Brain computer interface Rehabilitation and Virtual Environments in Functional Neurological Disorder (BRaVE-FND)

Participant information sheet: Main Document

NCT
IRAS: 349392

PARTICIPANT INFORMATION SHEET

Brain computer interface Rehabilitation and Virtual Environments in Functional Neurological Disorder (BRAVE-FND)

You are being invited to take part in a research study called 'Brain computer interface Rehabilitation and Virtual Environments in Functional Neurological Disorder (BRaVE-FND)'. This study is being undertaken as part of a PhD project. You do not have to take part and if you decide not to your care and treatment will not be affected in any way.

Before you decide, it is important for you to understand why the research is being done, what your participation will involve and what the potential benefits and risks to you are. **Taking part will involve a time commitment of attending 10 sessions over 3-to-4 weeks.**

Please take time to read the following information and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. You can take as much time as you like to decide. Part 1 tells you the purpose of this study and what will happen if you take part. Part 2 gives you more detailed information about how the study is run.

This is a photo of the g.tec recoveriX brain-computer interface (BCI) being used in a rehabilitation session. This is the device that we will be using for this study.

Part 1

What is the purpose of this study?

The purpose of this study is to determine whether rehabilitation using a device called a brain-computer interface can change the level of control people feel over bodily movements, in functional neurological disorder.

What is the background to this study?

Brain-computer interfaces (BCIs) are devices that measure brain signals to control output on a computer device through a process called 'neurofeedback'. One application of this is wearing an electroencephalogram (EEG) headset and thinking of moving your hand. The device can then decode your intention to move your hand and use the signal to make either a robotic limb move, or make an onscreen avatar move their limb.

This approach has been studied for potential use in rehabilitation for conditions such as stroke and spinal cord injury. To date nobody has explored their use for rehabilitation in functional neurological disorder (FND).

FND is a condition where there is a breakdown in how the brain sends and receives signals from the body, without there necessarily being any structural damage to the nervous system. It is incredibly common, being the second most likely reason for someone to visit a neurologist (after headache).

The condition manifests in a variety of ways, including motor weakness, tremors, seizures, sensory disturbances, and pain. From research about FND, we know that there is a disruption in perceived sense of control (or agency) of bodily movements.

This study will explore whether BCI based therapy can alter this sense of agency over bodily movements in people with FND. It will also be the first ever study of the use of BCIs in FND. Every person who is enrolled in the study will undergo a 10-session course of BCI based rehabilitation.

We are looking for 24 participants aged 16 and over with FND with motor weakness (predominantly weakness in at least one of the following: hand, arm, leg, foot).

Who is eligible to take part?

We are looking for people aged 16 and over who can engage with face-to-face rehabilitation. To be eligible you need to:

- Have a medical diagnosis of FND and be experiencing motor symptoms (predominantly weakness in at least one of the following: hand, arm, leg, foot).
- Have active FND motor symptoms which are at least moderately severe (this will be confirmed through an assessment by a doctor if you are invited to screening).

You may also be experiencing other functional neurological symptoms or subtypes, including functional seizures or functional cognitive symptoms (i.e. memory problems). **We will not be recruiting people with FND who do not have any motor weakness.**

You will also need to be able to tolerate 10 BCI rehabilitation sessions which involve an EEG recording (please see 'BCI rehabilitation' section below), which will require sitting still for three blocks of 15

minutes each session, with an EEG cap on your head, and wet gel at different points of your scalp. During the EEG recording there will also be a gentle electrical stimulation of either both arms, or one arm and one leg, to trigger flexion of the wrist or ankle.

There are some reasons why you may not be eligible for the study even if you fit the above criteria. You won't be eligible for the study if:

- You have a **current diagnosis of a severe mental illness**. This does not include mild or moderate anxiety or depression but does include severe depression, bipolar disorder, psychosis, personality disorders, or drug or alcohol dependence or harmful use.
- You have **certain neurological conditions**, like epilepsy, dementia, or learning disability. If you have autism spectrum disorder you will be able to participate as long as your sensory sensitivities do not impact on your ability to take part in the study.
- You have **certain physical health conditions** such as having a pacemaker, an implantable cardioverter-defibrillator or any other implanted electronic or metallic device that would mean you would not be suitable for inclusion. The reasons we will not be including people with any of these factors is because BCIs are still an experimental approach, and we do not want to destabilise anyone who may have a pre-existing vulnerability.
- You regularly take **certain medications** such as high dose benzodiazepines which can alter your brain signals and ability to use a BCI.
- You are **currently pregnant**.
- You are **currently enrolled in another clinical trial**.

