Report on a problem studied in the N-CODE Study Group March 2023
(https://www.n-code.org/events/events-first-n-code-stakeholder-led-study-group/)

Study Group Report template

Please complete your report template and return to ncode@contacts.bham.ac.uk. Reports should ideally be received by Friday 16th April, but at the latest by the onward funding deadline of Thursday 27th April.

NB: This report is a summary of the activities that took place at the Study Group and the inclusion of further work on new models/solutions is not required.

Challenge: Non-invasive Brain-computer-interfaces for Remote Rehab and Training of Motor Skills

Katja Kornysheva, Anna Sadnicka, Amin Rahmat, Fei He, Drummond Masterton, Atif Shahzad

Date: 27/04/2023

Abstract

Motor deficits caused by several neurological or neurodevelopmental conditions can result in severe disability and loss of function. The management of neurological diseases, both in adults and children, requires an ever-increasing commitment of resources for the national healthcare system. We investigated the challenge of rehabilitation and recovery of motor function in patients such as stroke and Parkinson's Disease (PD).

Studies suggest that the natural logarithmic pattern of functional recovery can be modified by intensive task-oriented practice. This includes more complex and challenging tasks such as typing on a keyboard, handwriting and fine individualised movements of fingers. Sequence planning is an integral part of motor sequence control which is repeated in task-oriented practice. It has been previously demonstrated that the competitive state of sequential movements during sequence planning can be read out behaviourally through movement probes. Competitive pre-activation is established gradually during sequence planning and predicts sequence skill. This forms a foundation for a rehabilitation support system that provides feedback on the pre-planning of actions using a brain-computer-interface (BCI).

We studied existing literature and discussed design strategies to establish a user-centric affordable BCI-enabled rehabilitation support system for Stroke and PD patients. This system will provide a solution for long-term rehabilitation provision outside the hospital environment as a portable neurotech that assists patients in enhancing or recovering their ability to perform skills with fluency and accuracy.

1 Introduction (1 page)

Skilled actions such as typing on a keyboard, handwriting, and driving a car are key building blocks of human goal-directed behaviour. They are essential for maintaining independence and quality of life in daily activities. A variety of neurological (e.g. stroke, spinal cord injury), and neurodevelopmental conditions (e.g. dyspraxia, stuttering) affect the execution of skilled actions in multiple ways and with varying severity. Access to effective rehabilitation protocols over prolonged periods of time and outside the clinic are lacking, although recommended in clinical guidelines (e.g. Stroke guidelines). While invasive brain-computer-interfaces (BCIs) have been used for prosthetic control, closed-loop brain stimulation, and neurofeedback, they come with multiple health risks and costs with only a small proportion of patients being eligible. In contrast, current non-invasive brain recording technology, such as functional infrared spectroscopy (fNIRS) and EEG, have so far focussed on decoding simple movements rather than more complex naturalistic action sequences and their associated neuronal activity.

In this study group, we investigated the major factors concerning the rehabilitation of motor function in several clinical conditions including Stroke and Parkinson's Disease. A swift and full recovery of motor function is found to have a significant impact on a patient's life with them being able to carry out routine everyday tasks. We reviewed and analysed the available literature for the feasibility of encoding and decoding of complex tasks and retraining via a BCI system. Building on the progress made in the study group, we established a roadmap for the development of a rehabilitation support system and a BCI-enabled non-invasive prosthetic control system. The first stage of the development, a "seed project", involves the feasibility and codesign of the BCI system with a group of patients and clinicians over next 12 months. The seed project aims to deliver the groundwork towards a first prototype of a portable EEG application that allows a participant to monitor their covert action planning and organisation in real-time and train to the desired level through corresponding sensory feedback to optimise action performance. The readout and feedback on the internal action-related electrophysiological patterns may facilitate innovative neurotechnological advances for remote rehabilitation of patients with impairment of manual coordination to train beneficial preparatory patterns prior to initiating and action and help provide remote, individualised, patient-centred training.

