PB-PG-0807-14152 – NIHR Research for Patient Benefit Programme – Final report

Project title: A novel neurofeedback based intervention to reduce neglect and improve function in stroke patients.

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Plain language summary

Following a stroke, some people are not aware of the space around them (called hemispatial neglect). Typically this occurs when the stroke affects the left hand side of the body. It is frequently associated with not being very alert, and there is research evidence that would suggest that rehabilitation that increases alertness could be effective in reducing the extent of hemispatial neglect.

The brain produces electricity which can be detected by electrodes placed on the scalp, this is called the EEG. The EEG tracing is a little like the ECG that records electrical activity from the heart. There is more than one type of electrical activity or waveform recorded with the EEG. Two of these are called theta and beta waves. Alertness is associated with decreased theta and increased beta waves. It has been suggested that showing people their EEG (called neuro-feedback [nf]) and training them to increase theta waves and decrease the beta waves may increase alertness and reduce the neglect.

The primary aim of this research was to assess the potential of NF using EEG to improve alertness and improvement in day to day activities in people with neglect. Other outcomes were to measure how easy it was to use NF and is it safe and thirdly to look at the changes in the brain associated with such recovery. This was to be investigated by using functional MRI.

The study planned to provide a 30 minutes session 5 days a week for 6 weeks. Patients were to be randomised between EEG NF and a sham session.

The research confirmed the reduced Beta wave activity in patients with neglect, and that over the six week period of NF some patients increased their level of Beta wave activity, it was not possible to conclude that the use of NF provided any benefit over and above spontaneous recovery. We found that the use of NF with EEG was not feasible in the acute phase of stroke, due to patients being clinically unwell and very tired, lacking in energy.

It was not possible to undertake the third part of the study, as it required the use of the research MRI in a separate building to the stroke unit. Logistically it was not possible to access the department.

In conclusion, this study has shown two things; 1) hemispatial neglect is associated with decreased beta waves. As neglect improved Beta wave activity increased, due to stroke recovery. 2), the study was more difficult to undertake than anticipated due to patients being less medically fit than anticipated

Keywords
EEG, EEG neurofeedback training, Hemispatial neglect, Rehabilitation

Summary of research findings
Hemispatial neglect is a complex neurological disorder, most commonly occurring after right hemisphere stroke, which manifests as an inability to attend to stimuli presented in the contralesional side of space. With over two-thirds of right hemisphere stroke patients suffering from the debilitating effects of hemispatial neglect a greater understanding of this condition and the development of effective rehabilitation interventions are vital. A small percentage of patients who present with neglect in the acute stages post-stroke do spontaneously recover completely (approximately 9%) and around 43% of patients show some improvement in a 2-week period post-stroke. However, there remains a large percentage of patients who are left with debilitating symptoms which can greatly hamper the rehabilitation of other neurological deficits that may be unrelated to neglect, such as hemiplegia. Despite the fact that neglect is the best single predictor of poor recovery from stroke, there remains no satisfactory consistent form of rehabilitation for this deficit. A growing body of research suggests that non-spatial deficits, such as sustained attention, may underpin hemispatial neglect rather than it being a purely spatial disorder. This is supported by recent findings that children with ADHD, a disorder associated with a disrupted attention system, often exhibit a leftward spatial bias similar to stroke-induced neglect. Given that EEG neurofeedback (EEG NF) has proven to be an effective treatment for ADHD there is potential that it could also be applied to patients with hemispatial neglect.

EEG NF is a technique that has previously been employed to normalize EEG in clinical populations by teaching individuals to modulate specific EEG frequencies. Learning is achieved by presenting the individual with an online representation of their brain activity in the form of a simple audio-visual display, such as a computer game or video. When the individual successfully increases or decreases specific brain frequencies they receive a positive audio-visual reward. This positive reinforcement gradually leads to better self-regulation of brain activity through learning achieved over repeated sessions. Several NF studies have reported behavioural, cognitive and neurophysiological improvements as a result of beta-reward protocols in subjects with ADHD and hence the same protocol was employed in this study.

The aims of the study were:

1. Assess the potential of EEG-NF in improving sustained attention and improvement in performance on everyday tasks in stroke patients with neglect.
2. Assess the feasibility of using EEG-NF for stroke patients with neglect

3. Identify cortical mechanisms that may underlie recovery of neglect in stroke patients, which will provide a mechanistic insight into developing and refining interventions for improving neglect and disability in these patients.