In order to confirm your eligibility, we will request that you fill out a baseline questionnaire, and we will need to have a meeting with you (either face-to-face or remotely over Teams depending on what would be convenient for you), so we can get to know you and your current situation.

We will also need your GP to provide us with a copy of your medical history, which will include a summary of medical problems over your lifetime. This information will be stored securely on a KCL server. You must be registered with a UK GP for the duration of the study.

It's important to emphasise that many people, for various medical or personal reasons, turn out not to be eligible for the study. Whilst we do not want to discourage you volunteering, please take the time to read this information sheet fully so you can decide if this study is right for you. Please feel free to ask us any questions if anything is not clear.

You can be based anywhere in the UK to take part in the study, and we will reimburse you for reasonable travel expenses. Given the number of in-person sessions (10) taking place over a 3-to-4 week period, and that the sessions will be taking place at Denmark Hill in London, we suggest that you only volunteer if you think it would be feasible for you to travel in regularly to this location.

Do I have to take part?

No, you do not have to take part. If you decide not to take part your care and treatment will not be affected. If you do decide to take part, you can withdraw at any time by emailing bravefnd@kcl.ac.uk.

What will happen to me if I take part?

We will send you a link to complete a short survey online. This survey will ask you some basic information about yourself and your FND and should take no longer than 10 minutes to complete. The survey will be hosted by the online software Qualtrics; this is a secure software which has been approved for use by KCL.

Pre-screening survey data will be held by the investigators on a secure server at KCL. The data is held solely for the purpose of screening for the BRaVE-FND trial. It will not be shared anywhere. Data will be deleted by default after six months, or at the end of the study period, whichever is earlier. For a link to the Qualtrics privacy notice, please visit https://www.qualtrics.com/privacy-statement/.

If we think you may be suitable from the survey, we will invite you to an online 1.5-to-2-hour meeting where we will talk to you about your history and current circumstances in depth. We will also ask you to complete some questionnaires during the meeting. These will include questionnaires relating to:

- Your mental health.
- Tour level of function.
- Your expectations of treatment.
- Your capacity for visual imagination (for more information on questionnaires, see the below "Questionnaires" section).

We will also ask for your consent to contact your GP or healthcare team to ask them to share the information they hold about you with us. This first meeting will take place online using Microsoft Teams. You will be able to take breaks if needed.

A doctor will then go through the information gathered and make a decision about your suitability for the study. The final decision about your suitability is taken by a panel which consists of the study doctors and physiotherapists who meet each week during the study period. You will be informed of the outcome within 1-to-2 weeks. If you are enrolled into the study, we will contact you to arrange a schedule of visits over a 3-to-4 week period. We will also need to notify your GP that you are enrolled in this study. This notification of enrolment will stay in your GP records.

If we think you are suitable at this point then you will be invited to the first face-to-face visit. All face-to-face visits will take place at the NIHR/Wellcome King's Clinical Research Facility (CRF), Cheyne Wing, King's College Hospital, Denmark Hill, London, SE5 9RS.

During this first visit at the CRF you will need to:

- Take part in a virtual reality (VR) task.
- Undergo a physical neurological examination (assessing the degree of weakness).
- Complete a button pressing task whilst an EEG tracing is recorded.
- Undergo your first BCI rehabilitation session which will also involve an EEG recording.

The first visit will last approximately 3-to-4 hours. There will be ten visits in total, spread out across 3-to--4 weeks (i.e. **you will attend 3-to-4 visits per week**).

Visits 2 – 9 will take approximately 1 and a half hours each and will each contain one BCI rehabilitation session and a short questionnaire. On visit 5 there will be a repeat physical examination.

