Chronic Stroke Rehabilitation: Exploring Technology and Neuromodulation Across Domains

26 June 2017
University of Surrey

Welcome

Welcome to this one-day workshop on Chronic Stroke Rehabilitation at the University of Surrey. We hope that you will find the programme interesting, engaging and also challenging. The papers being presented at the workshop will share empirical and theoretical work, as well as use a range of methodological approaches to explore this topic.

We are very pleased to have such a variety of speakers, from a range of disciplines. We hope that there is lots of opportunity for interactive discussion and sharing insights from our own experiences with stroke rehabilitation in a clinical or research context. We additionally hope that there will be chance to discuss methodological challenges in exploring rehabilitation with this patient group.

We extend our grateful thanks to the Institute of Advanced Studies for sponsoring this event, and for all those who have been willing and enthusiastic in their participation to help deliver such a stimulating array of talks. We do hope you enjoy the discussion, and we hope that it helps inform future research. We look forward to meeting you all.

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Programme

Time	
09:00	****Registration opens (tea and coffee)****
	Theme One: Vision
09:30	Brain Stimulation for neglect rehabilitation
	Pierre Petitet and Jacinta O'Shea, University of Oxford
09:55	Transcranial magnetic stimulation as a therapeutic approach for neglect rehabilitation
	Raquel Viejo Sobera, Universitat Oberta de Catalunya Barcelona
10:20	Brain stimulation of vigilant attention in stroke *Elena Olgiati, Imperial College London*
10:45	****Morning tea and coffee break****
	Theme Two: Motor rehabilitation
11.15	**Motivating stroke motor rehabilitation using digital musical instruments**
	Pedro Kirk, Goldsmiths
11:40	Insights into mechanisms of performance change due to proximal upper limb training in a robotic manipulandum in chronic stroke
	Ulrike Hammerbeck, University of Manchester
12:05	The role of sleep in neuromuscular rehabilitation
	Annette Sterr, University of Surrey
12:30	****Buffet lunch (provided)****
	Theme Three: Language
13:30	Neurostimulation in Chronic Stroke Aphasia: Issues around performance measurement, behavioural treatment, and stimulation site
	Anna Woollams, University of Manchester
13:55	Speech facilitation in aphasia using transcranial direct-current stimulation
	Jenny Crinion, UCL
14:20	Randomized trial of iReadMore word reading training and left IFG anodal tDCS in central alexia
	Sheila Kerry, UCL
14:50	****Afternoon tea and coffee break****
15:15	Training semantic associations in patients with comprehension impairments
	Glyn Hallam, University of York
15:40	EVA Park: Aphasia therapy using an online virtual word
	Richard Talbot, Niamh Devane and Jane Marshall, City University
16:05	Multidisciplinary computer-based motor and language therapy
	Holly Robson and Lotte Meteyard, University of Reading
16:30	****final remarks and close****

Abstracts

Theme One: Vision

Brain stimulation for neglect rehabilitation

Pierre Petitet

Oxford Centre for Functional Magnetic Resonance Imaging of the Brain (FMRIB),

Wellcome Centre for Integrative Neuroimaging (WIN),

Nuffield Department of Clinical Neurosciences, University of Oxford, U.K.

It is known that adaptation to a rightward prismatic shift can improve neglect symptoms after right hemisphere stroke (Frassinetti, Angeli, Meneghello, Avanzi, & Làdavas, 2002; Rossetti, et al., 1998; Serino, Barbiani, Rinaldesi, & Làdavas, 2009). However, not all patients respond to prism therapy, and in those that do the therapeutic benefits are transient (typically ~ 1 day). We developed a non-invasive brain stimulation protocol that aimed to potentiate motor memory formation in circuits controlling the adapting right arm. We predicted that this protocol would enhance consolidation of both the prism after-effect and the transfer gains for neglect. We performed an initial scientific proof-of-concept test of this hypothesis using an experimental medicine approach. Experiments in healthy volunteers were conducted first to identify the optimal brain stimulation protocol, which was then translated to patients to assess clinical response.

