DOI: 10.1093/brain/awh293 *Brain* (2004), **127,** 2419–2426

Pre-operative verbal memory fMRI predicts post-operative memory decline after left temporal lobe resection

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Summary

Functional MRI (fMRI) of cognitive tasks depends on technology widely available in the clinical sphere, but has yet to show a role in the investigation of patients. We report here the first demonstration of a clinically valuable role for cognitive fMRI. Temporal lobe epilepsy (TLE) is commonly caused by hippocampal sclerosis and is frequently resistant to drug treatment. Surgical resection of the left hippocampus in this setting can cure seizures, but may produce significant verbal memory decline, which is hard to predict. We report 10 right-handed TLE patients with left hippocampal sclerosis who underwent left hippocampal resection. We compared currently used data for the prediction of post-operative verbal memory decline in such patients with a novel fMRI assessment of verbal memory encoding. Multiple regression analyses showed that fMRI provided the strongest independent predictor of memory outcome after surgery. At the individual subject level, the fMRI data had high positive predictive value for memory decline.

Keywords: fMRI; memory; hippocampus; epilepsy; surgery

Abbreviations: fMRI = functional MRI; IAP = intracarotid amytal procedure; MTLE = mesial temporal lobe epilepsy

Received May 6, 2004. Revised July 9, 2004. Accepted July 10, 2004. Advanced Access publication September 30, 2004

Introduction

Epilepsy is the most prevalent serious neurological disorder, with a prevalence of 0.5–1% (Hauser, 1998). Approximately 30% of people with epilepsy continue to have seizures despite antiepileptic drug treatment; the majority suffer from focal epilepsy (Crawford, 2000). In this context, neurosurgery to resect the epileptic focus is an important and under-used treatment option. The first randomized trial of surgery versus optimal drug treatment in temporal lobe epilepsy (Wiebe *et al*., 2001) demonstrated a seven-fold increase in the likelihood of being seizure-free in the surgically treated group, with an associated highly significant improvement in quality of life.

The most frequent pathology identified in drug resistant epilepsy patients is hippocampal sclerosis, giving rise to the common syndrome of mesial temporal lobe epilepsy (MTLE). Despite a seizure-free outcome, many patients suffer a significant decline in memory ability after temporal lobe resection, especially for verbal memory following left-sided resection in right-handed patients. Decline correlates inversely with severity of hippocampal sclerosis in the surgical resection specimen (Hermann *et al*., 1992; Sass *et al*., 1994) and with severity of hippocampal sclerosis assessed by left hippocampal volume measured on pre-operative MRI (Trenerry *et al*., 1993).

Pre-operative memory performance is also a predictor of post-operative memory decline, with better performance predicting worse decline (Helmstaedter and Elger, 1996; Jokeit *et al*., 1997). Concern about memory decline and current limitations in its prediction play an important role in limiting the number of patients undergoing potentially seizure-curing surgery. Memory may suffer in this context because hippocampus and related mesial temporal lobe (MTL) structures are crucial to long-term episodic memory function (Squire and Zola-Morgan, 1991; Squire, 1992; Lepage *et al*., 1998; Cabeza and Nyberg, 2000).

Patients judged at risk of post-operative amnesia undergo the intracarotid amytal procedure (IAP or 'Wada test'), during which sodium amytal is injected into each internal carotid artery in turn, allowing selective anaesthesia of each cerebral hemisphere. The ensuing period of unilateral hemispheric anaesthesia enables the memory capacity of the un-anaesthetized hemisphere to be examined in isolation. This test is crude and limited due to of the brevity of the anaesthesia, dysphasia during dominant hemisphere injection and patient sedation. It is also highly invasive and carries a significant risk of adverse outcomes, including stroke. Although IAP provides a reasonable index of the risk for amnesia, it is a poor predictor of the extent of verbal memory decline, although some studies have shown modest predictive value (Loring *et al*., 1995; Jokeit *et al*., 1997; Lee *et al*., 2003).

