Computerised Cognitive Rehabilitation in Multiple Sclerosis May Result in Improved Working Memory

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TARGET AUDIENCE: Clinical and research based neuroscientists with an interest in cognition, neuroplasticity and multiple sclerosis.

PURPOSE: Multiple sclerosis (MS) is a common inflammatory condition affecting the central nervous system (CNS). MS is the most common cause of acquired, non-traumatic disability in young adults [1]. Many individuals with MS experience significant psychological, psychiatric and cognitive difficulties. Between 40-60% of individuals with MS may have evidence of cognitive dysfunction on neuropsychological testing [2-4]. Independent of the physical limitations imposed by the disease, cognitive dysfunction negatively impacts upon social functioning and quality of life (QOL) [5, 6]. Few studies utilising computer software based training have explored the structural and functional basis of neural plasticity in cognitive rehabilitation in MS [7-9]. We aim to investigate if a period of computerised, home-based cognitive rehabilitation is both feasible and effective in improving cognitive performance as well as QOL and patient measures of self-efficacy in managing their condition. We explore the functional and structural neuroimaging basis of any improvement in cognitive performance.

METHODS: This is a between-subject repeated measures placebo controlled study design in which adults with MS and evidence of cognitive impairment were randomly assigned to receive 45-minute, thrice weekly sessions of home-based computerised cognitive training for six weeks or a placebo condition (natural history DVDs). Forty adult patients with MS were recruited to the study. Patients were screened using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) test battery [10] for evidence of cognitive impairment. Participants are tested at 3 time points; at baseline (T1), after six weeks of intervention (T2) and after a further three months (T3). Here we present data on the first 17 patients (7 treatment, 10 placebo) with data at the first two time points (T1 and T2). MRI included structural and functional assessments. Only fMRI data are reported here. The task consisted of a visually presented n-back task [11], with n=0, n=1, and n=2 conditions, arranged in a block-design. Three 9-minute runs were recorded per session. The analysis was performed in SPM8. Data were realigned, normalised to MNI space and smoothed with a 8mm^3 Gaussian kernel. At first level, 2 contrasts were estimated to identify: 1) areas of increased activity in the 1-back compared to 0-back, and 2) areas of increased activity in the 2-back compared to the 1-back condition. At group level we estimated the group-by-time interaction, to evaluate areas of relative increase/decrease of activity after cognitive training versus placebo. Participants also underwent repeat testing with the BICAMS battery at each time point and completed a number of questionnaires examining QOL.

A repeat measures ANOVA test was performed to measure changes in the error rates between groups in the individual n-back tests, and changes in performance at the BICAMS.

RESULTS:

Figure 1 shows the main effect of 1-back>0-back and 2-back>0-back at group level. These maps are consistent with brain areas known to be involved in working memory [11]. No significant effects were detected in performance in the BICAMS cognitive assessment battery between T1 and T2, although there was a trend towards improvement in the treatment group. With respect to the n-back task, only patients in the treatment group showed an improvement at T2, with a lower number of errors compared to T1 (p=0.018). Figure 2 shows the group-by-time interaction in 2-back>1-back task, showing increased activation in the left frontal cortex in the control group relative to treatment group at T2 (p<0.005 uncorrected).

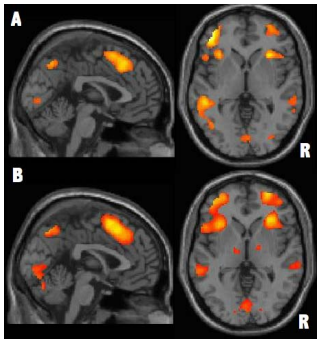

Fig 1. Group-level main effect of 1back>0-back (A) and 2-back>0-back (B).

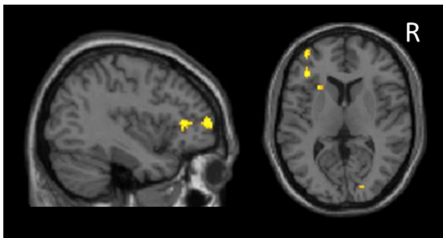

Fig 2. Significant group-by-time interaction (p<0.005, uncorrected, k>30)

DISCUSSION:

Our fMRI paradigm illustrates increased working memory load with increasing complexity of n-back task. Our preliminary data support the hypothesis that home based cognitive rehabilitation may be effective in improving cognitive performance in working memory tasks. Preliminary fMRI data suggests there may be an alteration in BOLD activity that underpins this improvement. It might be postulated that with cognitive training, less cognitive effort is required to perform working memory tasks as assessed on this n-back paradigm and as measured in a reduced error rate in performing the task.

References: References. 1. Anderson D, et al. Ann Neurol 1992; 31:333-6; 2. Rao, SM et al. Neurology 1991; 41:685-91; 3. Rovaris M, et al. AJNR 2000; 21:402-8; 4. Lyon-Caen O, et al. Arch Neurol 1986; 43:1138-41; 5. Rao, SM et al. Neurology 1991; 41:692-6; 6. Cerasa et al, Neurorehabil Neural Repair 2013; 27:284-95; 7. Sasre-Garriga, et al. Mult Scler, 2011. 17:457-67; 8. Filippi et al. Radiology, 2012. 262:932-40; 9. Langdon D, et al. Mult Scler, 2012. 18:891-8; 10. Sweet et al. Hum Brain Mapp 2006. 27:28-36; 11. Smith E, et al. Cogn Psychol 1997;33:5-42.