Optimizing memory function in temporal lobe epilepsy.

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Abstract

Purpose

The study aimed to assess whether engagement in a memory training programme and performing internet brain training exercises improve memory function in people with temporal lobe epilepsy (TLE).

Methods

Seventy seven people with TLE, complaining of memory difficulties, completed the study. Participants ranged in age from 19 to 67 years and 40 had left TLE. Participants were randomized to one of four conditions; group 1: traditional memory training , group 2: Lumosity, an on-line cognitive training programme, group 3: traditional memory training and Lumosity, group 4: no training. Memory efficiency and mood were assessed at baseline and three months later.

Results

Group analyses indicated improved verbal recall after training ($p<0.001$) and improved subjective ratings ($p<0.007$). More participants reported a lessening of the memory burden ($p<0.007$) after training; differences were significant between groups 1 and 3 compared to group 4. Lumosity use was not associated with changes in the memory outcome measures but there was a relationship with depression ratings and the number of memory games played ($p<0.01$). Conventional memory training, IQ and post-surgical status were associated with positive memory outcomes.

Conclusions

The study indicates traditional memory rehabilitation techniques can help reduce the burden of memory impairment in TLE. There was no evidence that Lumosity the on-line cognitive training programme had specific advantages. Positive change was not universal and larger studies will be required to explore factors associated with successful outcomes.

Key words:

epilepsy, temporal lobe epilepsy, memory, memory rehabilitation, on-line cognitive training

1. Introduction

Memory decline is a major concern for people with epilepsy and their families. Memory impairment in association with epilepsy and its treatment has been a consistent finding of neuropsychological research over many decades, with temporal lobe epilepsy identified as a high risk factor (1). The role of memory rehabilitation in reducing the burden of memory problems was highlighted more than 150 years ago (2) and yet has received limited attention with the number of reviews advocating research exceeding the number of well-designed outcome studies(3-10). Research undertaken with other neurological populations and related meta-analyses have provided some evidence for the efficacy of memory rehabilitation (11-14).

Brain training exercises in the form of activities such as reading, doing crosswords and suduko have been advocated as likely to improve memory function. The last decade has witnessed a dramatic rise in the availability of internet cognitive training programmes designed and marketed specifically as brain training techniques. These are promoted as tools to maintain or improve memory and other cognitive functions through mental exercises and stimulation. It is often assumed that any effects of practice will generalise outside the immediate training context and this greatly widens their appeal. As Rabipour and Davidson write '*The promise of brain training enhancing function has created a booming scientific field and a billion dollar commercial industry neither of which shows sign of abating' (1*5). The evidence to support the brain function improving claims made for these programmes remains equivocal due to methodological weaknesses such as inadequate controls and a failure to demonstrate generalisation effects (15-17) We previously found inconsistent findings on our memory outcome measures in people with left TLE and healthy controls following up to 40 brain training sessions using Lumosity, a commercially available mental training programme (18).

Memory rehabilitation in clinical practice refers to a range of approaches and includes guidance in the use of external memory aids and the teaching of mental and mnemonic strategies which aim to improve memory function directly. Most interventions have an educational component that includes increasing awareness of factors that can affect memory function such as mood, physical exercise, and sleep. In this study we wanted to explore whether these techniques, common components of memory rehabilitation, would have a beneficial impact on memory function of people with TLE complaining of memory difficulties. In addition we wanted to explore the impact on memory function of using Lumosity, a commercially available internet brain training programme. Memory training studies in epilepsy have been criticised for their failure to demonstrate generalisation effects and this also has been a concern of critics of the internet brain training companies. For this reason it was considered vital to have, in addition to objective memory test performance as an outcome measure, some indication of memory performance in daily life.

We aimed to explore

1. whether a memory training programme drawing upon techniques used in clinical practice would improve verbal memory test performance and subjective ratings of everyday memory function in people with TLE complaining of memory difficulties.

2. whether Lumosity an internet brain training programme alone or in combination with conventional memory training techniques would improve verbal memory test performance and subjective ratings of everyday memory function in people with TLE complaining of memory difficulties.

2. Methods

This was a randomised un-blinded controlled trial.