Functional MRI (fMRI) is attractive as a tool to examine memory in patients because of its wide availability and minimal risks. A small number of studies has shown patients with left MTLE preferentially activate right hippocampus in tasks assumed to require left or bilateral hippocampal function (Detre *et al*., 1998; Dupont *et al*., 2000; Jokeit *et al*., 2001; Golby *et al*., 2002). None of these studies used a design that allowed memory specifically to be examined in isolation.

Only one previous study from our group (Richardson *et al*., 2003) has shown that right-handed patients with left hippocampal sclerosis preferentially activate the right hippocampal formation in a verbal memory encoding task. We also showed that, in left hippocampal sclerosis patients, there is a distribution of activity between left and right hippocampi during this verbal encoding task that reflects the severity of left hippocampal sclerosis. Thus, patients with mildly affected left hippocampi showed relatively greater activity in left hippocampus than right hippocampus while patients with more severe pathology showed relatively more activity in right than left hippocampus (Richardson *et al*., 2004).

Two studies have revealed the potential for fMRI of a memory-related task to predict clinical outcomes in MTLE patients: (i) fMRI combined with IAP correctly predicted which patients undergoing anterior temporal lobe resection would become seizure-free (Killgore *et al*., 1999); and (ii) in the same group of patients, there was a correlation between mesial temporal fMRI activity and recognition memory change following surgery (Casasanto *et al*., 2001).

To date, there are no clear demonstrations that fMRI has a better predictive value for clinical outcomes compared with other established tests in any neurological field. Our aim in this study was to investigate the utility of event-related fMRI as a predictor of verbal memory decline in right-handed patients with left hippocampal sclerosis undergoing left anterior temporal lobe resection and to compare fMRI with existing techniques.

We previously recruited 26 right-handed patients with left hippocampal sclerosis who underwent evaluation for possible surgery in our centre (the pre-operative data for 24 of these were reported previously (Richardson *et al*., 2003, 2004). Ten of these subjects underwent surgery, became seizure-free and had histopathologically proven hippocampal sclerosis. The predictive value of pre-operative fMRI for post-operative memory decline in these subjects is reported here.

In this study, we examined encoding of neutral words. We show that the severity of post-operative verbal memory decline is strongly predicted by a multiple regression model which includes left hippocampal volume, pre-operative verbal memory score and the difference in successful encoding activity between left and right hippocampus. We show that hippocampal encoding activity difference is the strongest independent predictor and has high predictive value at the level of individual patients.

Methods

Subjects

Twenty-six consecutive subjects with an MRI-based diagnosis of left hippocampal sclerosis were recruited prospectively from the epilepsy surgery programme of the National Hospital for Neurology and Neurosurgery, London, UK. All 26 subjects underwent an fMRI study during evaluation for surgery.

Inclusion criteria for the 10 subjects reported here were: drug treatment resistant MTLE; right-handed; normal right hippocampal imaging parameters; first language English; seizure-free at least 6 months following left temporal lobe resection; and histopathology of the resection specimen showed hippocampal sclerosis. We included all the subjects who fulfilled these criteria. In the other 16 subjects, surgery was deferred because of a number of factors, which included: significant risk of substantial memory decline or amnesia (according to structural imaging, neuropsychometry and IAP); patient choice; and substantial improvement in seizure control following a change in antiepileptic drug treatment. Participants gave written consent and the study was approved by the Joint Research Ethics Committee of the Institute of Neurology and National Hospital for Neurology and Neurosurgery.

Pre-operative neuropsychometry

To assess verbal memory, we used the List Learning and Story Recall subtests of the Adult Memory and Information Processing Battery (Coughlan and Hollows, 1985) as part of a larger neuropsychometric test battery used for routine pre-surgical evaluation. The List Learning test has an initial registration component (maximum score = 75) and a delayed component (maximum score = 15). The Story Recall Test compares immediate and delayed recall of a story and yields a percent retained score (maximum score = 100). We obtained three clinical neuropsychological measures: (i) list learning—immediate (pre-operative immediate list recall); (ii) list learning—delayed (pre-operative delayed list recall); and (iii) story recall (pre-operative story recall).