2 Description of the problem (1 page)

To restore the patients' independence, brain-computer-interfaces (BCIs) have been employed for prosthetic control and neurofeedback. For example, invasive BCI combined with state-of-the-art machine learning have enabled prosthetic control of handwriting and typing, speech, and assistive movements in patients without mobility (e.g. tetraplegic)[1–4]. Companies such as Neuralink are capitalising on these discoveries and investing in innovative engineering solutions to make these invasive devices more durable and widely available. However, the risk profile and costs of invasive methods are substantial. Clinical risks can include infection, haemorrhage and mechanical brain tissue damage and the longevity of implants underneath the skull or directly in living brain tissue is not well known[5]. Further, there is a significant cost of the neurosurgical intervention and the long-term follow-up of implanted patients. Correspondingly, invasive BCI technology is only considered for a very small

pool of patients with severe disabilities, conditions that are refractory and have extensive side effects to medications.

In contrast, patients with milder forms of stroke and those with neurodevelopmental conditions affecting skilled action learning and control are largely excluded from BCI-based applications due to a disadvantageous risk-benefit ratio of invasive neurotech. Meanwhile, there is an acute need of rehabilitation outside the hospital environment, due to the severe economic and logistical pressures on the NHS. The development of home and remote neurorehabilitation technology, e.g. interactive neurorehabilitation delivered in the community clinic or the patient's home which is safe and led by therapists remotely would alleviate such pressures and potentially broaden access to long-term patient care. Consequently, there is an acute clinical need for research and development around non-invasive BCI for skilled action rehabilitation, training and prosthetic control.

Whilst there has been a push towards utilising non-invasively recorded brain signals such as functional infrared spectroscopy (fNIRS) and EEG for BCI, results so far have been modest compared to invasive BCI applications. This is partly due to the focus on decoding basic movements, such as flexion and extension movements of the left or right hands one movement at a time, rather than on more skilled naturalistic multi-step action sequences such as typing, handwriting and speech, directly relevant to patients' daily tasks and activities. Meanwhile, recent research utilising machine learning of MEG and EEG signals in healthy individuals has shown that activity preceding and accompanying complex action sequences carries a much richer informational signal about multi-step actions than previously assumed. This enables a non-invasive read-out of the organisation of movements and thought[6–8], e.g. during movement sequence planning and production when participants retrieve and prepare movement sequences from memory. Such an approach provides direct insight into action organisation before incorrect movements are executed, which can corrupt movement skill representations through use-dependent plasticity[9]. Finally, decoded preparatory activity has been shown to predict the individual's skill level and thus may be a target for future neurorehabilitation, neuroprosthetic and neurofeedback applications.

In summary, there is an acute clinical need for the development of state-of-the-art non-invasive BCIs for stroke and neurodevelopmental conditions. Specifically, we need to develop technology that offers a safer, more versatile alternative to invasive BCIs, which could be administered remotely outside the hospital to deliver neurotraining at scale. Advances in this field would have the potential to improve the lives of a broad set of patient groups with mobility impairments.

3 Solutions proposed (split into sections as required e.g. approaches considered to solve the problem, any mathematical model development and relevant results, technological solutions, etc.) (5 pages)

We systematically explored concepts of potential solutions to the challenge with specific consideration of usability, affordability and functionality. Several ideas for hardware (sensing and feedback wearable systems) and software (mathematical models and data processing) were discussed. Literature surveys suggested that the primary motor and premotor cortices plays a vital role in motor recovery, and the primary activity in the motor cortex region (Figure 1) can be used as a signal in rehabilitation. Specifically, beta oscillations observed in contralateral motor-related cortical areas are known to reflect Gamma-aminobutyric acid (GABA) mediated inhibition of local neuronal

populations, and are pathologically increased in stroke and PD patients who show impairments of fluent movement initiation and control[5]. Specifically, beta power from sensorimotor areas is known to decrease during movement preparation and execution, and then sharply increase after the end of the motor task and the lack of beta power modulation during movement has been associated with clinical conditions such as stroke, as well as poorer motor skill performance[10].

