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Research Article

A neuropsychological study of near infrared spectroscopy hemoencephalography neurofeedback treatment in amnestic mild cognitive impairment

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Abstract

Background: Cognitive impairment in amnestic mild cognitive impairment (AMCI) appears associated with decreased brain activation in prefrontal cortex (PFC). Near infrared spectroscopy hemoencephalography applied to cortex can be used to provide biofeedback signals enabling voluntary control of brain activation, this is known as neurofeedback training (NT). **Aims:** We conducted a pilot study of NT of the PFC in AMCI in order to establish tolerability and treatment protocols. **Method**: Ten patients completed 12 weekly NT sessions. **Results:** All patients were able to obtain voluntary control of PFC activation. NT was well tolerated and only mild self-limiting headache was reported in two patients. In this small preliminary sample repeated behavioural measures revealed near significant trends for improved immediate and episodic memory and medium effect size for the same variables. **Conclusions**: These initial results indicate that NT of relevant cortical areas in AMCI warrants further investigation.

Key words

amnesia, hemoencephalography, infrared spectroscopy, mild cognitive impairment, neurofeedback, treatment

Introduction

There is increasing evidence that vascular impairment plays a significant role in Alzheimer's disease pathology.[1] Vascular impairment; abnormal cerebral blood flow, metabolism and activation occur in AD and in those with normal cognition who are at increased genetic risk of AD,[2] along with Amnestic Mild Cognitive Impairment (AMCI).[3]

The degree of decreased activation in the prefrontal cortex (PFC) is thought to be correlated to the degree of impaired task performance in AMCI.[4,5]

Regional brain blood flow changes in response to neuronal activation can be measured using non-invasive bed-side techniques.[6] Near-infrared spectroscopy hemoencephalography (NIRS-HEG) utilises the differential light frequency absorption of oxyheamoglobin and deoxyheamoglobin to measure changes in cortical blood oxygenation, thereby providing a proxy measure of brain metabolism and activity.[7,8] The technique involves placing light sources (red and infrared) and a sensor some distance apart on the skin overlying an area of interest. Light penetrates the cortex via the skin, skull and brain membranes and scattered light reaches the sensor via the reverse path.

NIRS-HEG can be used to provide real-time biofeedback of cortical activation to a person who can then learn to gain voluntary control of activation in a specific cortical area. This technique is known as neurofeedback training (NT). During NT the individual voluntarily increases and maintains blood flow to a cortical area and this has been associated with symptomatic improvement of some conditions.[9]

We conducted a pilot study to (i) assess the tolerability and feasibility of neurofeedback training in patients with AMCI, (ii) to establish optimal treatment protocols and to (iii) collect sufficient data for a power calculation for a randomised controlled study.

Methods

Patients with AMCI were recruited from the UCL Essex Memory Clinic. All patients fulfilled operationalised diagnostic criteria for AMCI.[10] Detailed psychiatric assessments including history, mental state examination and physical examination were completed for all participants. Routine neuropsychological testing included the National Adult Reading Test (NART), Mini-Mental State Examination (MMSE), Revised Cambridge Cognitive Examination (CAMCOG-R), Logical Memory Test, and Halstead Trail Making test (TMT)

Neurofeedback training

Subjects received 12-weekly supervised NT sessions during which left and right prefrontal cortical sites were trained for 10 min each. Frontal sites were identified as F3 (left prefrontal) and F4 (right prefrontal) of the 10-20

international EEG system. Prior to commencing the treatment, subjects spent five minutes listening to binaural beats in the beta range (16-24 Hz) to encourage a stable repeatable mental state at the end of which a baseline oxy-deoxyheamoglobin ratio (HEG ratio) was captured. Continuous feedback signals were provided by visual analogue scales and digital readouts of the HEG ratio. Increases in the HEG ratio, as measured against a 30 second delayed moving average, received positive reinforcement. Positive reinforcement comprised of an emotionally neutral film clip with sound that played when the real-time HEG ratio was above the delayed moving average ratio. When the HEG ratio went below the moving average ratio, a monotonous low-pitched auditory tone (200Hz) was presented and the film was paused.