Pre-operative structural imaging

Structural MRI was carried out at 1.5 T (Horizon Echospeed, General Electric, Wilwaukee, WI, USA) as part of routine pre-surgical evaluation, including T1 volume and dual-echo whole brain T2-map (Duncan *et al*., 1996). Hippocampal volumetry was carried out according to a previously published protocol (Van Paesschen *et al*., 1995).

Pre-operative functional imaging

Functional imaging was performed according to a previously described method (Richardson *et al*., 2003, 2004). In brief, subjects were scanned at 2 T (Siemens VISION, Siemens, Erlangen, Germany), acquiring T2*-weighted image echo planar imaging (EPI) volumes, providing blood-oxygenation-dependent (BOLD) contrast [33 slices; whole brain; voxel dimensions $=3 \times 3 \times 3.67$ mm; TE (echo time) = 40 ms; TR (repetition time) =2.5 s]. SPM99 was used for image analysis (Friston *et al*., 1995). The images were realigned, corrected for slice timing differences, transformed to the standard anatomical volume and smoothed (8 mm kernel).

A verbal encoding task was used. During scanning subjects were visually presented with 255 single words, including 36 emotionally aversive words (e.g. 'cancer', 'rape', 'terrorist') (Strange *et al*., 2000), one every 4.5 s. The word pool from which these were drawn is available on request. Subjects pressed a right-hand button to indicate whether the word was 'living' or 'non-living', and were not asked to memorize the words. Ninety minutes after scanning, subjects performed a surprise recognition memory test (not scanned): subjects were asked to indicate whether the word was definitely remembered (R response); if the word seemed familiar (K response); or was new (N response) (Tulving, 1985). The encoding stimuli were then conditionalized according to subjects' recognition responses. Recognition accuracy (D′) was calculated for stimuli labelled 'R' as (hit rate) – (false alarm rate).

To test for subsequent memory effects, imaging data were analysed within a two-level random-effects analysis employing an event-related design (Friston *et al*., 1998). At the first level, trial-specific responses were modelled and each subject's movement parameters were included as confounds. Contrasts of parameter estimates were calculated to produce a 'contrast image' for each subject of R minus K for neutral items only; we have showed previously that the responses to emotional words were dependent on amygdala pathology, which was not correlated with hippocampal pathology (Richardson *et al*., 2004).

We created for each patient a voxel-by-voxel image of left minus right encoding activity (R minus K) difference; these 'encoding asymmetry' images were used for further analyses. At the second level, simple regression was used to examine effects within the group. We chose $P < 0.05$ corrected for peak height both across the whole brain and within the small volume of left hippocampus using a 5 mm radius sphere centred on the peak activation in the left hippocampus in normal subjects in our previous study (Richardson *et al*., 2003) as the threshold for significance.

Post-operative neuropsychometry

At 3 months post surgery, each subject was tested on parallel versions of the List Learning and Story Recall; these parallel versions have standardized equivalent difficulty. We again collected three neuropsychological measures: (i) list learning—immediate (post-operative immediate list recall); (ii) list learning—delayed (post-operative delayed list recall); and (iii) story recall (post-operative story recall). Using these three measures, performed pre-operatively and repeated post-operatively, we calculated measures of verbal memory change between the first pre-operative and second post-operative assessment (pre-operative—post-operative change in immediate list recall, pre-operative—post-operative change in delayed list recall, pre-operative—post-operative change in story recall).

Data reduction

We expected that there would be a high degree of intercorrelation amongst the measures of memory. Therefore, we used principal components analysis to identify a factor accounting for the largest component of variance amongst these scores. Thus, the three pre-operative measures (pre-operative immediate list recall, pre-operative delayed list recall, pre-operative story recall) were entered into a principal components analysis, from which the first principal component was extracted. Likewise, the three memory change measures (pre-operative—post-operative change in immediate list recall, pre-operative—post-operative change in delayed list recall, pre-operative—post-operative change in story recall) were entered into a principal components analysis, from which the first principal component was extracted.

Prediction of change in memory score: model optimization

We entered the variables predictive of verbal memory outcome into a stepwise linear regression to identify the most important predictive variables.

