continuous power variations, it allows for a more detailed analyses on modulations of specific burst waveforms. It also provides time-specific features during a single trial, which power lacks when looking at the ERD. Even though ERD and other power based features are generally more studied for BCIs, bursts can offer complementary information and potentially improve classification of motor activity during MI.

3. Methods

In this thesis, I analyse data collected from non-invasive EEG signals collected during MI tasks with an animated hand on a screen as feedback, see Figure 2.1. The BCI in this project had 62 EEG electrodes placed on the surface of the scalp of stroke patients (actiCHamp, Brain Products), with the remaining two electrodes used for horizontal eye movements and reference. Additional sensors such as electrooculography (EOG) for vertical eye movements, electromyography (EMG) for arm muscle activity, and accelerometers for finger and hand movements were simultaneously used during the sessions. The data was processed in an online fashion and machine learning models were created to classify and predict motor activity. In this specific study SVM was used, as it is fast and handles multiple dimensions well. Feedback was determined by the SVM with successfully predicted MI activity giving positive feedback by moving the hand on the screen frame by frame in the desired direction.

3.1 Intervention setup

The results in this thesis are derived from two different neurofeedback interventions, a pilot study and a main study. The pilot study was a proof-of-concept intervention in which two stroke patients practices MI with an EEG-based BCI over a period of multiple weeks. An in-house BCI was developed to provide the patients with instructions, analyse and decode data, and provide feedback to the patients. The main study was based on the early findings of the pilot, from which the BCI was refined and improved. In this study, 16 stroke patients were recruited to a similar intervention as the pilot study, spanning over 10 weeks. However, only 14 patients completed the neurofeedback training and results from these will be presented in this thesis.

3.1.1 Pilot study

The pilot study included two patients with chronic ischemic stroke in the left hemisphere (<6 months prior to study entry). They undertook an intervention consisting of three EEG calibration/baseline recordings during the first week of the EEG measurements, followed by 12 BCI training sessions over four weeks, and lastly one evaluation session. Clinical test sessions were performed at baseline (once/week during three weeks), during the BCI training

(once/week) and at evaluation (once) by a trained physiotherapist. Lastly, two fMRI (functional MRI) recordings were conducted, one before and one after the BCI training phases.

In each EEG session, the patients sat in front of a screen with a surface mounted EEG cap applied on their head as shown in Figure 2.1. The protocol in the calibration and evaluation sessions (as well as the fMRI sessions) involved multiple MI and ME tasks in which the patient was instructed to imagine or attempt to grasp and release the paretic hand. The neurofeedback sessions included only MI and idle tasks. During MI, the patient received feedback in the form of a moving hand on the screen. The screen hand moved based on predefined features in the brain data that were predicted using Support Vector Machine (SVM). The SVM model was built from data during the calibration sessions and a short calibration session held before every neurofeedback session. A more detailed description of the pilot study can be found in paper A.

3.1.2 Main study

From initial results of the pilot study, an intervention with a larger sample of patients was initiated. A total of 14 patients with chronic stroke completed the intervention and the project followed a similar structure as the pilot study with some differences in the protocol. In terms of EEG, it was comprised of 3 baseline sessions (once/week), 12 neurofeedback sessions and 3 evaluation sessions, spanning 10 weeks. The baseline and evaluation sessions were the same as the pilot study, using a refined protocol for instructions. We substantially changed the procedure for building the classification models used for determining the feedback. The SVM models for the neurofeedback sessions did not include data from the baseline session. The models were instead adaptive and the weights were retrained every new MI trial during the BCI sessions. The main reason for the change was to allow for the model to follow evolving cortical activity across the intervention. As well as to reduce the recording time by eliminating trials only used for model training. Every session also starts from a blank model, which adapts to the state the patient is in at that specific time, giving a more personalised experience. This study also included a new task during BCI training named Motor Observation (MO), where the patient watched the feedback received in the previous MI task. The idea was to complement the idle task by including a task where the visual stimuli are included. During the 10 weeks of intervention, the patients also had one clinical test session per week, as well as two fMRI sessions before and after the neurofeedback training sessions, to evaluate the progression of motor function and neural reorganisation throughout the intervention. A more detailed description of the main study can be found in paper B.

3.1.3 Ethical considerations

All patients participated voluntarily and could at any moment interrupt the sessions or cancel their involvement in the study. Collected data was pseudo-anonymised and patients were only referred to as untraceable id-numbers. All EEG recordings were performed at Danderyd Hospital, Stockholm, Sweden and instructions were received in case of emergency or need of medical help. Only stroke-related information was considered when screening for participants, e.g. ethnicity or gender was not considered.

The pilot study has been conducted in accordance with the principles embodied in the Declaration of Helsinki and complied with local rules and regulations according to the Swedish Ethics Review Authority (Dnr 2019-01577). The study was registered as a clinical trial at clinicaltrials.gov (NCT03994042). Both participants signed a written informed consent form before participating in this study.

The main study adhered to the Declaration of Helsinki and was approved by the Swedish Ethical Review Authority (Dnr 2022-00713-01) as well as the Swedish Medical Agency (CIV-21-10-037847). The study was registered as a clinical trial at clinicaltrials.gov (NCT04847089). All patients participated voluntarily and provided informed written consent.

4. State of the Art

When using BCIs for stroke rehabilitation, it is important to consider the individuality of each patient [56]. Current BCI studies often focus on classification accuracy and availability. Availability is of high importance for stroke rehabilitation and previous studies have made arguments for subject-independent EEG-based BCIs outperforming subject-specific ones, when it comes to classification accuracy on the healthy population [48]. However, subject-independent models would need more research on how effective they are for stroke patients due to their hemispheric asymmetry. Another solution is adaptive BCIs that have also seen recent development in accuracy, outperforming subject-specific models [46]. However, when it comes to MI stroke rehabilitation, high classification accuracy of the system does not necessarily equal to better recovery. Neurorehabilitation after a stroke is based on activity-driven neuroplasticity (the ability to reorganise the structure and function of the brain in response to activity and experience) [20], and having a system that provides successive challenges is of higher importance for recovery [19], [29]. In this thesis I introduce a method where the difficulty is adjusted based on the distance-to-bound of an SVM in order to offer progressive challenges.