Participants:

People were recruited if they had a diagnosis of TLE and were troubled by memory problems defined as a rating of 2 or greater on the Everyday Memory Failures Questionnaire indicating memory problems were a moderate or severe nuisance (details given below). Exclusion criteria were on-going or planned medication changes, a mood disorder and a globally impaired memory, defined as scores < 1st centile on verbal and visual memory tests. The latter criteria were used as previous studies indicate those with profound memory impairment are less able to benefit from conventional memory rehabilitation strategies.

The study was approved by the National Hospital for Neurology and Neurosurgery and the Institute of Neurology Joint Research Ethics Committee, and written informed consent was obtained from all participants.

Participants were recruited between May 2012 to July 2014 from the National Hospital for Neurology and Neurosurgery outpatient clinics. Eighty-eight people met the selection criteria and 77 completed the study. Reasons for discontinuation included unforeseen medication changes, poor seizure control, insufficient time to fulfil the study requirements and adverse life events.

Participants were randomly assigned to one of four groups: Group 1 Conventional Memory Training (CMT); Group 2 Lumosity Brain Training (LBT) ; Group 3 CMT and LBT combined; Group 4 No Training (NT). People in group 4 were advised they would receive memory strategy input and would be enrolled on to the Lumosity at the end of the study. Demographic and clinical details of the four groups are presented in table 1.

Table 1: Demographic and clinical characteristics of the four study groups.

	CMT	LBT	CMT + LBT	NT
Number	22	19	17	19
Age: median (range) mean(SD)	44 (22-60) 44.7 (8.1)	45 (23-61) 43.8(9.7)	41 (24-67) 42.5 (11.5)	46 (19-60) 42.4(13.3)
Gender M/F	13/9	11/8	11/6	11/8
IQ	100.6 (15.9)	100.5 (12.4)	100.4 (12.9)	101.8 (12.4)
Epilepsy				
Age of Onset	17.2 (12.4)	18.4 (12.8)	17.9 (15.0)	17.9 (12.8)
Seizure free N	5 (23%)	5 (26%)	7 (41%)	8 (42%)
Seizure free years median (range) mean (SD)	 8 (2-13) 6.8 (4.8)	 4 (3-6) 4.0(1.4)	 9 (5-17) 10.5 (5.2)	 8 (2-17) 8.4(6.4)
TL Laterality				
Left	12 (55%)	11 (58%)	8 (47%)	10 (53%)
Right	6 (27%)	4 (21%)	5 (30%)	5 (26%)
Unclear/bilateral	4 (23 %)	4 (21%)	4 (23%)	4 (21%)
Post TL surgery	8 (36%)	8 (42%)	8 (47%)	9 (47%)
Number of different AEDs (range) mean (SD)	2 (1-5) 2.0 (1.1)	2 (0-4) 1.9 (1.2)	2 (0-5) 1.8 (1.0)	3 (2-3) 2.1(.9)
Seizures in the previous 3 months:				
Convulsions median (range) mean(SD)	 0 (0-7) .8 (2.0)	 0 (0-13) 1.6 (4.2)	 0 (0-4) .4 (1.0)	 0 (0-3) .2 (.7)
focal dyscognitive median (range) mean(SD)	 0 (0-25) 3.6 (6.2)	 0 (0-30) 5.1(9.0)	 0 (0-34) 3.3(7.5)	 0 (0-22) 3.4(5.7)

There were no significant differences between the groups for age, gender balance, IQ and epilepsy related variables. Twenty five had been seizure free for at least two years, thirteen of whom had undergone surgery. The ratio of seizure free / not seizure free participants was higher in groups 3 and 4 but this difference was not significant. There were more left than right TLE participants in each group. Fifteen different types of AED were prescribed in a variety of combinations and three people were not taking any medication.

All participants routinely kept seizure frequency records for their neurological outpatient reviews. For the purposes of this study seizures occurring in the three months before the study onset were recorded. Secondarily generalized convulsions and focal dyscognitive seizures were recorded separately. Auras were not documented. The median number of seizures is low and this is driven by the seizure free cohort.

Memory Training

Memory training was provided on an individual basis in up to two sessions and totalled a maximum of four hours. Following the last session participants were instructed to engage in the taught exercises, to use external memory aids demonstrated and/or to do the lumosity brain training exercises regularly over the next twelve weeks. Contact via telephone or via the internet, according to preference, was made to assess how things were going and to provide encouragement on a monthly basis. Due to the tertiary nature of our epilepsy service people often live a considerable distance away such that more regular attendance would have been expensive and for some logistically prohibitive. Other research has indicated that it is regular practice and the embedding of strategies into daily life that is a key component of effective rehabilitation (12, 14).