It was anticipated that given the prevalence of neglect in the acute stroke population, recruitment would be relatively straightforward. However many patients were clinically unstable during the recruitment phase or were suffering from fatigue, and as a consequence did not meet the inclusion/exclusion criteria. As a result all patients received the NF training intervention rather than allocating patients to an additional control group. Seven neglect patients completed the full twelve week study, six weeks of daily NF training sessions followed by six weeks with no intervention. Assessment sessions were conducted at 3 time points: Time 1 was conducted during the baseline week, immediately following consent, Time 2 was conducted in week 7 after the NF training period, Time 3 was conducted in week 12. The beta training protocol required patients to increase beta activity without simultaneously increasing theta or high beta activity. To study the effects of EEG modulation, several EEG variables were extracted from the session data: beta amplitude during baseline and feedback periods and theta and high beta activity (the inhibit frequency bands) during baseline and feedback periods. To determine whether patients showed evidence of EEG modulation as a direct result of the NF training, within-session learning effects were analysed in the form of increased beta power within the feedback periods. Without empirical evidence of within session training, despite an observed across session improvement in baseline beta activity, successful NF training could not be concluded. Instead the across session changes in EEG are more likely to be due to spontaneous recover alone.

In addition to assessing the therapeutic effects of EEG NF training, the design of this study permitted a broader, perhaps even more important, line of investigation into the recovery of neglected patients. Each NF session commenced with a three-minute baseline EEG recording (during which thresholds for the training period were set) meaning a continual dynamic record of resting state EEG would be obtained for each patient across the six-week period. Regardless of whether changes were induced as a result of the training or not, this is the first study to obtain such a detailed account of EEG activity over a prolonged period of time and allow correlations to be made with behavioural measures. Given the distorted EEG profile of neglect patients found in our initial analyses, it was hypothesized that recovery would be associated with a normalization of EEG activity with specific emphasis on an increase in beta activity.

Our analyses revealed that a subgroup of patients who showed an increase in tonic beta activity over a 6-week period also showed a corresponding significant improvement in NIHSS scores in comparison with patients who failed to show a change in beta activity. If beta activity is considered to be a measure of alertness, the findings of this study suggest that an improvement in alertness is associated with a general improvement in stroke-related deficits in neglect patients. In order to determine whether there were any factors distinguishing patients who showed increased beta activity from those who did not, baseline EEG and behavioural measures were compared across groups. Interestingly, anxiety proved to produce the only significant difference, with low anxiety corresponding to patients who showed an increase in beta activity over time relative to patients who showed no change in beta activity. This finding suggests that anxiety could be a predictor of EEG

normalization and behavioural recovery. This deserves further investigation in future studies as it has implications for rehabilitation studies. The second distinguishing group factor was baseline EEG activity. The initial beta activity was lower (but not significantly) in patients who went on to show increased beta over time. Both findings suggest a relationship between baseline EEG deviations and potential for normalization, with more extreme deviations in EEG associated with a higher rate of change over time. There was also a trend for patients who showed increased beta activity across sessions to have more severe neglect, as measured by the BIT, although this was not significant. This tentative conclusion points to a relationship between neglect severity and EEG modulation. If patients are able to modulate their EEG despite having more severe neglect deficits this has significant implications for future therapy.

Each training session consisted of five 3-minute training periods during which patients were asked to maintain beta amplitude above threshold. In order to ascertain whether patients showed evidence that they were able to modulate beta amplitude with increasing success during a session, mean beta amplitudes for each 3-minute training period were extracted and averaged across all training sessions. Correlations were then conducted to see if there was a relationship between beta amplitude and training period. Five of the seven patients showed a trend, defined as a positive correlation coefficient, to increase beta amplitude across the five training periods of the sessions, however none of these correlations reached significance. Given the lack of significant increases in beta amplitude in any of the patients it is not possible to conclude that NF training has induced neuroplastic changes in these right hemisphere stroke patients in the acute post-stroke phase.

Patient and public involvement

The role of PPI involvement prior to the study commencing was invaluable. Insights were provided that helped to structure the study to maximise recruitment of people. The difficulties experienced were more due to methodological and logistical reasons. Rather than a refusal to take part. We would welcome the input of trained PPI in future studies.

Data sharing statement

See link [https://www.nihr.ac.uk/documents/nihr-position-on-the-sharing-of-research-data/12253] for the NIHR position of the sharing of research data. The NIHR strongly supports the sharing of data in the most appropriate way, to help deliver research that maximises benefits to patients and the wider public, the health and care system and which contributes to economic growth in the UK. All requests for data should be directed to the award holder and managed by the award holder.

Disclaimer

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This project was carried out between June 2010 and July 2013. This final report has not been peer-reviewed. The report was examined by the Programme Director at the time of submission to assess completeness against the stated aims.