A BCI system can be tiring to use, especially for stroke patients who are already susceptible to brain fatigue [16]. A decrease in beta activity can be an indication of mental fatigue [3]. In a previous study, including eleven stroke patients, they used an MI-BCI system with visual feedback, evaluating the efficiency of the system and the correlation between accuracy and mental fatigue [26]. They found a strong correlation in frontal and central channels between the relative beta power and the accuracy of the MI-BCI performance. The results of this study show that the use of a BCI system might potentially cause mental fatigue in stroke patients, using visual feedback. In this thesis, I evaluate the effects of visual feedback from a dual task perspective. Specifically, it may be challenging for the user to perform both a mental task and at the same time process the information from the feedback.

The literature is limited on the effects of feedback in neurorehabilitation for stroke patients and more research is needed. One study is planning a double-blinded randomised controlled trial where they will compare neurofeedback with a sham BCI for subacute stroke, claiming there is not enough research on the effect of neurofeedback for that subgroup [34]. However, there are no results as of writing this thesis. Earlier studies have shown improved clinical function after the use of neurofeedback-driven BCIs compared to a control group. One study saw an increase in upper limb Fugl-Meyer-Assessment score

(FMA) after the use of BCI compared to a control group [43]. Similarly, another study observed a lasting reduction in impairment when using functional electrical stimulation (FES) as feedback for their BCI system compared to a group using a sham FES [14]. All of these studies compare two different testing groups, focusing on the difference between the groups. In contrast, I use an intra-patient approach and analyse differences in sensorimotor activity with and without feedback (specifically visual feedback) during the same task. This puts the focus on the underlying neural activity that may potentially explain the reason for the differences found in the earlier studies.

To obtain functionally relevant and useful outcomes from the BCI training, it is important that the underlying features in the data, reflected in the feedback, are related to the intentions of the user. Recent research is questioning conventional methods of extracting features from averaged band-limited power over trials, as they do not reliably represent underlying mechanisms of the brain, specifically in the beta band [7], [17]. Instead, in individual trials, it has been demonstrated that beta activity occurs as transient bursts, labelled in the community as beta bursts [53]. Using this theory, a pipeline has been developed for signal processing and feature extraction for MI-EEG data [39]. They show that their method offers better decoding performance and improved decoding speed when compared to conventional methods. In this thesis, I have applied beta burst feature extraction and evaluated how bursts are characterised in the brain of stroke patients, with the aim of evaluating its potential in BCI rehabilitation after stroke.

5. Research overview

5.1 Problem formulation

In this thesis, I aim to investigate a novel rehabilitation method that utilises MI-BCI to help stroke patients reorganise neurons in the brain and promote motor function in the upper limb extremities. MI together with neurofeedback-based BCIs have already shown promising results in targeting and reorganising neural activity in motor areas [51]. However, finding relevant features in the signals and adapting to individual variability are challenges not yet resolved [10]. Consequently, utilising MI-BCI for stroke patients is still in its infancy and needs more research in order to be fully developed. I want to investigate key components of the BCI in order to provide relevant feedback for self-regulation of neural substrates to promote stroke rehabilitation of hand movements using MI.

Everyone has different brain profiles, but for stroke patients the difference is even larger due to the heterogeneity of the lesion (location and extent) and variability in neural reorganisation following the stroke [28]. Having a BCI that adapts the difficulty to the user level is crucial to make the neurofeedback rehabilitation accessible to all. A conventional neurofeedback system uses frequency band-limited features from EEG data to be used as information for the feedback [39]. This activity varies substantially between subjects and can cause the system to give positive feedback only to high performers. Many users will experience the feeling of unresponsiveness that can lead to a drop in motivation, which reduces the chances of learning [44]. This will restrict many users from utilising the full potential of the BCI and will result in less positive clinical outcomes. It is important for the system to provide feedback based on the level of the user to promote motivation and learning.

Receiving relevant feedback is crucial for a successful neurofeedback system. However, there are still unknown effects that feedback can have while performing a task simultaneously [34]. A posterior alpha decrease has previously been observed when visual neurofeedback is provided online [50]. This could potentially disrupt the concentration of the users and reduce their engagement within the given task. The research on how visual feedback should be provided within a BCI framework is scarce. It is important to investigate how the feedback affects the targeted subject group and choose the feedback appropriately. Stroke patients often have reduced cognitive abilities and may experience difficulties concentrating on the task while processing feedback. Therefore, an understanding of how visual feedback impacts the cortical activity produced during MI is essential for the development of BCIs for stroke rehabilitation.

Further, BCIs often utilise machine learning or artificial intelligence (AI) to decode information from brain activity in real-time [18]. These models are used to predict the intention of the user and provide feedback accordingly. This enables a closed-loop neural learning environment in which patients can self-regulate their neural activity in order to achieve neural plasticity. AI does not only decode complex patterns of activity or facilitates a data-driven intelligent approach to generate feedback, it also allows the development of personalised protocols tailored to the user. However, when it comes to BCI rehabilitation, it is important that the neural substrates that underlie the AI model are functionally relevant for recovery. Applying AI for BCI rehabilitation is still uncharted territory and more research is needed to understand what features are appropriate for the model [6]. According to Szul et.al. sustained power over time does not reliably represent movement preparation and performance [53]. Many studies, including my own, use sustained power to predict motor activity, but it does not give accurate enough features to distinguish certain movements, such as opening and closing the hand [55]. Investigating alternative methods for feature extraction is crucial for a fully adaptable BCI system. Beta bursts are unexplored in stroke patient data and could provide further information on the reorganised neurons around the lesioned area.

Different brain profiles in stroke patients suffer various restrictive effects and it is important to evaluate the system design thoroughly to make sure the neurofeedback BCI training is relevant for recovery. The key factors investigated in this thesis are the adaptability of the protocol of tasks, the interference of the feedback provided, and the potential of using beta bursts as more relevant features in stroke patient data for neurofeedback systems.

5.2 Research Questions

Protocol setup, feedback, and feature extraction are all key factors when designing a BCI. Personalising the BCI is of high interest, especially for stroke patients due to their heterogenous brain profiles. This thesis aims to investigate these key factors of the BCI with the intention of obtaining a better understanding of what promotes learning. I further aim to suggest methods to personalise the experience for the user. The analysis and results of this thesis are based on the following research questions:

- **RQ_1: How can the difficulty-level during BCI training be adjusted and adapted online?**
  All BCIs include a protocol that guides the user in performing the tasks during training. The cortical activity of the patient is often directly translated to feedback in various forms. Each individual is different and will perform the tasks differently. If the protocol is designed to provide feedback directly related to the cortical activity, users with lower classification accuracy might experience lack of responsiveness. This could

reduce motivation and give negative effects to the learning outcomes. If instead the system adapts to the performance of the user, this might increase motivation and allow patients to better improve during training. This RQ is addressed in paper A in which a distance-to-bound approach is explored.