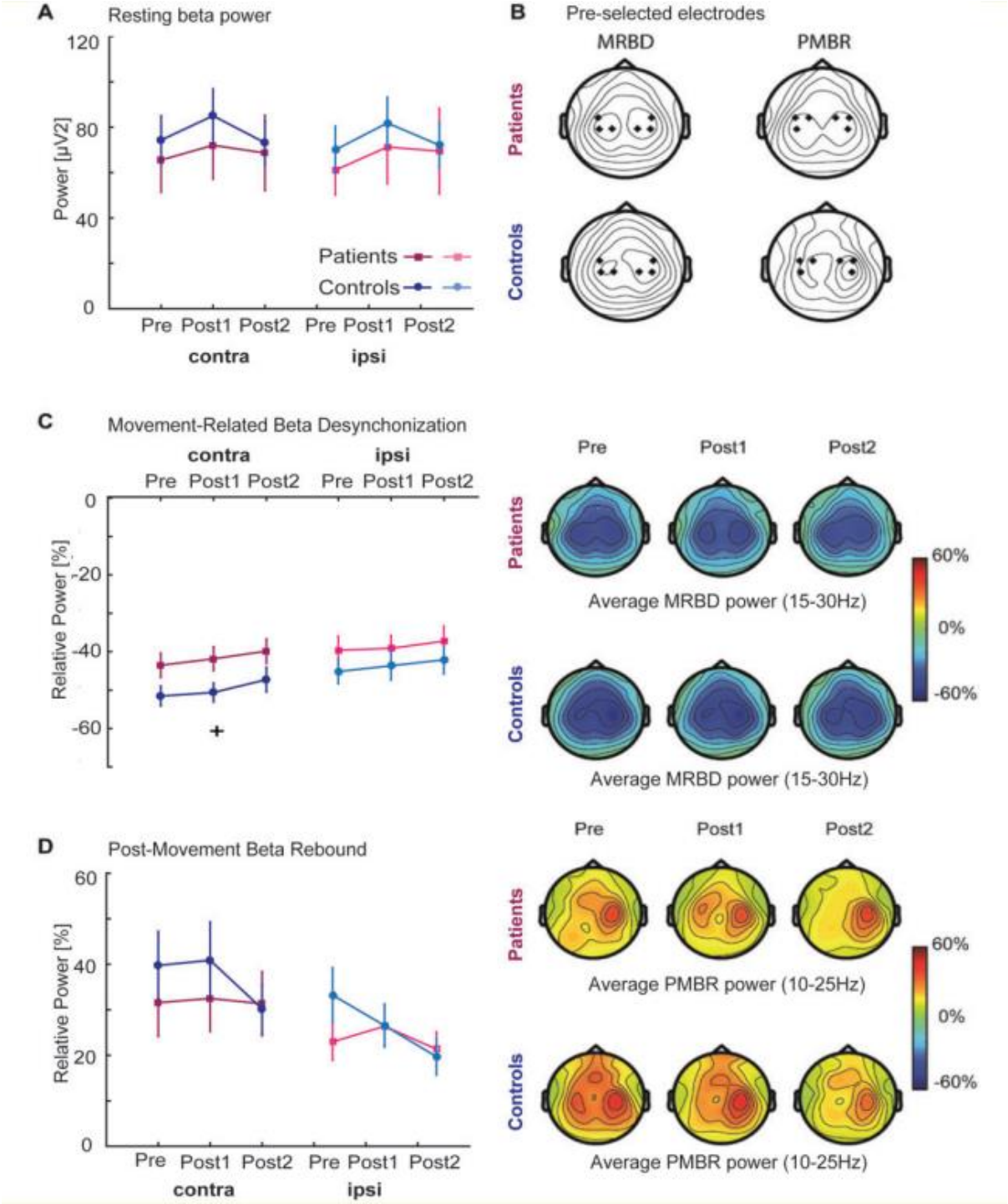

Figure 1. Skilled movement-related EEG beta power reduction and post-movement rebound above motor cortical regions in ipsilateral and contralateral hemispheres. Stroke patients showed comparable levels of baseline beta power, but less

change in beta power in the peri-movement phase associated with poorer skill learning. Adapted from Espenhahn et al. 2020. [10]

This leads to one of the most important design factors for EEG data sampling in mobile settings. We explored design ideas for a minimalist and easy-to-wear EEG headset (as a headband or integration into audio headset) that will form a seed concept in our stakeholder co-design meetings.