The tenth and final visit is similar to the first visit. During the final visit you will need to:

- Take part in a virtual reality (VR) task
- Undergo a physical examination
- Complete a button pressing task whilst an EEG tracing is recorded
- Undergo your last BCI rehabilitation session which will also involve EEG recording

Study visits may be filmed (on a camera and stored on the KCL secure network) for safety and/or training purposes, however participants will have the option to ask us to switch this off if they feel uncomfortable and non-consent to this aspect will not affect enrolment. Video and audio recordings will be downloaded from the camera and stored on a secure KCL server as soon as is feasible after the recording has been made and will then be deleted from the camera. Videos will be edited to hide the identity of the participant and will remain saved on the secure KCL server for up to five years and be used for education, training and safety purposes.

Below is a table to help you understand the time needed for you to be a participant in this study. We can be flexible within certain limits (usually between 1 and 3 days) about the specific days that you visit, but if you think you are not going to be able to attend more than 1 of the study visits, then please tell us at the first visit. We will pay your travel expenses, but we cannot pay you for the time commitment for the study.

The total time commitment for you will be about 24 hours spread over 10 visits over the course of 3-4 weeks, depending on your circumstances.

If visits take longer than expected (such as if you wish to take additional breaks or take longer to complete questionnaires), then refreshments e.g. drinks and a sandwich, will be offered.

Visit number	V0 Screening	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10
Location	Phone / Teams	King's College Hospital, Denmark Hill, London									
Visit length (hrs)	2	4	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	4
Phase length		3 – 4 weeks									
Extras		VR, EEG, heartbeat tracking task									VR, EEG, heartbeat tracking task

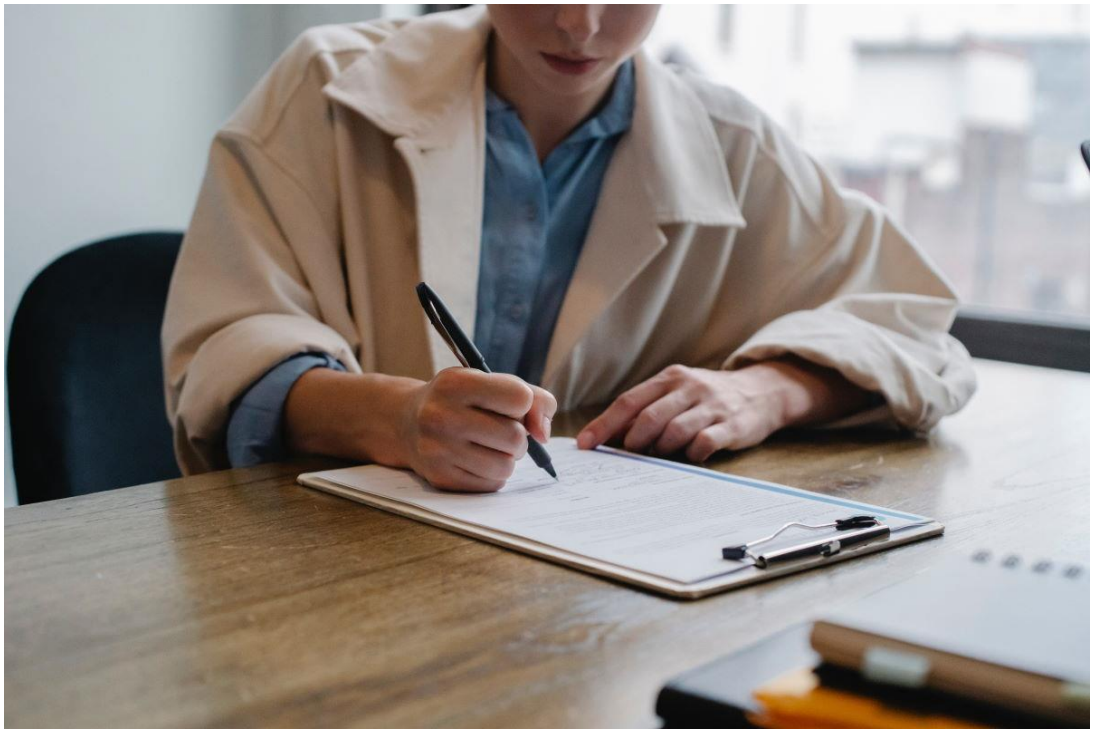
Questionnaires

The following questionnaires will be completed in the screening phone call (Visit 0):