- **RQ_2: How does continual and simultaneous visual feedback influence the ability to perform Motor Imagery tasks for stroke patients?** Feedback is a vital part in a neurofeedback system. It is supposed to guide the user to self-regulate the neural substrates and boost learning. However, there are still many unknown effects feedback can have on the subject. Performing MI tasks simultaneously as receiving feedback could create confusion and cause lack of concentration. Especially for stroke patients that suffer from reduced cognitive abilities. This RQ is addressed in paper B, which investigates the instantaneous neural effects of continual visual MI-neurofeedback in contrast to providing no feedback within the same trial.
- **RQ_3: How are transient and heterogeneous events in the beta band manifested in stroke patients during motor-related processes?** Recent studies on beta activity during motor activation show strong evidence that it is more accurately represented as heterogeneous bursts rather than sustained power over time. Sustained power has through the years been well studied for motor activity, compared to bursts. However, power lacks the individual temporal features, during a single trial, that bursts have, which is a limiting factor when used as the basis for a neurofeedback system. With a more accurate representation of the motor activity, I believe beta bursts can uncover features that can help personalise the BCI for the unique brain profile of the stroke patient. This RQ is addressed in the beta burst analysis section under thesis contributions, where a novel beta burst detection algorithm is applied on stroke data.

5.3 Research methodology

The research method used in this thesis is an explorative approach using quantitative EEG measurements. The research is based on previous work, in which the results sparked new theories with the need for further analysis. A larger project was formed from these theories that included methods to analyse them. Quantitative data was collected from a predefined BCI where the subjects performed tasks given by a set protocol. Further analysis was done post sessions to investigate patterns and anomalies from multiple subjects.

An empirical research process is used in this thesis. The research problem is first identified followed by a literature review and a research project to evaluate the problem. From the research project, the initial research questions are formed. EEG recordings have been collected continuously at the same time as

analysis of the recorded data. With the analysis, a proposed solution is formed and evaluated. The answer to the research question depends on the findings in the evaluation, and if needed a new problem formulation was formed.

6. Thesis contributions

6.1 Included papers

This section covers the overview of included papers in this thesis.

6.1.1 Paper A

Title: Exploration of using "distance-to-bound" to manipulate the difficulty during motor imagery BCI training after stroke – A clinical two-cases study
Authors: Jonatan Tidare, Martin Johansson-Alvarez, Jeanette Plantin, Susanne Palmcrantz, Elaine Astrand
Status: Preprint medXRiv
Abstract: Objective: Motor Imagery-based Brain-Computer Interfaces (MI-BCIs) is a promising technology for neurorehabilitation after stroke. However, many face challenges in using a BCI because they fail to produce discriminable patterns in their brain activity. Personalizing the BCI task difficulty could help the learning process of these users but there is currently very limited knowledge on which methods can be used online. Our aim was to explore a distance-to-bound approach for adapting MI BCI task difficulty in real time.

Approach: Two chronic stroke patients performed 12 BCI training sessions over 4 weeks during which they performed MI of open- and close hand movements and received continual visual feedback based on multivariate decoding of ongoing electroencephalogram (EEG) activity. We increased the difficulty and maintained it by adapting it in real time based on distance-to-bound decoding metrics and using a multiple-session design we investigated the stability of this approach and how it related to MI-related EEG activity of each patient.

Main results: We show that patients had to produce stronger alpha and beta event-related desynchronization (ERD) activity across the sensorimotor cortical areas of the brain to receive positive feedback. In addition, we show that the online adaptation converged within sessions as well as accommodating for drift in the data both within and between sessions. We suggest that the distance-to-bound approach can effectively be used to control BCI task difficulty and potentially guide patients to produce functionally relevant activity patterns. However, from our results, stronger sensorimotor ERD activity did not consistently correlate to improved motor function. Clinical assessments showed that both patients improved in motor function (+4 and +8.7 change in Fugl-Meyer assessment for upper extremity), however, the correlation to sensorimotor ERD activity was positive for one patient and negative for the

other (Pearson's rho = 0.95,-0.80, p = 0.05, 0.18). These results indicate that the translation of distance-to-bound outputs to feedback needs to be individually tailored considering the stroke lesion and EEG activity profiles for each patient.

Significance: This study provides valuable insights and considerations for BCI difficulty adaptation in the aim of developing more effective training protocols in BCI-based stroke rehabilitation.

My contributions: I performed analysis on the data already collected that led to some of the results presented in the paper. In particular, I contributed to the results of the adaptive threshold analysis. I also participated in the the draft and final writing process.

6.1.2 Paper B

Title: Instantaneous neural effects of continual visual neurofeedback after stroke

Authors: Martin Johansson-Alvarez, Jeanette Plantin, Susanne Palmcrantz, Elaine Astrand

Status: Pending for submission to a journal

Abstract: Objective: Neurofeedback training using motor imagery-based brain-computer interfaces (MI-BCIs) show promising but variable outcomes in chronic stroke rehabilitation. However, little is known on the dual task effects of feedback when simultaneously performing a mental task. This becomes especially relevant for cognitively challenged patient groups. This study aims to investigate instantaneous effects of continual visual feedback on neurophysiological activity while stroke patients practised MI during BCI training.

Approach: Fourteen chronic stroke patients participated in a 10-week long intervention, with 4 weeks of intense MI-BCI training. During each MI training trial, patients were instructed to mentally imagine either opening or closing their paretic hand while being provided continually updated visual neurofeedback only during the last part of the trial (after 4 seconds). We analysed patient-specific spatial and temporal dynamics of peak frequency power related to MI with and without feedback, and analysed the correlation of changes to blink rate, and clinical motor- and cognitive abilities.

Main results: Individual MI-related peak frequency of event-related desynchronisation (ERD) across sensorimotor areas was mainly found within the Alpha band. Two peak ERD patient profiles were observed: dominant ipsilesional (43% of patients) or contralesional ERD (57% of patients). Independent of ERD profile, we show weakened ERD in anticipation of visual feedback, followed by a restrengthening shortly after feedback onset, not significantly different from the prior no feedback phase. However, bilateral occipital decrease in individual peak frequency suggests increased information processing shortly after feedback onset. Furthermore, ERD was weakened during the last

part of the trial (with feedback). This reduction was correlated to increased blink rate, and we show a tendency of higher cognitive ability for patients with greater reduction in ERD during the end of the trial. These results indicate that visual feedback does not interfere, nor significantly help the practice of MI during BCI training.