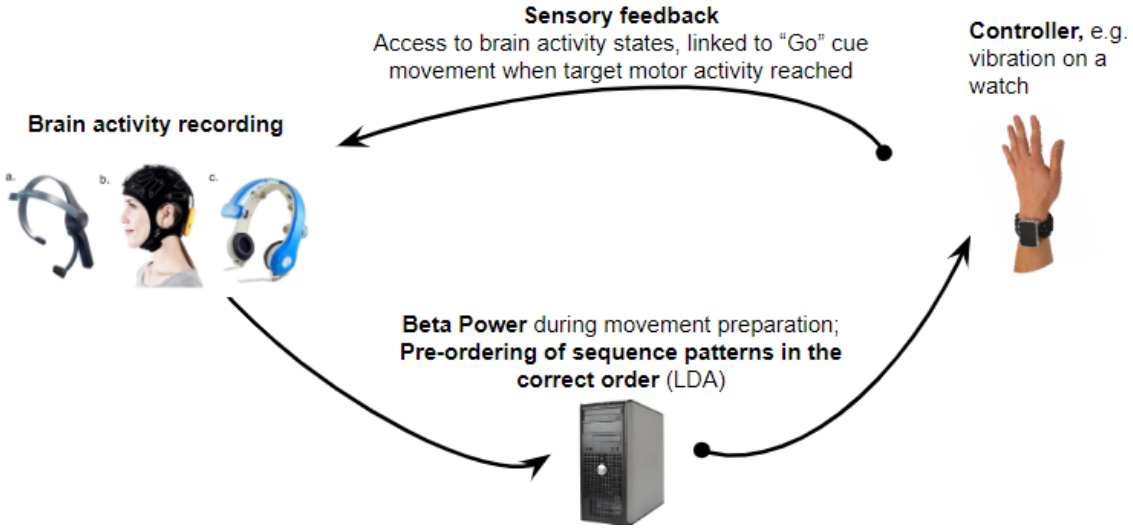

Figure 2. Block Diagram of the proposed solution for rehabilitation and retraining of motor skills

The proposed solution consists of a brain activity recorder (EEG wearable headset), a mobile data processor, and a feedback device (Figure 2). A clinical co-creation phase will involve three 2h meetings with a small group of stakeholders, including patients, patient advocates, and rehabilitation providers. Meetings will cover rehabilitation needs, feedback on the proof-of-concept setup, and identifying features for a portable device. Stakeholders will be invited through existing contacts and patient databases (Co-I: Dr Anna Sadnicka, UCL) and we aim to assemble small, but diverse and inclusive groups in terms of gender, ethnicity, and clinical severity.