Questionnaire / Questions	**Estimated average time to complete**	**Estimated maximum time to complete**
Medical history	30 minutes	45 minutes
Prior & Ongoing Medications	1 minute	2 minutes
Mini Neuropsychiatric Inventory v7.0 (MINI)	50 minutes	60 minutes
17 Item Hamilton Depression Rating Scale (HAM-D-17)	5 minutes	10 minutes
The Clinical Global Impressions Scale (CGI)	<1 minute	1 minute
TOTAL ESTIMATED TIME	**87 minutes**	**118 minutes**

The following questionnaires can be completed in your own time, online before Visit 1 (we will send you a link to online questionnaires hosted securely on Qualtrics):

Questionnaire	**Estimated average time to complete**	**Estimated maximum time to complete**
Stanford Expectations of Treatment Scale (SETS)	2 minutes	5 minutes
Multiscale Dissociation Inventory (MDI)	7 minutes	10 minutes
Maudsley 3-Item Visual Analogue Scale (M3VAS)	<1 minute	1 minute
Generalised Anxiety Disorder Scale (GAD-7)	3 minutes	5 minutes
Adverse Childhood Experiences (ACE)	3 minutes	5 minutes
Traumatic Experiences Checklist (TEC)	7 minutes	10 minutes
Short Assessment of Personality Scale (SAPAS)	<1 minute	1 minute
Multidimensional Assessment of Interoceptive Awareness – Version 2 (MAIA-2)	3 minutes	5 minutes
Short Suggestibility Scale (SSS)	3 minutes	5 minutes
Spontaneous Use of Imagery Scale (SUIS)	3 minutes	5 minutes
EuroQoL-5D-5L Scale (EQ-5D-5L)	3 minutes	5 minutes
Work and Social Adjustment Scale (WSAS)	1 minute	2 minutes
TOTAL ESTIMATED TIME	**37 minutes**	**59 minutes**



We will also ask you to complete some brief questionnaires during some of your visits (Visits 1, 5, 10)

VR task

During the first and tenth visit, you will be asked to put on a Quest 3 virtual reality headset and to complete a task involving dragging a ball in a circle. We will ask you to repeat this multiple times and assess how much control you feel over your movements during the task.

This is a photo of the VR headset we will use in this study, the Meta Quest 3.

This is what you will see in the VR task. You will see a wireframe of your hand holding a ball, and you will have to drag this in a circle.

EEG task

During the first and tenth visit, you will put on an EEG cap with gel in the channels of the EEG cap so that we can measure a trace of your brain activity. Whilst we measure your brain activity, we will ask you to look at a computer screen, on which you will be given cues to press either a right keyboard button, or a left keyboard button. We will measure your reaction times, as well as your brain activity in response to cues. This will take approximately 45 minutes. The EEG data will be uploaded to the secure clinical system at the CRF before pseudoanonymised versions of the EEG data are analysed.

This is a photo of the EEG cap you will be wearing. An electrode will be clipped onto your ear, this should not be uncomfortable, but if it is we can reposition it. EEG gel will be injected into each of the 16 electrode channels, so your hair will get wet. We will provide paper hand towels to wipe your scalp clean.