Conventional Memory Training (CMT)

Sessions covered information about the brain, memory functions and factors affecting memory in epilepsy. Ways of using compensatory methods including environmental adaptations and external aids were outlined, drawing upon those methods advocated by memory rehabilitation practitioners and those with an evidence base to support their potential acceptability and utility (12, 14, 19). Participants were given advice on how to optimize the use of external memory aids such as prompts including calendars, watch/phone alarms and apps. Ways of using memory aids to store information in the form of diaries and notepads and the use of mobile phones and computer programmes to record information, such as contact details and autobiographical events were outlined.

Cognitive strategies were selected from methods found to be effective in previous studies (13, 14, 19). These were demonstrated and practised. Strategies employed required the mental manipulation of new information and the focusing of attention and mental elaboration to make memories more robust. Participants were encouraged to use visual imagery to enhance the recall of people's names and to use this method to try and remember new people they met. For participants who found this method straightforward and effective the more advanced Method of Loci visual imagery technique was introduced. This entails visualising prominent features on an established route and then pairing these with 'to be remembered' items to form a new image. Subsequent retracing of the journey has been shown to assist the recall of new items. The Story Method was introduced as a verbal elaboration technique. This involves the subject embedding the 'to be remembered' information in a personally created story. First letter mnemonics was demonstrated as a way to remember new information when the order of items is crucial such as remembering a recipe, directions or lists.

Participants were provided with a training manual outlining the content of the sessions and providing homework exercises. Participants were encouraged to incorporate the external aids and cognitive strategies into their daily lives**.** For example, the Method of Loci training exercises consisted of practise in using the identified personalised familiar journey with lists of unrelated items of increasing length; beginning with three to maximise success and increasing in multiples of three. Behavioural tasks set as homework included using visual imagery to recall names of people met each week and checking diary entries daily. People were encouraged to share and practice the strategies with a friend or family member and some participants attended the session with a relative.

Lumosity Brain Training (LBT)

Lumosity is a commercially available series of mental exercises delivered via the internet. Outcome studies of the programmes efficacy have been variable but with a recent randomised trial reporting positive findings in people with mild cognitive impairment (20). In an earlier pilot study we found the programme was user friendly and several participants enjoyed the challenge the games afforded (18). Lumosity has the considerable benefit of providing a log of the number of games played and a tally of the number of days engaged on the programme. Performance scores were available for memory, attention, speed and problem solving games together with a measure of the rate of change. Participants were encouraged to perform the Lumosity exercises regularly and they were provided with on line reminders.

Outcome measures

Memory function and mood were assessed at the study outset and at an interval of 12 to 14 weeks.

Memory tests

Two verbal memory subtests from the BIRT Memory Information Processing Battery (BMIPB) were used (21); the List Learning and the Story Recall tests. Parallel versions were used on each of the two assessment sessions.

In the List Learning task the participant is read aloud 15 common words on five consecutive occasions. Following each presentation as many words as possible have to be recalled. The total number of words recalled over five trials is recorded. The participant is then presented with a second 15 word list and asked to recall as many words as possible. Following the second list participants are asked to recall the original list. The performance indicators used were verbal learning, the total number of words recalled from the five trials (maximum =75) and verbal recall, the total recalled after the second list (maximum score = 15).

In the Story Recall task the participant is read aloud a short prose passage. Free recall is tested immediately and again after a forty minute delay. The performance indicator used was the delayed recall score as it has the best test retest reliability (Pearson $r = 0.74$). Previously we have found prose recall to be associated with memory complaints (22).

Subjective Memory measures

The Everyday Memory Questionnaire (EMQ) was used to provide an indication of the nature and frequency of memory failures encountered in daily life. This memory questionnaire has been developed in house and has been used over more than 20 years. It consists of 17 frequently reported memory failures (e.g. how frequently do you lose items around the house; how frequently do you forget to take your medication) and two infrequently reported memory failures (eg how frequently do you forget your date of birth or address). Subjects indicated the frequency of each memory failure over the preceding two months on a six point rating scale ranging from ‘not at all’ to ‘more than once a day’. In addition an overall memory nuisance rating is requested on a four point scale (0 = no concern to 3 = a serious concern) (22).