Significance: This study provides insight in the temporal and spatial dynamics of peak frequency ERD in response to visual feedback while stroke patients practice MI during BCI training. We believe the results will contribute to building a solid foundation of knowledge and understanding for the informed development of BCI technology in stroke rehabilitation.

My contributions: I gathered the majority of the EEG and fMRI data and performed most of the analysis. I was involved in the writing process from the original draft to the final manuscript.

6.2 Beta burst analysis

This section describes the analysis of beta bursts and its results that is not included in the papers presented above. All beta burst analyses were conducted on the three baseline EEG recording sessions from the main study. This includes both MI and ME trials, in contrast to the neurofeedback BCI sessions, which only include MI. These sessions were chosen as a start with the intention of investigating beta bursts during MI and ME to assess whether any differences can be found between those tasks for stroke patients. In addition, I wanted to provide a first characterisation of beta burst after stroke, comparing lesioned and healthy hemispheres.

6.2.1 Methods

Before I could investigate the bursts, the data had to be pre-processed in a different way than my previous pipeline. Since the bursts in question last only a few hundred milliseconds, it is important that the data are as clean as possible with high temporal and spectral resolution. First, I removed blink and unwanted muscle movement artifacts by applying Independent Component Analysis (ICA) from the Matlab EEGLab toolbox (version 2025.0.0). I ran ICA on bandpass-filtered data (between 2 and 40 Hz) and then removed components from eye and muscle movements with an accuracy of 80% or higher from the unfiltered data.

After this, I applied a broad bandpass filter between 1-120 Hz and a power line artifact removal algorithm based on a custom implementation of the Zapline function from the meegkit package (dss_line) in Python [39], [21]. Some trials and channels in the data still looked noisy and bad; therefore, I applied an automatic trial rejection and channel interpolation algorithm (autoreject package in Python) as well as visually inspecting all trials with a subset of channels and

manually rejecting trials with visually obvious artifacts. As a last step for the preprocessing, I re-referenced the channels by subtracting the average over all channels.

To perform the time-frequency decomposition of the filtered data, I used the superlets algorithm [38]. It gives a better trade-off between temporal and spectral resolution than other common methods, and has been shown to give better classification results for burst features [12]. The base Morlet wavelet was defined with 4 cycles and for the superlet, the minimum and maximum number of cycles was defined as 1 and 40, respectively. Applying the superlet algorithm transforms the data into the time and frequency dimensions, which allows for the beta-specific analysis.

I applied a novel burst detection algorithm, using a beta frequency range of (15-30 Hz) from channels C1-C4 and CP1-CP4 to cover the motor area of the brain. In short, the bursts were detected by finding the highest peak amplitudes in a time-frequency representation of each trial. Each detected burst was then modelled as a two-dimensional Gaussian, considering the full-width at half-maximum (FWHM) in both time and frequency domain. Then, the peak time is aligned with the filtered data and adjusted to the minimum phase point within 30 ms before and after the peak time. The waveform from a 260 ms window around this phase point is extracted and saved together with the peak duration, peak amplitude, peak frequency, and frequency span of the burst. The Gaussian is then removed from the time-frequency matrix, and the process is iteratively performed until no more peaks can be identified in the matrix over the noise floor [53]. This algorithm aims to identify a wide range of bursts to be used together with dimension reduction algorithms in order to find waveform specific features.

Principal Component Analysis (PCA) is a dimensionality reduction technique that can be applied to multivariate datasets to identify dominant patterns of variability while preserving as much variance as possible. Applying this to beta burst waveforms, I can transform the original waveform data into a set of orthogonal principal components (PCs). PCA captures the most dominant features of the burst waveforms in terms of variance around the mean waveform shape. The first principal component represents the waveform shape that accounts for the greatest variance across bursts, with subsequent components capturing progressively less variance while remaining uncorrelated.

6.2.2 Results

As a first validation of the burst detection pipeline, I plotted the distributions of burst peak duration, peak amplitude, peak frequency, and frequency span. I decided to separate MI and ME, and to compare the distributions between the lesion and healthy side. These distributions are visualized in Figure 6.1. Burst duration and amplitude generated similar distributions between the lesioned