Hypotheses to be tested

We tested the following hypotheses:

(i) Pre-operative verbal memory predicts verbal memory decline after surgery.
(ii) Left hippocampal volume predicts verbal memory decline after surgery.
(iii) Encoding asymmetry (derived from fMRI data) predicts verbal memory decline after surgery.
(iv) Encoding asymmetry (derived from fMRI data) is the best predictor of verbal memory decline after surgery.

Results

Demographic, clinical and memory data are summarized in Table 1. Nine of the 10 patients showed decline in at least two of the three memory measures between pre-operative scores and post-operative scores. There was decline in immediate list recall in six patients, no change in two and a slight improvement in two (mean change between pre-operative and post-operative scores was a decline of 5.7 points, ranging from a decline of 17 points to an improvement of 3 points; $P = 0.028$, paired *t*-test, 2-tailed). The delayed list recall showed decline in all but one, who had no change (mean change between pre-operative and post-operative scores was a decline of 3.6 points, ranging from a decline of 9 points to zero decline, $P = 0.002$, paired *t*-test, 2-tailed). There was decline in story recall in six patients and improvement in four, although overall this change was not significant across the group (mean change between pre-operative and post-operative scores was a decline of 14.2 points, ranging from a decline of 72 points to an improvement of 93 points, $P = 0.4$ paired *t*-test, 2-tailed).

Co-variation between memory scores

The recognition memory score derived from the recognition test carried out following pre-operative fMRI (D′) correlated

Table 1 *Demographic and clinical data for the subjects studied*

Patient	Sex	LHV (mm^3)	LHT2 (ms)	Age	Aetiology	Age at first febrile convulsion (months)	Age at onset of epilepsy (years)	Seizure types (frequency per month)	Drugs and dose (mg per day)	VIQ (WAIS-R)	PIQ (WAIS-R)	Age at completion of full-time education (years)	Pre-operative immediate list recall	Pre-operative delayed list recall	Pre-operative story recall	Post-operative immediate list recall	Post-operative delayed list recall	Post-operative story recall	Recognition accuracy following encoding fMRI
1	F	2026	96.4	30	Febrile convulsion	5	0.4	mTL CPS (4)	CBZ400 LTG450	86	112	18	39	9	83	26	5	100	0.416
2	M	1819	95.7	23	Febrile convulsion	9	0.75	mTL CPS (3)	VPA1500 TOP75	71	73	16	59	11	69	47	8	100	0.518
3	M	1408	94.1	44	Febrile convulsion	11	26	mTL CPS (8)	PHT400 VPA3000 GBP3600	102	110	20	36	5	65	36	0	14	0.324
4	F	1890	92.4	47	None known	-	3	mTL CPS (1)	TOP500 CBZ1500	73	67	16	49	10	92	49	6	40	0.373
5	F	1803	86.5	34	Febrile convulsion	15	15	mTL CPS (20)	LTG500 TOP325	85	95	16	47	6	40	40	5	133	0.440
6	F	1600	95.5	36	Febrile convulsion	12	8	mTL CPS (5)	CBZ1800 CLB10	89	92	18	48	8	94	50	8	75	0.603
7	M	2366	94.8	28	Febrile convulsion	15	6	mTL CPS (2)	CBZ800 VPA1200	90	117	19	56	11	91	39	2	50	0.427
8	F	1600	96.4	20	Febrile convulsion	12	4	mTL CPS (12)	LTG400 TOP400	92	102	18	45	11	92	40	7	71	0.318
9	M	1762	94.8	28	None known	-	4.5	mTL CPS (1), SG TCS (1)	GBP3600 LTG200 CLB10	92	92	16	35	8	86	27	3	14	0.303
10	F	1779	93.9	38	Febrile convulsion	30	2.5	mTL CPS (0.5)	CBZ2000 CLB30	83	89	16	21	3	54	24	2	37	0.092

CLB = clobazam; CBZ = carbamazepine; GBP = gabapentin; LHT2 = left hippocampal T2 signal; LHV = left hippocampal volume; LTG = lamotrigine; mTL CPS = typical mesial temporal lobe complex partial seizure; PHT = phenytoin; SG TCS = secondary generalized tonic-clonic seizure; TOP = topiramate; VPA = sodium valproate; WAIS-R = revised Weschler Adult Intelligence Scale.