Mood Ratings

A mood rating scale was included as an outcome measure. Low mood is a factor than can impact on subjective and objective memory function, a relationship that is likely to be bidirectional. The Hospital Anxiety and Depression Scale (HADS) a fourteen item mood screening questionnaire with established reliability and validity was selected to monitor (23) . Seven items relate to symptoms of anxiety and seven to symptoms of depression. Scores of >11 are considered indicative of a mood disorder.

Lumosity

The Lumosity programme registered how many times participants used the training exercises. It also provided feedback in the form of progress charts in each cognitive domain and an overall score the Brain Performance Index (BPI), the higher the score the better the performance.

Participant’s Programme Evaluation

At the end of the study participants were encouraged to provide feedback on their experience of the programme and its delivery. Groups 1 and 3 were asked to indicate the helpfulness of the external aids and cognitive strategies. Ratings ranged from not helpful to very helpful. In addition they were asked to respond to statements regarding how well the training was explained, how helpful the training had been, how easy it was to understand, how helpful and easy the training manual was to follow and how easy the homework exercises were to carry out.

Groups 2 and 3, who undertook the Lumosity programme, were asked how helpful it was, and how easy and enjoyable they found the games, how often they trained, whether they found the programme motivational and whether they would continue to use the programme at the end of the study.

Programme evaluation ratings were made on a five point scale ranging from completely agree to completely disagree.

Analysis:

Data was analysed using SPSS version 21. Power analysis dictated a minimum group size of twelve to detect a reliable pre/post intervention change in verbal memory test scores. The significance level for all analyses was set at $p<0.01$ (two-tailed).

Group differences in outcome measures at the study outset and change scores were analysed using parametric statistics for memory test scores, the EMQ score and HAD scores (t tests, ANOVAS and Scheffe's test for post-hoc comparisons) and non-parametric statistics for memory ratings (Kruskal Wallis and Mann-Whitney U test for post-hoc comparisons).

To assess for the clinical significance of post-trial changes in verbal learning, verbal recall and story recall participants' change scores were classified as improved or not on the basis of reliable change indices (RCIs) at a 90% confidence interval. Subjective memory ratings were classified as improved if a category shift in rating occurred in a positive direction (eg a change in rating from 3 a severe nuisance to 2 a moderate nuisance).

Relationships between change scores and clinical and demographic variables of interest were explored using Pearson's correlations for continuous data and Chi- square tests for categorical data

Predictors of meaningful memory change were explored using logistic regression analyses with meaningful gains in memory as calculated using RCIs for memory test scores and a positive category shift in memory rating as the dichotomous outcome variables

3. Results

Group analyses:

There were no significant differences between the groups in memory test scores at the study outset (Table 2). All groups were performing between one and two standard deviations below average. The frequency of reported memory failures, memory rating and levels of anxiety and depression were comparable between groups.

Differences between the groups approached significance for verbal learning ($F=3.1$;df=3;$p<0.03$) and achieved significance for verbal recall ($F=7.3$;df=3;$p<0.001$: pairwise comparisons group1 CMT versus group 4 NT $p<0.001$ and group 3 CMT and LBT versus NT $p<0.01$).

Table 2: Memory test performance and subjective memory and mood ratings of the four groups at baseline and at follow up.