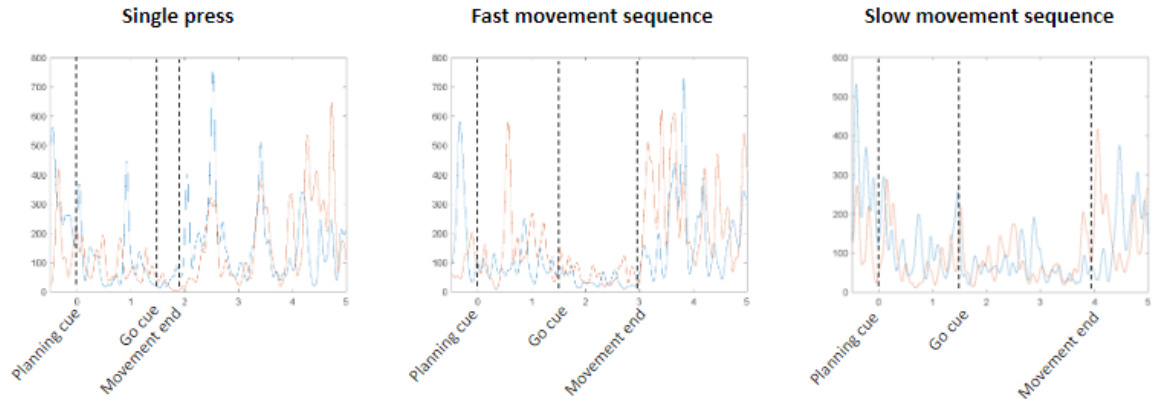

Figure 3. Trial-by-trial beta power in the EEG dataset. Representative trial examples for three conditions that vary in duration (single press, fast and slow finger press sequence).

Starting with the existing dataset collected previously by authors (Kornysheva et al.), we analysed the Beta power in planning, execution and post-execution of various scenarios of typing on a keyboard.

The dataset included MEG[7] (*N*=16) and EEG[8] (*N*=19) datasets recorded while healthy volunteers retrieved, prepared and produced typing-like sequences of finger presses from memory after two days of training (Figures 3 & 4).

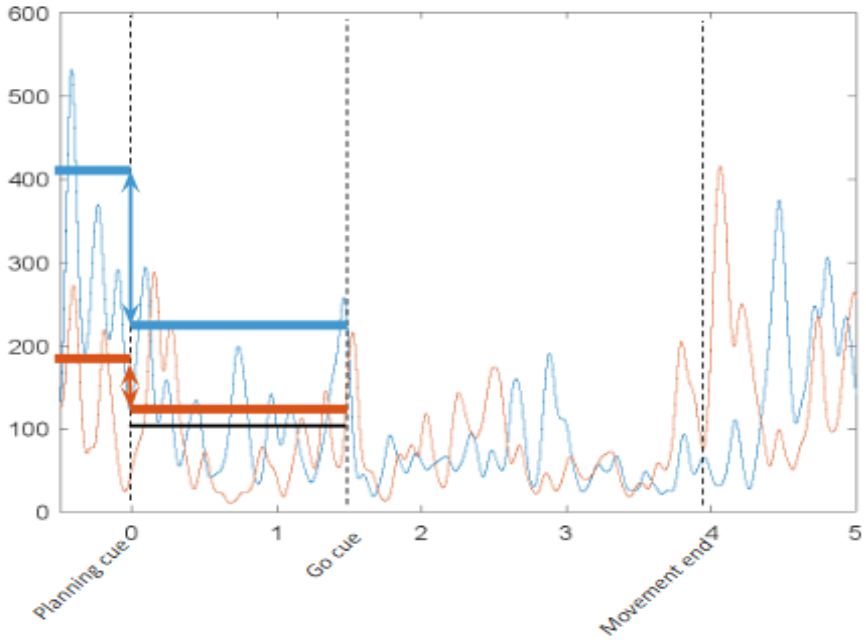

Figure 4. In line with findings by Espenhahn et al. 2020 (Fig. 1), we will focus on the relative changes in beta power as markers of skilled performance and clinical impairment. However, we will examine beta power during movement planning. Participants will be provided real-time feedback on the relative modulation of the beta power after the planning cue indicates the movement sequence to be performed.

This dataset offers the opportunity to improve existing and explore new machine learning algorithms to enable decoding of sequence planning from non-invasive brain recordings prior to motor execution trial-by-trial and in "real-time", which has direct relevance to future neurorehabilitation and training applications.