strongly with pre-operative verbal learning (pre-operative immediate list recall), $P = 0.005$ (Fig. 1A). The first principal component derived from the pre-operative memory scores ('pre-operative verbal memory') correlated strongly with pre-operative immediate list recall ($R^2 = 0.72$, $P = 0.002$) and with pre-operative delayed list recall ($R^2 = 0.65$, $P = 0.005$), but not with pre-operative story recall ($R^2 = 0.017$). Similarly, the first principal component derived from the pre-operative—post-operative memory change scores ('post-operative verbal memory change') correlated strongly with pre-operative—post-operative change in immediate list recall ($R^2 = 0.97$, $P < 0.001$) and with pre-operative—post-operative change in delayed list recall ($R^2 = 0.38$, $P = 0.05$) but not with pre-operative—post-operative change in story recall ($R^2 = 0.051$).

Prediction of memory outcome by structural imaging parameters

Post-operative verbal memory change was strongly predicted by left hippocampal volume ($R^2 = 0.53$, $P = 0.017$) (Fig. 1B).

Prediction of memory outcome by pre-operative memory scores

Post-operative verbal memory change was predicted by pre-operative verbal memory ($R^2 = 0.50$, $P = 0.021$) (Fig. 1C).

Prediction of memory outcome by functional imaging parameters (figure 2)

At the group level, a single mesial temporal region showed a correlation between left–right encoding activity difference and post-operative verbal memory change. This region corresponded to the left hippocampus [$(-36\ -20\ -22)$, $Z = 3.64$, uncorrected $P < 0.001$, small-volume corrected $P = 0.016$]. Across the whole brain, no other regions survived the threshold chosen.

From a clinical perspective, the power of any predictive test is most relevant at the single subject level. Thus, on an individual subject basis we examined sensitivity, specificity and positive predictive value of pre-operative fMRI in predicting memory decline. We took the simplest approach to this by defining a 'normal' test result as predominant left hippocampal activation [as we previously reported for normal subjects (Richardson *et al*., 2003)] and an 'abnormal' test result as predominant right hippocampal activation [as we previously reported for patients with more severe left HS (Richardson *et al*., 2004)]. We defined memory outcome either as 'decline' in memory test score or as 'no decline'. We used two different thresholds to show decline: either any decline greater than zero, or as a decline greater than one standard deviation from the group baseline values. We used a 2×2 contingency-table approach to examine the ability of an 'abnormal' test result to predict 'decline' (Table 2).