BCI rehabilitation sessions

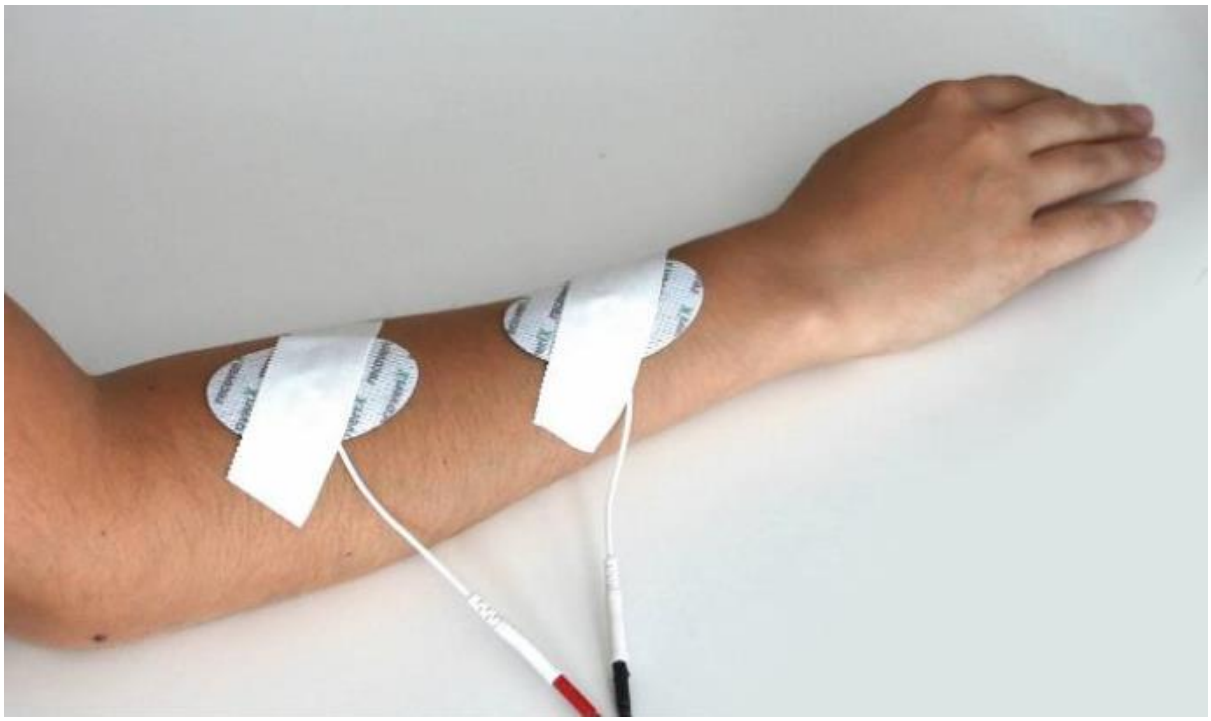
During each of the ten face-to-face visits, you will undergo a BCI rehabilitation session. This will involve wearing an EEG cap with gel in the channels of the EEG cap so that we can measure your brain activity. On visits one and ten this will be the same EEG cap that you wear for the EEG task.

We will place two sticky electrodes on your arm, and two sticky electrodes either on the opposite arm or the opposite leg. We will administer a gentle electric stimulus to your arm and leg, starting at 0mA and slowly increasing until we trigger a mild flexion of your wrist, and/or ankle. Once we are satisfied with the level of stimulation and have confirmed that this is not uncomfortable for you, we will begin the rehabilitation process.

You will be asked to look at a computer screen with an image of a person and their arms and/or legs (depending on which part of your body is affected by motor symptoms). You will hear a voice saying

either “right” or “left”, and an image will appear on the screen. After this cue you will be expected to think of moving either your right hand/foot, or your left hand/foot (without actually moving it). Your brain activity of imagining the movement (motor imagery) will be measured and if it is accurate enough, the avatar on screen will move their respective limb, and the electrodes on your arms and legs will trigger real world movement/flexion of your wrist or ankle.