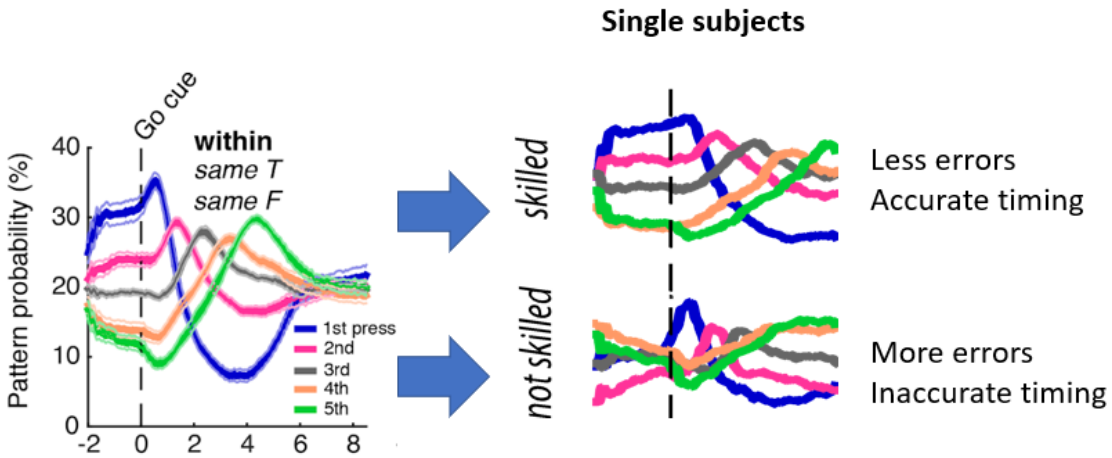

Figure 5. Our previous work indicates that neural patterns related to subsequent movements in a sequence are already pre-ordered during planning[7], in the absence of movement at the periphery (fingers). A pre-ordered pattern during sequence planning is predictive of subsequent performance (representative individual participant examples). Beta power changes relative to baseline will be quantified and evaluated as a predictor of the decoded content during motor

preparation (linear discriminant analysis: LDA). This will provide a direct mapping between oscillations, the decoded sequence organisation and behavioural performance to advance future BCI applications.

Previous computational and neurophysiological work suggests that movements in a sequence are planned as parallel graded activations and selected for output through competition. Sequence planning is an integral part of motor sequence control. It has been previously demonstrated that the competitive state of sequential movements during sequence planning can be read out behaviourally through movement probes. Studies suggest that competitive pre-activation is established gradually during sequence planning and predicts sequence skill, rather than the temporal structure of the motor sequence (Figure 5). These results form the foundation of motor skills training via our proposed wearable BCI system, which will enable swift and better recovery of patients to their full potential.

4 Future work (1 page)

Our vision is to close the gap in long-term rehabilitation provision outside the hospital environment and develop portable neurotech that assists patients in enhancing or recovering their ability to perform skills with fluency and accuracy. This will be achieved by enabling the affected individuals to identify and learn brain states of movement preparation that are beneficial for initiating and producing movement sequences fluently and accurately. Building on the first phase of BCI for rehabilitation and recovery of motor function, we aim to establish a non-invasive BCI-enabled prosthetic control system for patients with loss of major periphery function. This will be achieved by combining sensory information from multiple wearable sensor modalities including EEG and EMG, and mathematical modelling, to identify action specific signatures.

The (phase I) seed project will deliver the technical groundwork (software and hardware development) towards a first prototype of a portable EEG neurofeedback application that allows a participant to monitor and learn to control their hidden neural action planning activity in real-time in order to optimise action performance. The readout and feedback on the internal action-related electrophysiological patterns may facilitate innovative neurotechnological advances for remote rehabilitation of patients with impairment of manual coordination to train beneficial preparatory patterns prior to initiating and action and help provide remote, individualised, patient-centred training.

The work will be divided into three work packages (WPs) that will each feature stakeholder engagement, technical development, and output. WP1 is focused on laying the foundation for the project in terms of the patients' rehabilitation needs and neurophysiological data required to build for an effective neurofeedback/BCI application. WP2 involves the development of a proof-of-concept neurofeedback brain-computer-interface (BCI) device. The engineering (Task 2.1) will begin after the first stakeholder engagement, but in parallel to the data stress test and software development in WP1 as the hardware aspects of the application are not co-dependent on WP1. WP3 will focus on designing and refining the proof-of-concept design towards a prototype neurotech application.