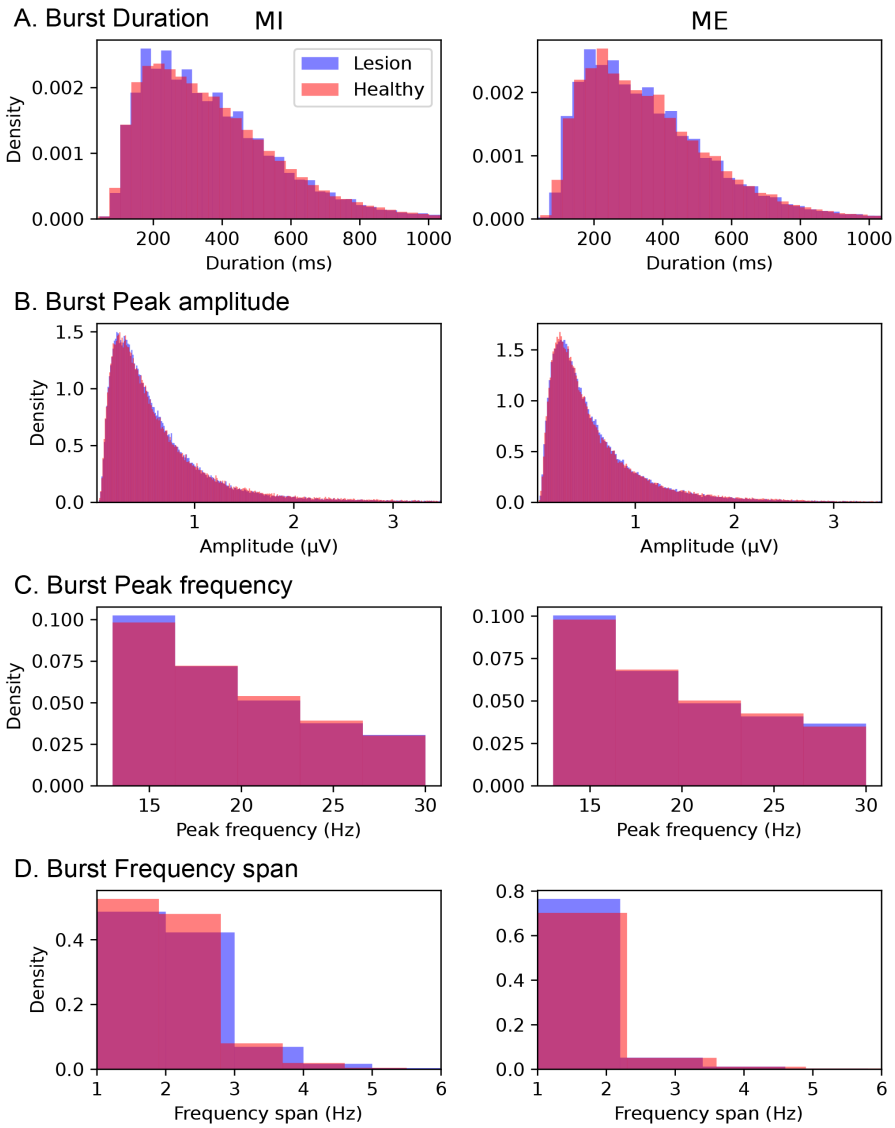

Figure 6.1. Distributions of bursts from all subjects, split between MI and ME tasks. The blue bars are busts from channels over the lesioned hemisphere while the red bars are bursts over the healthy hemisphere. The bursts are represented as burst peak duration (A), peak amplitude (B), peak frequency (C), and frequency span (D). The general shape of each distribution is similar between MI and ME as well as lesioned and healthy channels.

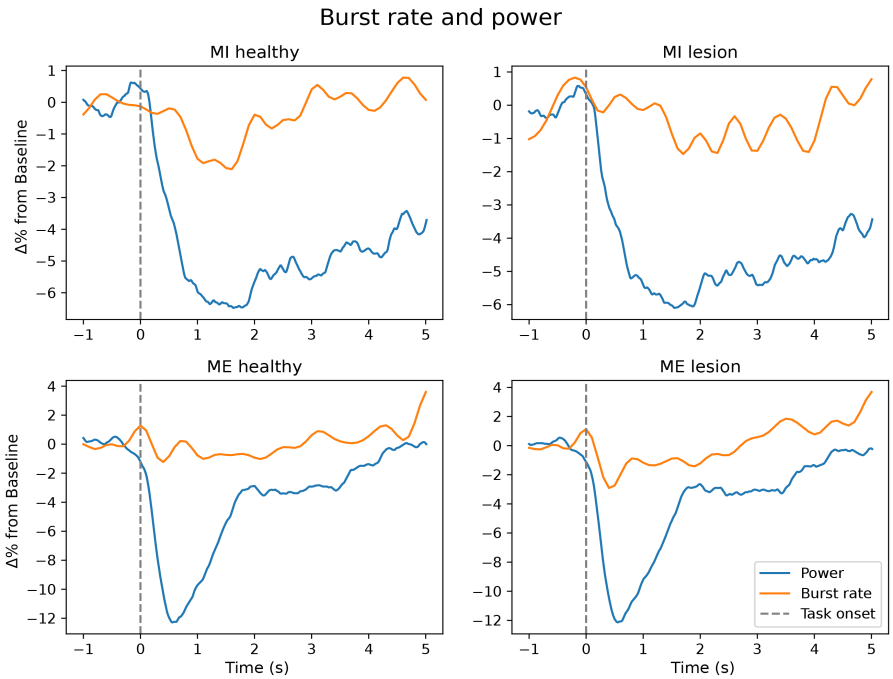

Figure 6.2. Average burst rate and power over all subjects (n=14) represented as percentage change from baseline (average amplitude between -1 and 0 seconds). The plots are separated between MI and ME, as well as lesion and healthy hemisphere.

and healthy hemisphere, both during MI and ME tasks. The same goes for burst peak frequency, with most bursts found in lower beta regions. Most of the peak frequency spans are also short for both MI and ME. These distributions are comparable with other studies [53], and bursts were reliably found in both hemispheres, independently of task. A total of 437,409 bursts were found throughout the whole dataset.

Next, I wanted to investigate whether the rate of bursts throughout single trials correlates with ERD activity. Here I once again split the detected bursts between MI and ME as well as lesion and healthy hemispheres. To compare burst rate and ERD I first computed the average amount of bursts in bins of 100 ms from trial onset until the end, over all trials and channels for the selected task and hemisphere. Time-frequency power from the superlet algorithm was also averaged over trials and channels for the selected task and hemisphere, as well as frequencies 13-30 Hz. Then I baseline-corrected the burst rate and power as the percent change from the mean value of 1 second before task onset (1000 ms time window). In Figure 6.2 burst rate and power are plotted separated between MI, MO, and lesioned and healthy hemispheres. It can be observed that burst rate generally follows the power dynamics during both MI