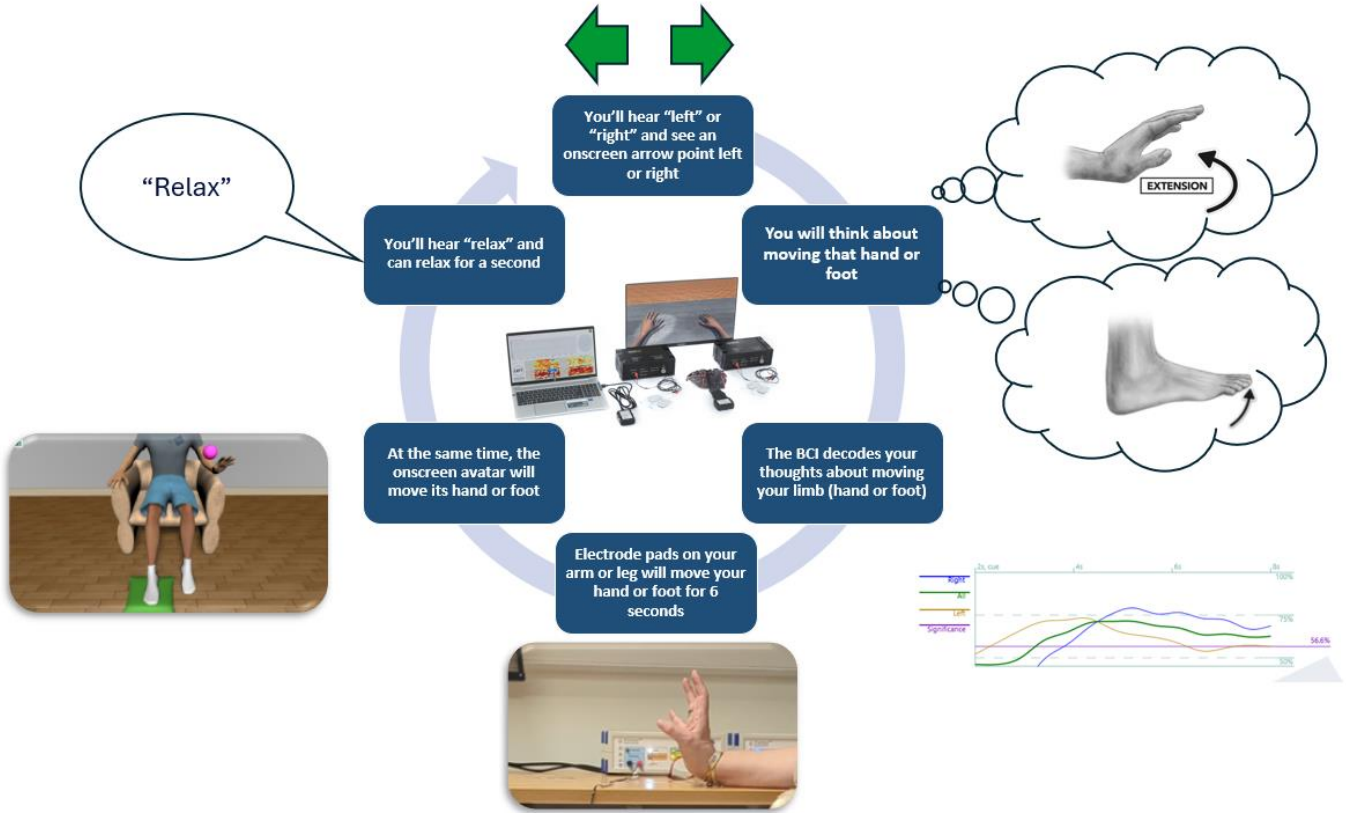
Every seven and a half minutes you will be able to take a break for two minutes. In total the process will be split into three sections and so will take roughly 55 minutes total. If you need us to pause the process, we can do this at any point.



We will place two sticky electrodes on your arm and two other sticky electrodes on the opposite arm or opposite leg.

If you are having both arms stimulated then you will see the image of two arms on the screen, and the virtual hands will move when you imagine moving your hands. If you are having one arm and one

leg stimulated then you will see the image of a person sat in a chair, and the avatar will move their hand or foot when you imagine moving your hand or foot.



Flowchart of the process you will go through during the BCI rehabilitation sessions.

Optional interview

If you are suitable for the study, we will ask you whether you would like to take part in an optional interview. You don't have to consent to this to take part in the study, but if you do it will help us further understand how this intervention might work.