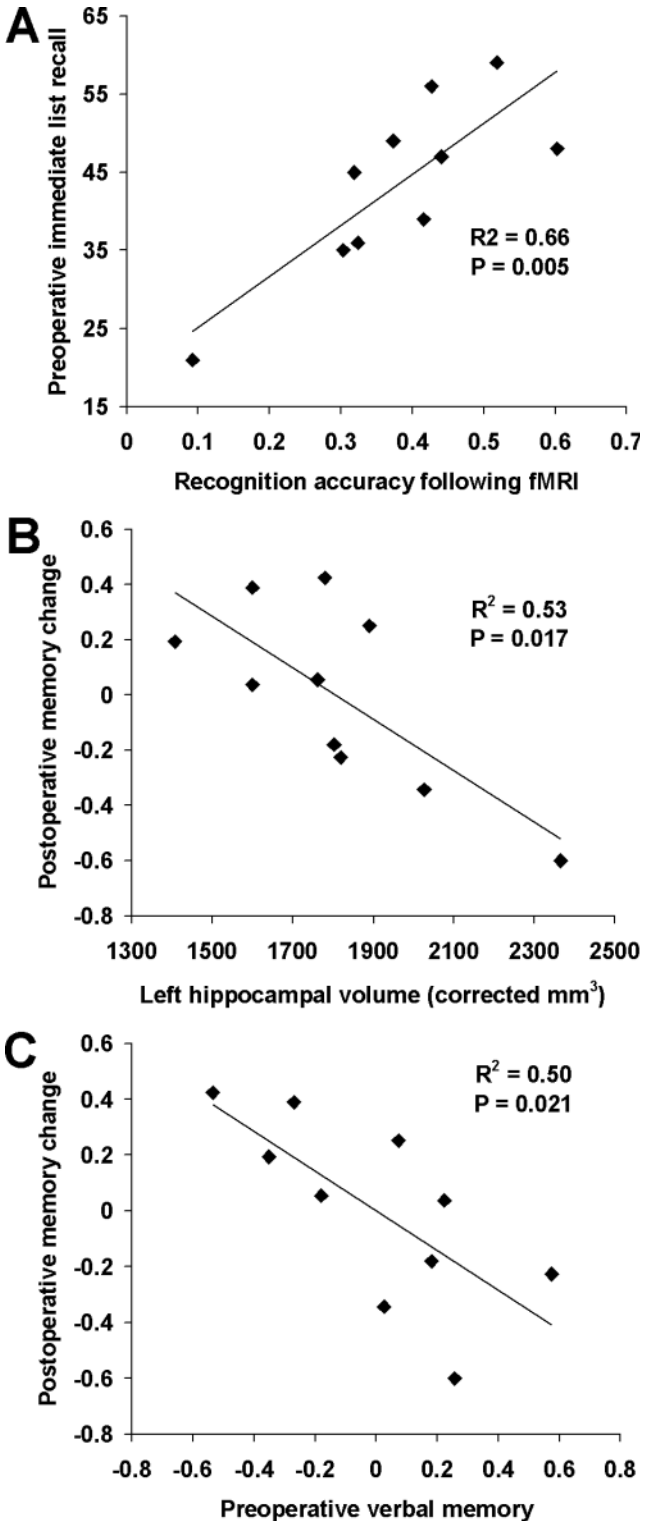

Fig. 1. (**A**) Correlation between recognition accuracy following fMRI (D′) and pre-operative immediate list recall. (**B**) Correlation between left hippocampal volume (corrected for total intracranial volume) and post-operative memory change (1st principal component of verbal memory change measures; see Methods). (**C**) Correlation between pre-operative verbal memory (1st principal component of pre-operative verbal memory measures; see Methods) and post-operative memory change (1st principal component of verbal memory change measures; see Methods).