	CMT Pre Post	LBT Pre Post	CMT+LBT Pre Post	NT Pre Post	p values	50th centile**
List learning mean (SD)	 41.8 46.2 (11.5) (13.9)	 46.2 49.0 (14.1) (13.9)	 44.9 51.5 (10.6) (12.4)	 45.1 43.6 (6.3) (9.4)	 F=3.1 p<0.03	 53.2 (10.2)
List recall mean (SD)	 7.2 9.9 (4.0) (3.3)	 8.4 8.8 (3.7) (4.3)	 8.2 10.5 (3.5) (4.6)	 8.6 7.2 (2.5) (3.3)	 F=7.3 p<0.001	 11.2 (3.0)
Story recall mean (SD)	 16.7 25.3 (7.6) (10.5)	 16.0 22.9 (9.9) (13.5)	 15.7 21.8 (10.5) (14.3)	 17.7 20.2 (8.9) (10.1)	 F=1.5 p>0.01	 25.2 (9.3)
EMQ failures* mean (SD)	 62.0 51.5 (15.8) (14.4)	 61.0 55.3 (18.8) (17.4)	 61.0 52.3 (17.8) (19.5)	 60.0 62.3 (21.0) (18.8)	 F=3.7 p<0.02	
EMQ rating* mean (SD)	 2.4 1.8 (0.6) (0.8)	 2.1 1.7 (0.8) (1.0)	 2.4 1.7 (0.7) (0.7)	 2.0 2.1 (0.7) (0.7)	 X^2 =16.6 p<0.001)	
HADS : Anxiety mean (SD)	 6.1 6.9 (3.7) (5.3)	 7.5 6.9 (5.1) (4.5)	 8.0 7.2 (3.0) (4.4)	 7.7 7.6 (3.4) (3.9)	 F=.68 p >0.01	
Depression mean (SD)	 4.2 4.4 (3.6) (3.4)	 5.4 4.1 (4.0) (0.7)	 4.5 4.1 (3.3) (3.1)	 4.4 4.1 (3.8) (3.7)	 F=1.0 p>0.01	

*higher score denotes less favourable memory evaluation

** BIMPB manual normative values

Participants estimates of the frequency of memory failures indicated a reduction over the trial compared to the previous three months which approached significance for a reduction in the frequency of reported failures (F=3.7;df=3;p<0.02) and achieved significance for subjective ratings of the memory burden (X^2 16.6;df =3; p<0.001; pairwise comparisons were significant for CMT+LBT group 3 versus NT Group 4; U=66,p<.002).

Individual analyses:

Eighteen participants were classified as having improved memory function on the basis of RCIs for verbal learning, 20 for verbal recall and 18 for story recall. The differences between the groups approached significance for verbal recall (X^2 = 8.3; df=3;p<0.04); pairwise comparisons were significant for CMT+LBT group 3 versus NT Group 4; U=103,p<.01).

Thirty-one participants were classified as having improved memory based on a downward grading in the memory nuisance rating. Differences between the groups were significant (X^2 = 12.1;df=3;p<0.007); pairwise comparisons were significant for CMT+LBT group 3 versus NT group 4; U=83.5,p<.002 and for CMT group 1 versus NT group 4;U=106.5,p<0.002).

Table 3: Numbers and % of participants classified as showing improved memory function on the basis of memory test score change and subjective ratings.

	CMT	LBT	CMT+LBT	NT	X^2 (df=3)
Verbal learning Number (%)	7 (33%)	3 (15%)	5 (29%)	3 (16%)	P >0.01
Verbal recall Number (%)	8 (38%)	4 (20%)	7 (41%)	1 (5%)	8.3; p <0.04
Story recall Number (%)	7 (33%)	3 (15%)	4 (24%)	4 (21%)	P >0.01
EMQ rating Number (%)	12 (57%)	7(35%)	10 (59%)	2 (11%)	12.1; p<0.007

Relationship between memory test performance and subjective ratings

A positive correlation which approached significance was observed between the change in verbal recall and the reported frequency of memory failures with improved performance associated with a reduction in the reported incidence of everyday memory failures (Pearson correlation -.27;p<0.03). No relationships were observed for verbal learning and story recall.

Lumosity

Table 3 gives the number of days participants in groups 2 and 3 used Lumosity and the number of games played during the intervention. Uptake of the programme was variable but there was no significant difference between the LBT and the LBT and CMT combined groups.

There were no significant correlations between the number of days or games played and changes in memory test performance or subjective ratings of memory. There was an association which approached significance between the changes in the depression rating and the number of games played. The higher the total number of games played the greater the reduction in the HAD depression score (r = 0.23; p<0.05). Cognitive domain analysis indicated a significant relationship with depression scores and memory games (r = .28; p<0.01). No relationships were observed for anxiety rating change and indices of lumosity use.