In a series of experiments in healthy volunteers, we identified a transcranial direct current stimulation protocol that increased prism after-effect persistence from < 24 hours to a timescale of multiple days. By assessing inter-individual covariance of behaviour with brain imaging data, we could also identify neurochemical correlates of the stimulation-induced behavioural change. Next, this stimulation protocol was translated to test for clinical effects in three chronic, severe, treatment-resistant neglect patients in four longitudinal case series. We observed: 1) enhanced retention of the prism after-effect, and 2) a significant increase in the magnitude and longevity of therapeutic response. When exposed to prism therapy combined with sham stimulation, patients showed no improvement. However, when the therapy was combined with stimulation, all patients exhibited significant improvements in neglect that lasted for weeks to months and did not return to baseline.

These findings challenge consensus in the literature that because the left hemisphere is pathologically over-excited in neglect it should be suppressed. They further demonstrate that the normally transient after-effect of prism adaptation can be transformed into a long-lasting memory trace that is therapeutically significant. Stimulation during visuomotor adaptation can unmask latent plastic potential in the damaged brain that durably improves attention deficits after right hemisphere stroke.

Transcranial Magnetic Stimulation as a Therapeutic Approach for Neglect Rehabilitation

Dr Raquel Viejo Sobera

Faculty of Health Sciences

Universitat Oberta de Catalunya

Barcelona

For many years, clinical research has been conducted to develop new and effective rehabilitation strategies for neglect rehabilitation. Nowadays, transcranial magnetic stimulation (TMS) is a relevant tool in this regard, and it should be considered as a therapeutic intervention in combination with other rehabilitation approaches.

A systematic review was conducted in the MEDLINE and Web of Science databases in order to find all the existing evidence of TMS in the rehabilitation of neglect.

The studies focused on ameliorating the negelct symptoms in stroke patients have been conducted by applying stimulation over the intact hemisphere posterior parietal cortex using inhibitory TMS protocols, such as low frequency repetitive TMS (58% of the studies) or continuous theta burst stimulation (42%). Most of the studies used figure-eight coils (79%), but round coils were also used with positive results (21%). The treatments varied from 1 session (37%) to up to to 20 sessions (16%).

All the published studies have positive results with improvements lasting from a few hours to up to 6 weeks after the end of the treatment in two cases (11%). The absence of negative findings alerts us about to the high risk of publication bias.

Although the evidence for considering TMS as a new therapeutic tool is still scarce, the findings so far are encouraging. TMS is a promising technique in the treatment of neurological syndromes, but more clinical trials with larger samples are essential to determine the real potential of TMS as a rehabilitation approach.

Brain stimulation of vigilant attention in stroke

Dr Elena Olgiati

Faculty of Medicine

Imperial College London

Sustained or vigilant attention is the ability to maintain attentional focus when confronted with prolonged cognitive effort. Converging evidence from primate neurophysiology, lesion studies and functional imaging has shown that right frontal and parietal regions play a key role in maintaining attention over time (Posner & Petersen, 1990). Right hemispheric stroke can cause a deficit in sustaining attentional performance, especially when a spatial component is incorporated into a task (Malhotra et al., 2009). Importantly, sustained attention deficits have been shown to contribute to the disability and the severity of spatial neglect.

Here, we explored the effect of non-invasive brain stimulation on different attention measures in stroke patients and age-matched controls, following on recent evidence showing that tDCS can improve vigilance in young volunteers (Nelson et al., 2014). Participants performed a vigilance task under conditions of real/sham tDCS, in a double blind sham-controlled crossover design. A weak direct current (1mA, 10 minutes) was applied over the right dorsolateral prefrontal cortex using 3 circular (1.5cm diameter) rubber electrodes. A brief set of cognitive tests was administered immediately before/after the application of real/sham tDCS. In addition, participants underwent resting-state fMRI whilst receiving real/sham tDCS to examine whether vigilance, and its responsiveness to brain stimulation, was linked to any particular patterns of brain network activity. In my talk, I will present preliminary evidence from this study and address the role of brain stimulation in boosting sustained attention in stroke patients.