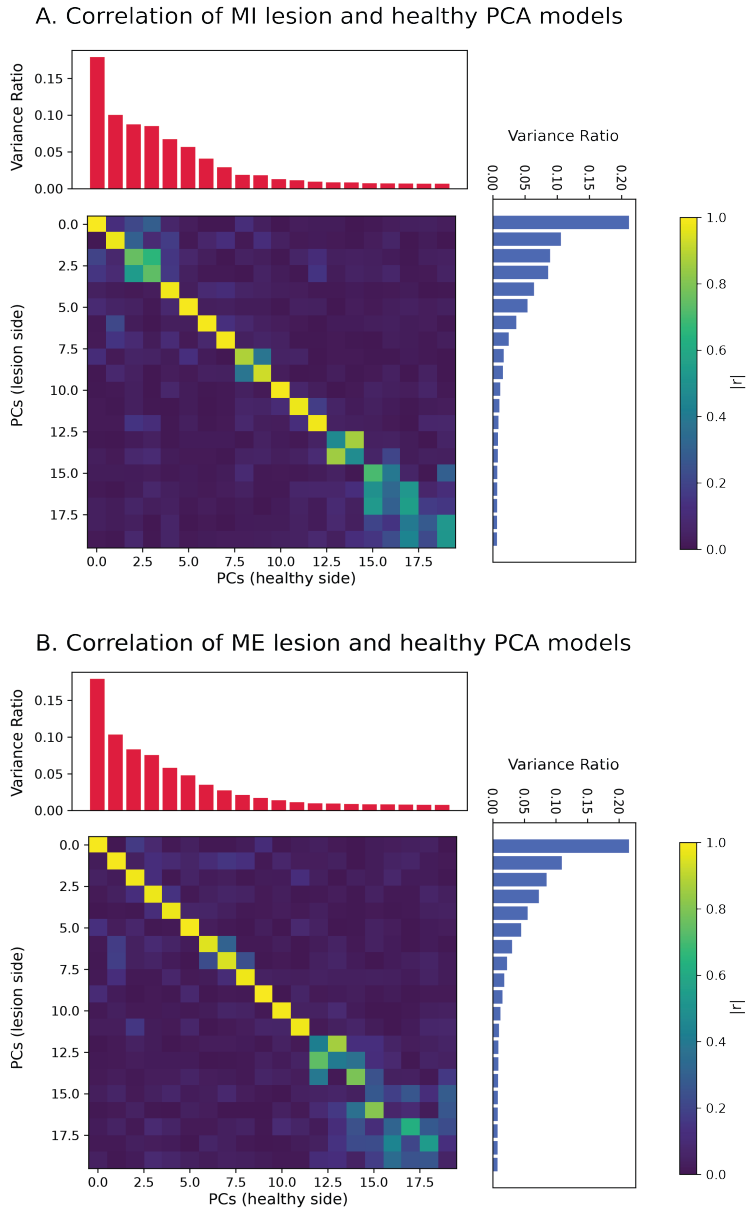

Figure 6.3. Spearman rank correlation of the loadings for each PC from the PCA models of waveforms over the lesioned and healthy hemisphere. A) Correlation of the PCs for MI waveforms. B) Correlation of the PCs for ME waveforms. The bar graphs show the proportion of the total variance in the dataset explained by each principal component.

and ME trials. However, an interesting difference in power can be observed between MI and ME. MI is generally more sustained than ME which generates strong ERD early, but subsides fast. Burst rate has a slight trend of reducing after task onset and slowly increases at the end of the trial, following power. Burst rate during MI on the lesioned side seems to decrease a bit later than for the healthy side. However, it is difficult to evaluate what this implies when analysing the rate of all bursts, independent of waveform.

This burst detection method detects a wide range of bursts, not only bursts with high amplitude, meaning that it is not surprising that the overall burst rate does not directly correlate with power fluctuations. Since I aim to find features that can be represented with other means, instead of power, having many bursts and investigating the specific waveforms, instead of overall burst shape and rate, allows me to do that. I chose to apply PCA to reduce the number of dimensions, since it has been successfully utilised in previous work [39], [53]. First, I wanted to investigate whether the same PCA model can be used for both hemispheres, particularly since the stroke lesion creates very different brain profiles between the hemispheres. To make this comparison, I ran PCA with 20 PCs on normalised waveform data from the MI-lesion, MI-healthy, ME-lesion, and ME-healthy datasets. Figure 6.3 shows the Spearman rank correlation of the loadings (magnitude of how strongly a variable contributes to a PC) for each PC between the PCA models of the two hemispheres, with MI and ME plotted separately. The models show high correlation for components between the two PCAs, up until principal component 12, which means it is highly efficient to use the same model on both the lesioned and healthy hemisphere.

The final step covered in this theses was to analyse the waveforms from each principal component. Since I could not find any significant difference between the burst distributions or rate, and the hemisphere-specific models showed high correlation, I once again performed PCA although this time on all bursts. Only 12 principal components are of interest since the models separated by hemispheres did not show a high correlation beyond that, and the majority of the total variance in waveform shape is explained by the first 12 principal components. In Figure 6.4, each PC represents a distinct axis of variation, capturing specific features of waveform shape that differ across bursts. In this reduced-dimensional space, each burst is assigned a coordinate that reflects its projection onto these components, effectively summarising its shape with a lower-dimensional vector (scores) than the original waveform. Each line in Figure 6.4 represents the mean waveform shape within each quartile of scores for that PC. This is the first step towards separating bursts according to their shape, thereby enabling a more detailed analysis of how different types of bursts behave during ME and MI in the lesioned and healthy hemispheres of stroke patients.