Table 4: Lumosity programme uptake for group 2 LBT and group 3 LBT and CMT combined

	LBT		CMT+LBT	
Days played: median (range) mean(SD)	 65.5 58.5	 (15-88) (19.5)	 56.0 54.0	 (10-97) (28.5)
games played:				
Total median(range) Mean(SD)	 368 436	 (114-949) (214.1)	 364 417	 (619-273) (391.2)
Attention Median(range) Mean(SD)	 87 95	 (20-243) (54.3)	 61 89	 (9-273) (80.3)
Memory Median (range) Mean(SD)	 74 86	 (23-201) (41.9)	 75 85	 (16-213) (65.6)
Speed Median (range) Mean(SD)	 62 67.7	 (13-172) (38.9)	 47 64	 (6-361) 83.6
Problem solving median(range) mean(SD)	 56 68	 (18-225) (49.9)	 50 66	 (4-350) 80.2

Factors affecting memory rehabilitation outcomes

Participants classified as having improved verbal learning had significantly higher IQs (t=3.7; p<0.002) and with a trend observed for more likely to have had surgery (X^2 = 5.4;df=1;p<0.02). Improvements in verbal recall were associated with receiving CMT (X^2= 7.1; df=1;p<0.01). No associations were found for Story recall. A decline in the memory nuisance rating was associated with receiving CMT.

No association was found between positive memory outcomes and age, gender, HAD anxiety or depression scores, Lumosity use, age of epilepsy onset and duration, TL laterality, seizure free status and number of years seizure free.

A logistic regression analysis was performed with improved memory test performance as the binary outcome defined as RCI gains in one or more of the memory test scores (verbal learning, verbal recall and/or Story recall). Variables entered were CMT, IQ and surgical status. The model explained 29% of the variance and classified 71% of participants as improved. A second analysis using the memory rating and the same three variables classified 59% as improved but explained only 19% of the variance.

Seizure frequency

There were no differences in seizure frequency between the groups during the intervention.

Programme Evaluation

CMT

Evaluation sheets were completed by 36/39 participants. The majority indicated they found external strategies more helpful than mental strategies (83%). Of the mental strategies ratings in order of perceived helpfulness were word retrieval strategies (70%), Chunking methods (67%), story methods (64%), visual imagery/association techniques for names (63%), other picture methods (57%), Method of Loci (51%) and other retrieval strategies (49%). Ratings on the delivery of the programme were high (97%), 86% rated the programme easy to follow, 75 % found the manual helpful and 67% indicated the exercises were easy to carry out.

LBT

Evaluation sheets were available for 34/36 participants who were signed up for the lumosity training programme. 82% found the programme was easy to use and 60% indicated they found it helpful with 30% reporting an associated improvement in their memory. 68% found the games easy to understand and 53% found the Lumosity training reminders helpful. 32% reported using the programme on a daily basis and 68% reported finding the programme motivational. 44% indicated they would sign up to use the programme in the longer term.

4. Discussion

The memory training interventions were associated with improved memory function. We observed improvements in memory test scores for one in three participants and better subjective ratings in one in two following an outpatient based memory training programme, compared with one in five in the control group. Improvements were most evident in association with instruction in conventional memory training techniques and there was no evidence that the internet brain training programme employed had specific benefits although it was associated with positive changes in mood ratings.

Our findings provide some support for the efficacy of memory rehabilitation techniques in general (12, 13) and adds to the evidence base of their role in people with TLE (13, 24-28). As a class II study our results strengthen the tentative conclusion from a recent review that memory rehabilitation is *'possibly effective for individuals with seizure related deficits in attention and memory'(6).* The changes recorded in subjective ratings provide an indication the intervention had an impact in everyday settings and not just in memory test performance. The training programme had stressed the importance of applying the strategies routinely in home and community settings and provided homework exercises to encourage this. There was however no indicator of the amount of practice undertaken as there was for the Lumosity programme. The positive changes in memory outcomes following up to two outpatient sessions seem at least comparable to those recorded following a more intense residential programme (25) . The study was not designed to evaluate the relative effectiveness of different strategies but in the study evaluation participants indicated external aids including mobile phone functions and diaries were most helpful. A review of memory rehabilitation methods also found compensatory strategies to be associated with larger effect sizes than cognitive strategies (29)and in a recent study mobile phone functions were credited as being particularly helpful (30).