The interview will last 1-to-2 hours and will focus on your experience of being part of the study, including your experiences during the rehabilitation sessions. It will take place after the final rehabilitation session and will be done remotely over Microsoft Teams. The interviewer will ask you pre-specified questions such as:

- How did you find the BCI sessions?
- How would you describe the experience of the BCI sessions to a friend?
- Were there any changes to your FND symptoms during the BCI rehabilitation?
- What are your thoughts about BCI neurofeedback as a possible treatment for FND?

There are no 'right answers' to these questions, and so the interviewer will let you talk for as long or short a period as you feel comfortable. In general, it might take around 60 – 90 minutes to complete this interview, but it could be less. This interview will be audio (not video) recorded via Microsoft

Teams and it will immediately be uploaded to the King's College London secure cloud platform. It will later be transcribed into writing by a member of the study team before the audio file is deleted.

Your responses to the interview questions will be anonymised and brought together with responses from others to form 'themes'. Direct quotes may be taken from answers and used in research reports or presentations (particularly in any paper summarising the qualitative interviews) but will be brief and anonymised. We will ask you to consent for direct but anonymised quotes to be shared in any subsequent publications. If you would prefer not to consent to this, it will not affect your enrolment into the study or to the interview.

What are the possible benefits of taking part?

1. You will be helping with clinical research, which may help others in the future.
2. The BCI rehabilitation may be a positive experience.

What are the possible risks of taking part?

1. Some people who volunteer for this study will, for one reason or another, turn out not to be eligible. Your eligibility for this study will not be confirmed until shortly before the first rehabilitation day and the study team reserve the right not to administer the rehabilitation if they think it is not in your best interests. It could be very disappointing and frustrating for you if you volunteer for this study and then are excluded shortly before rehabilitation starts. This does not happen often, but please consider this possibility before deciding whether to take part in this study.
2. The rehabilitation may be tiring given the effort and concentration required over each 45-minute rehabilitation session.
3. It may take several sessions for you to get used to the BCI rehabilitation process. During the first session it is possible that you won't be able to make the onscreen avatar move at all. This might feel discouraging and upsetting, even though the evidence suggests that most people get used to the process and are able to make it work after a few sessions.
4. The BCI will administer a very low level of electrical stimulation to make your wrist and/or ankle flex. You may find the electrical stimulation uncomfortable. If you find that you are unable to tolerate this discomfort, we ask that you tell us this immediately so that the electrical current through the system can either be reduced to a level you find acceptable or stopped altogether. You will be the one to decide what is an acceptable level.
5. Some people find VR experiences can make them feel dizzy. Whilst we will endeavour to ensure that conditions are optimised to avoid this (you will be sat down, stationary) there is always a potential risk.
6. We will ask you questions about your life history and current circumstances. This can include personal questions about traumatic events that may be distressing.

Will the costs of my travel be covered?

We will reimburse participants and their carers for reasonable travel expenses (up to a maximum of £50 per visit, contingent on receipts being provided.)

What happens when the research study finishes?

We will keep in touch with you to let you know the results of the study if you wish and we will organise events to help raise awareness about the results of the study. We will ask for your consent to contact you about other studies in functional neurological disorder or with BCIs and VR that might interest you. Information collected about you during the study may be used to support other research in the future and may be shared anonymously with other researchers.

What about media interest?

Because BCIs have been featured in the news, it is possible that the media may be interested in this study. We will never tell the media that you are involved in the study. However, if the media approach you, then please do not talk to them. Refer them to the Principal Investigator of the study, who is Dr Paul Shotbolt.

Can the study team stop me from participating in the study?

Yes. The study team and the sponsor of the study can stop your involvement at any time. For example, this may happen because we are concerned for your safety if you continue in the study.

Part 2

What if relevant new information becomes available?

It is possible that whilst performing normal medical checks we may identify a significant problem that you didn't know you had. If this occurs, we will inform you. Sometimes during a research project, new information becomes available about the device. Although unlikely, if this happens, a member of the research team will tell you about it and discuss whether you want to continue in the study.

If you decide to continue in the study, you may be asked to sign an updated consent form. If the study is stopped for any other reason, we will tell you why

What will happen if I don't want to carry on with the study?