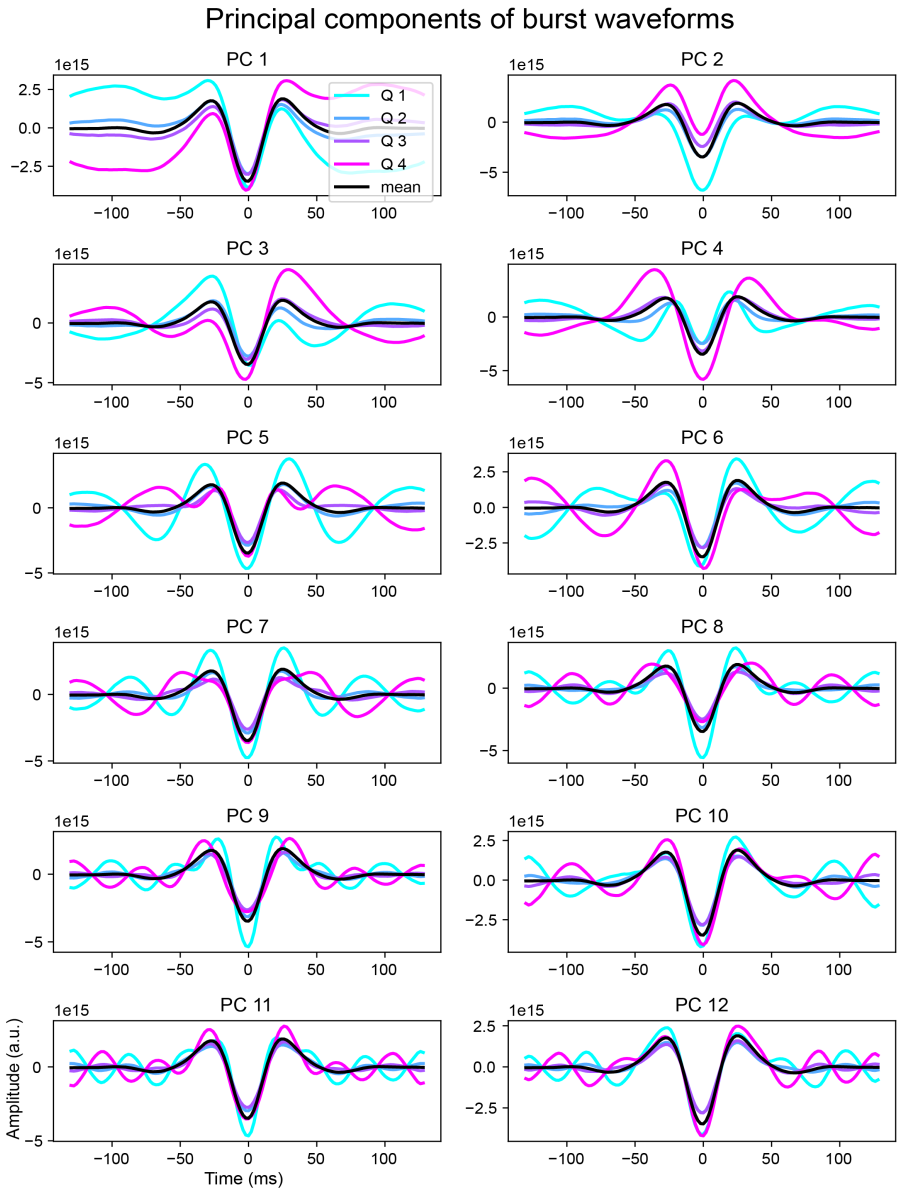

Figure 6.4. The first 12 principal components of beta waveforms from all patients. The coloured lines represent the mean burst waveform shape with a score within the 0-25th (Q1), 25-50 (Q2), 50-75 (Q3), and 75-100 (Q4) of all burst scores for that component. The black line is the mean of all burst waveforms.

6.3 Research contributions and Discussion

Each paper and complementary burst analysis contributes to the three research questions as follows:

6.3.1 RC_1: Controlling BCI task difficulty using the "distance-to-bound" approach is shown feasible

Paper A (Exploration of using "distance-to-bound" to manipulate the difficulty during motor imagery BCI training after stroke – A clinical two-cases study) addresses **RQ_1: How can the difficulty-level during BCI training be adjusted and adapted online?**

In this paper, we propose a novel approach in which the threshold used to calculate the distance-to-bound (the distance of a data point from the decision boundary of an SVM classifier) is dynamically adjusted to maintain consistent classification accuracy throughout a session. Two chronic stroke patients performed MI-BCI training with this approach. The threshold was set to reflect the 60th percentile of the SVM classifier output score values for MI trials (positive scores), yielding an average accuracy of 40%, and thus on average 40% positive feedback. This feedback threshold was updated every 5 MI trials using all available data to maintain the level of difficulty during the session.

The "distance-to-bound" approach was successfully applied and kept the difficulty at a stable 40% classification accuracy for both patients throughout the sessions. Although the difficulty was set very high (by maintaining 40% accuracy), we show that the patients received positive feedback primarily for producing stronger alpha and beta ERD centred around sensorimotor areas. I believe this reinforced them to produce this activity and assuming that it is more difficult to produce strong ERD, this result suggests that the BCI task difficulty was effectively adjusted.

Other studies suggest that a 70% or higher BCI classification accuracy is necessary to feel in control of the BCI system [5]. However, for stroke rehabilitation, the use of BCI is not necessarily required as an assistive tool. Instead, the introduction of progressively challenging tasks has been shown to facilitate recovery [19], [29], suggesting that increasing the difficulty within the BCI application may enhance neural rehabilitation outcomes in stroke patients. By keeping a steady 40% accuracy, patients with high performance is still presented with challenging tasks to facilitate recovery. In contrast, patients with low performance might experience more responsiveness by providing easier feedback since they might normally have had lower than 40% accuracy. This shows that the method adapts to the individual and gives a similar opportunity to all patients. In addition, both patients experienced an increase in the Fugl-Meyer assessment for upper extremity after the neurofeedback training. The

cross-patient average improved score was +6.35 FMA-UE, which is comparable with other studies [9], [15]. However, modulations in the MI-related EEG power correlated with motor improvements for one of the patients, but anticorrelated with the other. This showcase the necessity of personalised BCIs. To my knowledge the "distance-to-bound" approach has not been used to adapt difficulty for BCIs in stroke rehabilitation before. In my work, I contribute:

- methodologically by showcasing the feasibility of adapting the difficulty during an MI-BCI task using a distance-to-bound approach.

These findings adresses $\mathbf{RQ}_1$ by showing the potential of the "distance-to-bound" approach in adapting difficulty for the individual within an online setting. However this was an explorative study including only two patients and more research is therefore needed. I do however believe that this work contributes conceptually to the BCI community by highlighting the importance of personalisation in terms of difficulty adaptation.

6.3.2 RC_2: Continual visual feedback does not interfere with MI-related ERD over sensorimotor areas for stroke patients

Paper B (Instantaneous neural effects of continual visual neurofeedback after stroke) addresses **RQ_2: How does continual and simultaneous visual feedback influence the ability to perform Motor Imagery tasks for stroke patients?**

In this study, neurofeedback data from MI tasks were analysed both with and without feedback within the same trial. Fourteen chronic stroke patients participated in a four week long neurofeedback training period (three sessions/week). The task was designed so that each MI trial contained a period of time both with and without neurofeedback.

Within the patient group in this study (n=14), there was an interesting split in the peak frequency ERD patterns. Six patients generated generally more bilateral ERD over motor areas, with majority of the effect in the ipsilesional hemisphere, while eight patients generated a more centralised contralesional ERD. Other reports show that ERD over sensorimotor areas are dominantly on the contralateral side (opposite the paretic hand) during the performance of upper-limb MI, in the healthy population [37], [41]. This suggests that the split found in our group may be due to the hemispheric asymmetry caused by the lesion, which has also been observed in stroke patients in earlier studies [45], [54].

Independently of these groups, we can see a strong increase in ERD during no feedback, followed by a weakening in what seems to be in anticipation of the feedback onset, and then a restrengthening during early feedback. Antic-

ipation of behaviourally relevant cues has been observed in studies before in a healthy population [47]. However, the restrengthening of ERD during early feedback does not exceed the initial increase after trial onset. In the literature, it is still unclear what effects visual feedback has on the sensorimotor activity. I hypothesised that the feedback would have strengthened the ERD further, and there are studies suggesting this [57], [2]. However, our study shows clear evidence this is not the case for continual visual feedback in a group of stroke patients.