We found no support for an independent effect of the Lumosity on-line cognitive training programme. In an earlier pilot study our findings had been inconsistent although it was possible insufficient time had been spent engaged in the exercises to adequately assess efficacy (18) . In our previous study exposure to the programme had been variable, and was limited to a maximum of 40 sessions with few participants utilising their full quota. In the current study participants had unlimited access for three months. Furthermore, we failed to find a relationship between the number of games played and changes in the memory outcome variables. Our results concur with those of a recent meta-analysis of memory rehabilitation in stroke and TBI that found no evidence that internet based applications had better efficacy over traditional methods (31) . Findings of the benefit of internet cognitive training have been mixed. Limited data on generalization effects has been highlighted (15, 16, 32, 33) although a recent large scale study found positive changes in activities of daily living in older people following regular engagement in on – line cognitive games (34) . Most of our participants indicated they had found the Lumosity training exercises easy to understand and use and 1 in 3 believed Lumosity had some memory benefits with 1 in 2 reporting they had signed up to the programme in the longer term. The subscription payment for Lumosity was covered during the study but for continued use people had to commit to a monthly charge and financial costs need to be considered in any evaluation of value given the limited incomes of several participants.

We did find a positive association between Lumosity use and mood ratings. The more memory games played the greater the drop in depression ratings. Most participants indicated the games were fun and motivating. One participant, who chose to continue using the programme, however found his enthusiasm waned after he stopped making progress. Mental games such as those in the Lumosity programme are likely to be positively reinforcing and psychologically stimulating when gains in performance occur and are underscored by the graphics provided. When improvements are no longer forthcoming the programme may have a negative psychological impact. Clinical depression was an exclusion criterion and the reduction in depression ratings occurred in individuals with low pre-trial mood scores. The decrease in depression scores possibly reflects uplifting effects of Lumosity in non-depressed individuals.

Our study was not designed to explore whether pre-operative interventions had advantages over post-operative interventions although this clearly is an important research question. Forty-three percent of our participants had undergone surgery and we found that post-surgical status was associated with better memory outcomes. Subsequent post-hoc analyses did not support a prior suggestion that such a finding might be driven by those individuals who had undergone right temporal lobe surgery (25) . Significantly more individuals in the surgical group were seizure free, had less frequent focal seizures during the course of the study and had a lower medication load, all potential factors contributing to the better outcomes in association with post-surgical status. Our sample size was too small to adequately assess the relative contribution of these factors.

Up to a half of participants did not derive significant benefit from the programme and accordingly our findings cannot be used to endorse its universal application to people with TLE troubled by memory problems. Memory rehabilitation is expensive in terms of manpower and there are increasing pressures to make financial efficiency savings in the National Health Service in the UK. Being able to identify people who are most likely to benefit has major clinical relevance. Our findings were disappointing in this regard as most demographic and epilepsy factors were not predictive of outcome. Higher IQ was associated with better outcomes and there is some evidence that cognitive reserve may be a pertinent variable for other neurological groups (35). To become adept employing external aids and to learn and to embed cognitive strategies effectively is cognitively demanding and accordingly is likely to be affected by ability level.

Executive functions may be an important factor contributing to the success of cognitive training programmes. We lacked pertinent data to explore this hypothesis.

Our study had a number of limitations. To date we only have outcome data on short term effects and it is unclear how enduring any positive changes may be. The study was not blinded and there are likely to be biases, particularly in the subjective evaluation of the programme. Participants were made aware at the study outset of the potential interventions and people assigned to the control condition may have explored and taken up rehabilitation strategies independently. An additional consideration in psychological intervention studies is the time spent with the therapist rather than the nature of the input delivered. More time was spent with the psychologist in the three treatment groups but with less contact time for the Lumosity group. The outcome variables employed were restricted to verbal memory tests and questionnaires and broadening the assessment to include quality of life measures would have been a valuable addition. The failure to assess executive function at the outset prevented the consideration of the role of this potentially influential variable. We had data on the frequency of lumosity sessions undertaken but there was no data on the frequency and intensity of home-work sessions undertaken by groups 1 and 3. Our groups were mixed with respect to laterality of surgery and past treatment. The numbers in each intervention group were too small to evaluate whether these factors may influence the response to the rehabilitation approach offered.

5. Conclusion

Our research we believe provides sufficient evidence to support the use of memory training strategies with people with TLE in clinical settings. We would hope our findings may help to stimulate further research into the effectiveness of memory **training.** The interventions were not universally beneficial. Larger studies are warranted and these may better identify factors associated with successful outcomes. Temporal lobe epilepsy affects many young people with good cognitive reserves who have the potential to derive educational, occupational and psychosocial benefit from such programmes over many decades.

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