Theme Two: Motor rehabilitation

Sounds Within Reach: Enriched Environments for Physical Rehabilitation of the Upper Limb

Pedro Kirk

Department of Psychology

Goldsmiths

University of London

Stroke is a leading cause of adult disability disproportionately affecting people from poorer backgrounds (Mendis, 2013). Stroke survivors often have limited access to rehabilitation after discharge from hospital leaving them to self-regulate their recovery (Ashley, 2013). Previous research has indicated that several musical approaches can be used effectively in stroke rehabilitation (Altenmüller, et al., 2009; Schneider et al.,2007).

Music Therapy (MT) can be incorporated into stroke rehabilitation in a variety of situations and many techniques can be tailored to the physical goals and musical preferences of individual stroke survivors (Kadar, 2014). The use of digital-music interfaces, as opposed to traditional musical instruments, gives greater versatility and the opportunity to use machine learning approaches to tailor the protocol to an individuals' specific goals and improvement trajectory. Sounds Within Reach is a collaborative on-going project researching the role of bespoke digital musical instruments to aid in the physical rehabilitation of the upper limb for stroke survivors.

Insights into mechanisms of performance change due to proximal upper limb training in a robotic manipulandum in chronic stroke.

Dr Ulrike Hammerbeck

Division of Nursing, Midwifery and Social Work

University of Manchester

Recovery from stroke is often said to be the greatest early after the insult. Yet even in the chronic phase, training can improve performance. Here we probe the learning mechanism underlying accuracy improvements during reaching and test whether the speed at which movements are practised affects learning.

36 chronic stroke survivors trained over four consecutive days to improve endpoint accuracy in an arm-reaching task (420 repetitions/day). Half the participants trained using fast and the other half slow movements. The trunk was constrained allowing only shoulder and elbow movement for task performance.

At baseline, movements were variable, tended to undershoot the target and terminate in contralateral workspace (flexion bias). Training improved movement accuracy in both groups by reducing trial-to-trial variability however, the endpoint bias (systematic error) did not change. Improvements were greatest at the trained movement speed but in the fast training group generalised to other speeds. In the fast group small but significant improvements were observed in clinical measures.

Reduced trial-to-trial variability without an alteration to endpoint bias suggests that improvements are achieved by better control over motor commands within the existing repertoire. Thus, 4 days' training allows chronic stroke survivors to improve movements that they can already make. We further suggest that training needs to

be performed at a variety of movement speeds as generalisation is limited. Knowledge of the mechanism by which training alters behaviour will allow the design of more effective, tailored interventions.

The Role of Sleep in Neuromuscular Rehabilitation

Prof Annette Sterr

School of Psychology

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TBC

Theme Three: Language

Neurostimulation in Chronic Stroke Aphasia: Issues around performance measurement, behavioural treatment, and stimulation site.

Dr Anna Woollams

Division of Neuroscience and Experimental Psychology

University of Manchester

Neuroscience has offered a new framework within which to motivate treatment of deficits in chronic stroke aphasia, both in terms of the potential for plasticity and opportunities to enhance rehabilitation. This talk will first present a study where neurostimulation was combined with behavioural treatment for anomia in a case of chronic Broca's aphasia. Both the laterality and polarity of transcranial Direct Current Stimulation were systematically manipulated and compared to shame controls in order to determine effectiveness.

This work raises a number of issues concerning the treatment of anomia in chronic aphasia. The first concerns measurement of performance, and case series data will be provided that illustrates the scale of this problem. The second concerns the form of the behavioural intervention, which will be demonstrated by preliminary data from a recent case series computerised therapy study. The third concerns the optimal site for stimulation, and some suggestive case study data concerning the interaction of damage with treatment relevant to this issue will be presented. Overall, the neuroscience framework represents an exciting and productive approach that may help to overcome challenges in the treatment of chronic stroke aphasia.