Near infrared spectroscopy

Monochromatic light pulses at two near-infrared frequencies (660nm, 880nm) were emitted on the skin overlying a cortical area and detected 4.6 cm away in a horizontal plane (sampling rate 122Hz). The difference in light frequency absorption between oxy- and deoxyhaemoglobin was expressed as the HEG ratio (=Red x 200/Infrared light at the sensor) and used to measure changes in blood oxygenation from which changes in neuronal activation and local blood flow were inferred.

Statistical analysis

Data were compared using dependent t-tests. We conducted an explorative analysis of memory and attention related measures. Effect sizes were calculated for each dependent variable tested.[11] Analysis of data was done on SPSS-V14 on Windows-XP.

Results

Eleven patients with AMCI were recruited ten (7 females) completed treatment and one was lost to follow-up. The mean age of the AMCI sample was 64.1 with standard deviation 13.3 years. The mean pre-morbid IQ was 112.1; standard-deviation 9.3.

In total 120 NT sessions were completed and all participants were able to gain control over PFC activation. NT was generally well tolerated. Side effects occurred infrequent, were mild and self-limiting: headache lasting less than 3 hours was reported by two patients after the first training session.

Difference scores (baseline *minus* follow-up) on the cognitive measures revealed improved performance on remote memory, new learning, logical memory immediate and delayed recall, verbal fluency and trail making parts A and B. Larger effect sizes were observed for differences on new learning, logical memory immediate recall and orientation although none of the differences reached statistical significance.

Table 1. Behavioural results following neurofeedback training in AMCI.

T1 –T2 pair	Mean	SD	Lower CI	Upper CI	*t*	*df*	*p*	Effect size
CAMCOG-R	2.11	5.88	-2.41	6.63	1.08	8	0.31	0.36
Orientation	.89	1.54	-0.29	2.07	1.74	8	0.12	0.52
Remote memory	-.33	1.23	-1.28	0.61	-0.82	8	0.44	0.28
Recent memory	1.00	2.35	-0.80	2.80	1.28	8	0.24	0.41
Attention/Calculation	.22	1.09	-0.618	1.06	0.61	8	0.56	0.21
New Learning	-.78	1.20	-1.70	0.15	-1.94	8	0.09	0.57
Logical memory immediate	-6.22	9.27	-13.35	0.90	-2.01	8	0.08	0.58
Logical memory delayed	-3.44	8.29	-9.82	2.93	-1.25	8	0.25	0.40
Verbal fluency	-4.33	11.42	-13.11	4.45	-1.14	8	0.29	0.37
Categorical Fluency	.22	4.02	-2.871	3.316	0.17	8	0.87	0.06
TMTA	-6.78	30.55	-30.26	16.70	-0.67	8	0.52	0.23
TMTB	-16.88	40.12	-50.42	16.67	-1.19	7	0.27	0.41

CI: 95% Confidence Interval

The table 1 shows the difference scores (follow-up *minus* baseline) on cognitive measures indicating the treatment effects of neurofeedback training in AMCI. Scores are mean (SD) and effect sizes.

Discussion

The results from this pilot study indicate that neurofeedback training is feasible, safe and well tolerated in AMCI. We were able to establish a treatment protocol that was well tolerated as indicated by high treatment compliance rates. No serious adverse effects were reported.

Our explorative analysis of behavioural measures indicates overall trends towards improvement on measures of attention and executive functioning (TMT A and B) and episodic memory.

The results have enabled us to perform a power calculation for a randomised controlled trial. A sample size calculation, based on effect sizes for new learning

and logical memory immediate recall, indicates 27 participants will be required in each treatment arm.

NT of the PFC may improve attention and memory in AMCI and therefore provide an additional or alternative treatment option. The cost, size and portability of the NIRS-HEG device makes NT a practical treatment and our results indicate that it should be investigated to determine its efficacy in improving cognition in AMCI. We now aim to conduct a randomised double-blind sham-controlled NT treatment trial.

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