The seed project will aim to produce 2 manuscripts in neuro-engineering and computational neuroscience journals, 1 large scale grant application involving the team (EPSRC, MRC) and - if a prototype development in WP3 is achieved - a patent application supported by the University of Birmingham Enterprise.

5 Discussion and conclusions (1 page)

A large majority of Stroke and PD patients experience movement problems, preventing patients from re-entering work and remaining independent. NHS is under-resourced and bringing state-of-the art rehabilitation to all patients currently fails. We need methods in which the dose of therapy can be increased without requiring an increase in resources. There are therefore potentially broad and profound changes for the rehabilitation horizon of any individual in the neurological domain and the proposed technology can be flexibly adapted to assist the rehabilitation needs of a broad array of neurological disorders.

There is also much need for alternative inroads for brain repair, bringing the neuroscience of skill learning into the clinical domain. Access to planning information has never been available to individuals that require rehabilitation and the team of specialists that help patients recover. To date diagnostics of the cause of a motor deficit are the output itself or coarse clues offered by clinical neuroimaging in which the spatial distribution of lesions is sometimes helpful. Specifically decoding how actions are planned is an informationally rich context to allow targeted rehabilitation programs. Capturing changes in motor responses also closes the loop in terms of feedback so that more objective evidence for what works and what does not is provided. Specifically in PD, the robust relationship between Beta oscillations and bradykinesia strongly supports our use of methods that aim to characterise oscillatory behaviour associated with movement (EEG and MEG). In stroke, we will offer inroads for therapy of individuated finger movements. This puts the focus onto dextrous finger movements that are often neglected in the face of a patient population with profound motor deficits. However, the ability to regain dextrous finger movements will have enormous functional repercussions for activities of daily living.

We also anticipate that other specific patient groups with motor coordination disorders (such as dyspraxia, apraxia, and task-specific dystonia) would benefit from the proposed system. These are specific disorders of motor planning. We chose not to use these patient groups as our first working group as their prevalence in the general population is lower. However, motor coordination disorders often remove an individual's ability to work, and thus they have an impact of significant societal and economic consequences that we would be able to reduce with the development of the tools we propose.

6 References

1. Willett, F. R., Avansino, D. T., Hochberg, L. R., Henderson, J. M. & Shenoy, K. V. High-performance brain-to-text communication via handwriting. *Nature* **593**, 249–254 (2021).
2. Hochberg, L. R. *et al.* Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* **442**, 164–171 (2006).
3. Anumanchipalli, G. K., Chartier, J. & Chang, E. F. Speech synthesis from neural decoding of spoken sentences. *Nature* **568**, 493–498 (2019).
4. Pandarinath, C. *et al.* High performance communication by people with paralysis using an intracortical brain-computer interface. *eLife* **6**, 1–27 (2017).
5. Klein, E. & Ojemann, J. Informed consent in implantable BCI research: identification of research risks and recommendations for development of best practices. *Journal of neural engineering* **13**, 43001 (2016).

6. Yewbrey, R., Mantziara, M. & Kornysheva, K. Cortical patterns shift from sequence feature separation during planning to integration during motor execution. *J. Neurosci.* (2023) doi:10.1523/JNEUROSCI.1628-22.2023.
7. Kornysheva, K. *et al.* Neural Competitive Queuing of Ordinal Structure Underlies Skilled Sequential Action. *Neuron* **101**, 1166-1180.e3 (2019).
8. Mantziara, M., Holland, P., Egan, C., Galea, J. M. & Kornysheva, K. Motor planning of sequences produced with different speeds: Evidence from EEG pattern decoding. in *Society for the Neural Control of Movement Virtual Conference 2021* (2021).
9. Doya, K. What are the computations of the cerebellum, the basal ganglia and the cerebral cortex? *Neural Networks: The Official Journal of the International Neural Network Society* **12**, 961–974 (1999).
10. Espenhahn, S. *et al.* Sensorimotor cortex beta oscillations reflect motor skill learning ability after stroke. *Brain Communications* **2**, fcaa161 (2020).