If you withdraw from the study, your usual care and treatment will continue as before. We will retain and continue to use any data collected before you withdrew.

How do I get help if I am concerned about anything?

If you have a concern about any part of this study, you should ask to speak with a member of the study team, who will do their best to address your concerns. You should report any adverse events or medical occurrences that you experience whilst in the study to a member of the study team.

If you have any medical concerns that cannot wait until you can talk to a member of the team you should dial 111 to talk to NHS direct (24 hours a day), or speak to your GP or secondary mental health care professional using the information in this sheet to tell them about your participation in the study. In an emergency, you should visit A&E or dial 999.

What if there is a problem?

Any complaint about your experience within the study will be responded to and we will try to address any concerns you have as best we can. If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions [Dr Paul Shotbolt, Paul.Shotbolt@kcl.ac.uk, bravefnd@kcl.ac.uk].

If you remain unhappy and wish to complain formally, you can do this through the SLaM Patient Advice and Liaison Service (PALS) on 0800 731 2864, pals@slam.nhs.uk. In the event that something does go wrong, and you are harmed during the research, you may have grounds for legal action for compensation against King's College London and/or SLaM NHS Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Will my participation in this study be kept confidential?

Yes, however we need to tell other professionals involved with your care, for example your GP, that you are a part of this study and if any serious concerns arise. Similarly, we will ask them whether they have any concerns about you being in the study. They are bound by the same legal duty of confidentiality as the study team.

We will always try to ask for your approval before contacting your GP or other health professional if we have concerns about your safety or welfare. However, if we think that your safety and welfare is seriously at risk then we may not seek your consent beforehand, particularly if we think this would introduce unnecessary delay or cause unnecessary risk to yourself or others.

How will we use information about you?

We will need to use information about you, from your medical records, from your named carer or relative (support person) and from your GP for this study for this research project.

This information will include your:

- Name
- Initials
- Date of birth
- Contact details
- NHS number

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

King's College London and the South London and Maudsley NHS Foundation Trust are the co-sponsors of this research, and are both joint data controllers.

King's College London and the South London and Maudsley NHS Foundation are responsible for looking after your information. We will not share your information related to this research project with any other organisations

We will keep all information about you safe and secure by:

- We will write our reports in a way that no-one can work out that you took part in the study.
- Research data collected on paper will be stored securely in files in a locked cupboard, or in a locked office.
- Electronic research data and audio-visual data (including any videos) will be stored on secure computer servers located in the same country as the study itself.
- Only members of the clinical or research team or representatives from the Sponsor will have access to your data.

International transfers

Your data will not be shared outside the UK.

How will we use information about you after the study ends?

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for a maximum of 10 years. The study data will then be fully anonymised and securely archived or destroyed.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have

You have the right to ask us to access, remove, change or delete data we hold about you for the purposes of the study. You can also object to our processing of your data. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

You can find out more about how we use your information:

- our leaflet http://www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to bravefnd@kcl.ac.uk, or
- by sending an email to King's College London Data Protection Officer Mr Olenka Cogias, info-compliance@kcl.ac.uk (KCL) or via https://www.slam.nhs.uk/about-us/privacy-and-gdpr

What will happen to the results of the research study?

The results of the study will be published in academic peer-reviewed journals, presented at conferences and discussed at other public events. We will also produce a newsletter summarising the findings of the study which we will send to you and your clinical team. You will not be identified in any report or publication.

Who is organising and funding the research?

The study is organised by the Institute of Psychiatry, Psychology & Neuroscience, King's College London. The sponsors of the study are King's College London and the South London and Maudsley NHS Foundation Trust. Funding is provided by the KCL-Wellcome Mental Health Research for Health Professionals programme. The BCI is manufactured by g.tec. The researchers involved in conducting this study do not receive any financial incentives for including you in this study and do not benefit financially from this study.

Who has reviewed the study?

This research has been reviewed by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. We have also sought advice from FND patient representatives in the design and planning of this study.

Names of the study team

Principal Investigator: Dr Paul Shotbolt

Lead Investigator: Dr Hamilton Morrin

Contact us:

Email: bravefnd@kcl.ac.uk