Speech facilitation in aphasia using tDCS

Dr Jenny Crinion

Institute of Cognitive Neuroscience

University College London

Word-finding difficulties (anomia) are the most common and chronically disabling impairment after aphasic stroke. However, surprisingly little is understood about the contributions that different frontal brain areas make to anomia recovery, and how these areas function together as a network. The frontal language network overlaps considerably with those supporting other diverse cognitive functions such as cognitive control; both are likely involved in language learning/recovery. Here I seek to place spoken word production in the context of wider cognition and its underlying neural mechanisms to understand how common brain areas, and possibly common processes, support such disparate functions in the damaged brain. To address this I use whole-brain high-resolution structural and functional magnetic resonance imaging (fMRI) together with transcranial direct current stimulation (tDCS), plus neuropsychological examination and behavioural training of aphasic stroke patients.

Using factorial neuroimaging experimental paradigms paired with 'real-life' anomia training procedures I examine brain-behaviour relationships. My first series of experiments use fMRI to investigate the immediate modulatory effects of tDCS on healthy older subjects' frontal brain networks (including Broca's area) during easy and hard naming and cognitive control tasks. The second experimental series will investigate longer-term changes (consolidation) in these frontal brain networks after extended anomia training (hard becomes easy) and preliminary data where tDCS delivered to IFG in conjunction with extended anomia training facilitated speech relearning success. This approach may provide a powerful platform to understand the neural basis of cognitive and spoken language change following brain damage.

Randomized trial of iReadMore word reading training and left IFG anodal tDCS in central alexia

Sheila Kerry

Institute of Cognitive Neuroscience

University College London

Central alexia is an acquired reading disorder co-occurring with a generalised language deficit (aphasia). Despite the frequency and severity of reading impairments in post-stroke aphasia there is a lack of good evidence for the efficacy or mechanisms of potential reading treatments. This study tested the impact of a novel word reading training app, 'iReadMore', and anodal transcranial direct current stimulation of the left inferior frontal gyrus, on word reading ability in central alexia. 21 chronic stroke patients with central alexia participated.

A baseline-controlled, repeated-measures, crossover design was used. Participants completed two 4-week blocks of iReadMore training, one with anodal stimulation and one with sham stimulation (double-blind, block randomized and counterbalanced between participants). Each block comprised 34 hours of iReadMore training and 11 stimulation sessions. Outcome measures were assessed before, between and after the two blocks. The primary outcome measures were reading ability for trained and untrained words. Secondary outcome measures included semantic word matching, sentence reading, text reading and a self-report measure. iReadMore training resulted in an 8.7% improvement in reading accuracy for trained words but did not generalise to untrained words. Reaction times also improved. Reading accuracy gains were maintained three-months after training cessation. Anodal tDCS (compared to sham), delivered concurrently with iReadMore, resulted in a 2.6% facilitation for reading accuracy, both for trained and untrained words. iReadMore also improved performance on the semantic word-matching test. There was a non-significant trend towards improved self-reported reading ability. However, no significant changes were seen at the sentence or text reading level.

In summary, iReadMore training in post-stroke central alexia improved reading ability for trained words, with good maintenance of the therapy effect. Anodal stimulation facilitated learning and also generalised to untrained items.

Training semantic associations in patients with comprehension impairments

Dr Glyn Hallam

Department of Psychology

University of York

We present preliminary data from a training study of patients with stroke aphasia, who demonstrate impairments in semantic control tasks, that assessed whether training on a task requiring semantic control (e.g. associating the probe word 'garden' with target word 'shed', in the presence of related distractors) would lead to subsequent improvements on related measures of semantic control.