Additionally, during late feedback, towards the end of the trial, the ERD slowly decreases towards baseline. Attempting to validate this effect with various clinical measurements gave no correlation, which suggests that it is not due to stroke-related cognitive disabilities or mental fatigue. A potential answer is a change in the task nature towards the end. Instead of a dynamic MI, the patients produce a static imagery, reducing the power [52]. I was unable to validate this in this specific project. Nevertheless, as mentioned earlier, none of the patients in this study exhibited an increase in ERD throughout the trial after the initial increase around task onset. Comparing visual neurofeedback to no feedback has been done before [57]. However, these studies separate the feedback and no-feedback trials into different blocks. These reports does not take into account variations in sensorimotor activity over time, and neural reorganisation due to learning. Our study compares feedback and no-feedback within the same trial, allowing analysis of differences under equivalent cognitive states and thereby providing a more controlled and accurate comparison.

An additional occipital ERD is observed shortly after feedback onset that is not observed during no-feedback. However, it does not interfere, nor seem to significantly help increase ERD around sensorimotor regions during neurofeedback training. The findings in this paper provides valuable insight into the instantaneous impact of MI-related neurofeedback training on a trial level in stroke patients. In this work I contribute:

- scientifically by showing that continual visual feedback during neurofeedback training does not interfere, nor help increase ERD around sensorimotor regions.
- scientifically by showing that the two different stroke patient groups with opposite hemispherical power patterns do not differ in their response to visual neurofeedback.

This addresses $\mathbf{RQ}_2$, as I showcase similar ERD behaviour with and without feedback, independently of stroke patient groups. However, the long-term neurological response to feedback, for these patient groups, is still yet to be explored.

6.3.3 RC_3: Beta bursts show potential in explaining lesion-specific sensorimotor activity

The additional beta burst analysis included in this thesis targets **RQ_3: How are transient and heterogeneous events in the beta band manifested in stroke patients during motor-related processes?**

I applied a novel beta burst detection algorithm on MI and ME data from the baseline sessions of the main stroke study and compared the detected beta bursts from channels over the lesioned and healthy hemisphere. In addition, I applied a dimensionality reduction technique to analyse beta burst waveforms as an initial step toward identifying waveform-specific behaviours within bursts from stroke patient data.

Numerous bursts were detected throughout the data set. However, I could not conclude any difference between the lesioned and healthy hemispheres from the overall burst distribution, nor between MI and ME. This is in line with previous studies on beta bursts [53], which suggests that separating bursts according to their waveform shape is necessary for a more representative analysis. Consequently, the overall burst distribution exhibits a similar pattern to those reported in previous studies. Before investigating waveform shapes I evaluated the overall burst rate in comparison to beta power. I found that the beta power was in general more similar between hemispheres when compared to alpha power, which I showcased in paper B where the majority of ERD peak frequencies were in the alpha band. However, beta power differed substantially between MI and ME. This is most likely due to the nature of the movement. During ME, when physically grasping (or releasing), an early increase in ERD occurred. However, when the hand remains static in its end position the ERD quickly reduced as observed in other studies [52]. For the MI task this seems to not have been the case, and a slower reduction in ERD can be observed, suggesting a more dynamic imagined movement. The general trend of the burst rate follows the fluctuations of beta power. However, it is not strongly correlated. This is most likely due to the fact that not only bursts with high amplitude were extracted. My intention was instead to extract a wide range of bursts, even low amplitude, to be able to separate the bursts according to their general waveform shape. Despite this, a temporal shift of approximately 500 ms was observed in the reduction of burst rate between the lesioned and healthy hemispheres, indicating a potential rate asymmetry between the hemispheres.

When applying PCA as a dimensionality reduction technique on the burst waveforms, I saw a strong correlation between PCA models of the lesioned and healthy side respectively. This indicates that the features contributing to the variance within both hemispheres are aligned, meaning the waveform shapes are of similar nature. Going forward, it will be highly efficient to use

the same PCA model for both hemisphere. A more thorough waveform analysis is required to evaluate the potential differences found in burst rate.

Burst rate analysis on stroke patients performing MI-BCI rehabilitation training has not been conducted before as of writing this thesis. The method has demonstrated potential in other studies involving EEG and MI, where burst activity appears to contain behaviourally relevant features that could be leveraged for neurofeedback training [40], [39]. In my work, I contribute:

- by showing the feasibility of burst rate analysis for stroke patients.
- scientifically by showing a burst rate temporal shift between hemispheres not observed with beta power alone.

The findings in this study partly answers $\mathbf{RQ}_3$, as I find bursts with overall distribution and shape that manifest similarly to those of other studies. I also found evidence of differences in the burst rate between hemispheres; however, further waveform-specific analysis is required to confirm and evaluate what causes these findings.

7. Conclusion and Future work

A MI-BCI is a promising technology for helping stroke patients with motor recovery without the need for performing physical exercises. Together with neurofeedback, a BCI can guide the user to reorganise the neural substrates and promote motor recovery. This thesis presents results from two different experimental interventions. A pilot study consisting of two stroke patients and the main study including 14 stroke patients. A BCI was developed for the pilot study and updated for the main study based on the findings. In this thesis, I showcase results from evaluating the data during the practice of MI, performed by the patients. I present a promising method for adjusting the difficulty of a MI-BCI to help reinforce relevant activity for stroke rehabilitation. I also unveil the cortical impact when providing visual feedback during MI-neurofeedback training. Lastly, I investigate a novel feature extraction method to extract beta band burst waveforms that have the potential to help illuminate lesion-specific activity patterns. All of these contributions aim to provide the foundations for a fully adaptive BCI that will personalise the experience and give optimal neural reorganisation opportunities for different brain profiles, such as in stroke patients.

The opportunities for future work are plentiful. The data set from the main study is extensive and an evaluation of motor function recovery and activity profile changes over the span of the whole intervention has yet to be investigated. In the main study, a version of the distance-to-bound approach was also implemented with the intent of validating the approach on multiple subjects, and has yet to be analysed. Further investigations on the effects of feedback can be conducted, specifically on how it changes from early sessions to later ones. The difference in activity patterns found within the patient group is an interesting topic to further investigate, in particular if motor recovery over time differs depending on whether the subject exhibits strong ipsilesional or contralesional ERD. Further investigation of hemisphere-specific activity for stroke patients using beta bursts will be carried out. So far only overall burst shapes and rate have been explored. Waveforms were extracted, but waveform-specific rate was not included in this thesis and is something that will be further examined. Lastly, applying the burst detection algorithm on neurofeedback data will allow for further exploration of feedback versus no feedback, as well as a comparison of how well ERD and beta bursts explain changes in EEG activity throughout the intervention period for stroke patients.

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