Patients underwent 6 training sessions over a two week period. Results showed that patients improved in accuracy on the training task over the course of the study, though this was largely driven by an improvement on trials that

were repeated across the training protocol. Subsequent testing following completion of training showed an improvement on the Camel and Cactus test (which also tests semantic control).

Patients also underwent fMRI scanning before and after training to assess whether there was any correspondence between behavioural improvements and changes in brain activity. We found an increase in activity from baseline to post-training scan in the pre-supplementary motor area while participants performed variant of the Camel and Cactus test that corresponded to the behavioural improvement following the training.

Evaluating the benefits of aphasia intervention delivered in virtual reality

Richard Talbot

Division of Language and Communication Science

City University, London

Virtual reality (VR) is a computer-generated simulation of an environment with which the user can interact. It has many potential benefits for aphasia rehabilitation. Using simulated contexts in therapy may enhance functional communication and build confidence; and the opportunities to meet others 'in world' may reduce isolation. Despite this potential, few previous treatments for aphasia have deployed VR. Stark and colleagues developed a virtual house to promote language practice. Two programmes, Orla and AphasiaScripts, make use of a virtual therapist.

EVA Park is the first multi-user VR platform designed for people with aphasia. This study aimed to find out if an intervention delivered in EVA Park would benefit functional communication, word production, communicative confidence and feelings of social isolation. The accessibility and acceptability of the intervention was also explored. EVA Park was developed via a process of co-design involving people with aphasia. It has different locations including shops, restaurants, a hairdressers, houses, a bar and disco. There are fantastical elements such as elephants that can be ridden, and a mermaid under the lake. Users are represented by personalised avatars and talk to each other using headsets.

20 people with aphasia received 5 weeks of language stimulation in EVA Park. Each had daily sessions with a support worker addressing individual communication goals. They also had unlimited access to EVA Park in which they could potentially meet other participants. Activities included supported conversation, role plays and group discussions. The study employed a quasi-randomised design, which compared a group that received immediate intervention with a waitlist control group. Structured observations of participants using EVA Park and interviews explored accessibility and acceptability.

There were significant gains on the Communication Activities of Daily Living test. Gains were achieved by both groups of participants, once intervention was received, and were well maintained. Fluency naming and the Confidence Rating Scale also improved, but changes could not be attributed to intervention. Word retrieval in conversation and narrative did not change; nor did the Friendship Scale. The observation and interview results indicated good accessibility and acceptability.

Participants found EVA Park easy to use and were very positive about the intervention. Mixed outcomes may reflect the content of intervention and the suitability of the measures.

There were significant benefits for functional communication as assessed by the CADL-2. The skills explored by this measure are very close to those practised in Eva Park. Functional communication has been cited as the primary goal of aphasia therapy, since it reflects the ability to communicate in real world settings. The opportunity to locate intervention in simulations of such settings may be a key contribution of EVA Park to clinical practice. Other therapeutic applications of this novel resource now need to be explored.

Pilot data for computer-based motor & language therapy for chronic aphasia

Dr Lotte Meteyard and Dr Holly Robson

Department of Psychology

University of Reading

Neuroscience research has shown that the brain networks for language and movement overlap and are interconnected. Therefore, rehabilitation may benefit from combining language and motor activities together. However, treatment is currently separated across different health professionals (physiotherapists treat physical impairments, occupational therapists treat limitations in day to day life and Speech & Language Therapists treat language impairments). Therefore, many hours of therapist's time is actually provided separately.

The aim of this project is to develop a therapy software that can be used by more than one health profession to deliver therapy in a time efficient, personalised and motivating way. We present pilot data for a therapy software that combines treatment of language impairments with and motor actions, using motion-sensor technology (Microsoft Kinect) that is able to track how an individual moves. The software engages participants in rehabilitation exercises that require them to move their upper limbs in order to respond to language tasks (e.g. *Find the one that starts with '"s"*). We present data from a proof-of-principle study, in which the software has been trialled with 5 individuals with chronic impairments of language and upper-limb movement post-stroke