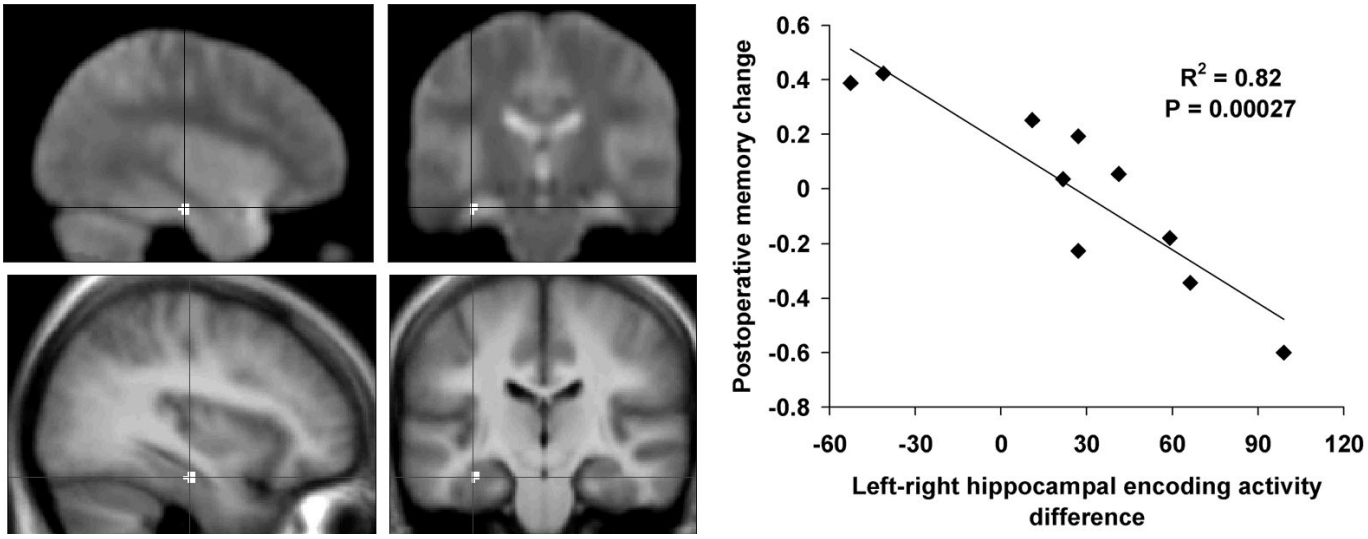

Fig. 2 Voxels showing a significant correlation ($P < 0.001$) between left-homotopic right voxel value and post-operative memory change (1st principal component of verbal memory change measures; see Methods) mapped onto average T2* image from all subjects (*upper left*) and average T1 image from all subjects (*lower left*). The correlation at the peak voxel is illustrated graphically on the right.

Table 2 *Sensitivity, specificity and positive predictive value of fMRI for the prediction of pre-operative post—operative change in memory score*

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
Cut-off: decline greater than zero from baseline values			
Immediate list recall	100	100	100
Delayed list recall	100	50	89
Story recall	100	20	56
Cut-off: decline greater than 1 SD from baseline values			
Immediate list recall	100	40	63
Delayed list recall	100	100	100
Story recall	100	40	63

Prediction of memory outcome: model optimization by stepwise linear regression

Three predictor variables were entered into a model with 'post-operative verbal memory change' as the dependent variable: (i) left–right hippocampal encoding activity difference; (ii) pre-operative verbal memory; and (iii) left hippocampal volume. This model predicted post-operative verbal memory change ($R^2 = 0.92$, $P < 0.001$). Stepwise linear regression showed only left—right hippocampal encoding activity difference made a significant contribution (significance R^2 change, $P > 0.1$ for the other variables).

To put this into a clinical context, we constructed an analogous model to predict pre-operative—post-operative change in immediate list recall (using left–right hippocampal encoding activity difference, pre-operative immediate list recall and left hippocampal volume as predictors). This model predicted pre-operative—post-operative change in immediate list recall ($R^2 = 0.84$, $P = 0.008$). In this model, stepwise linear regression again showed that only left–right hippocampal encoding activity difference made a significant contribution ($R^2 = 0.74$, $P = 0.001$).

Finally, we constructed a model to predict pre-operative—post-operative change in delayed list recall (using left–right hippocampal encoding activity difference, pre-operative delayed list recall and left hippocampal volume as predictors). This model predicted pre-operative–post-operative change in delayed list recall ($R^2 = 0.58$, $P = 0.13$). As in the other models, stepwise linear regression again showed only left-right hippocampal encoding activity difference made a significant contribution ($R^2 = 0.55$, $P = 0.015$).

Discussion

In this study, we confirmed previous findings that left hippocampal volume and pre-operative verbal memory function predict the extent of verbal memory decline in right-handed subjects with left hippocampal sclerosis undergoing left anterior temporal lobe resection because of intractable MTLE. Our novel finding is that relatively greater verbal memory encoding activity in left hippocampus compared with right hippocampus—as measured using fMRI—predicts the extent of verbal memory decline in the same subjects. Importantly, fMRI was by far the strongest independent predictor of memory decline and a powerful predictor of outcome for individual patients. We show these effects for two different standard clinical measures of verbal memory and even more strongly for a derivative (first principal component) of a range of standard clinical measures, which best accounts for the variability in measures within the patients studied. This is the first

time fMRI has shown a predictive value in a clinical setting over and above currently used tests.

Two functional imaging studies have shown prediction of memory outcome in patients undergoing temporal lobe resection for intractable MTLE. One study used blood-flow PET, a technique not generally available in clinical settings and, due to its poor temporal resolution, incapable of resolving activity associated with single events (Henke *et al*., 2003). Furthermore, only three of their subjects had left MTLE (the group in whom verbal memory decline is anticipated) and none of these experienced any decline in verbal memory. Hence, the study by Henke and colleagues primarily addressed non-verbal memory decline, which is less disabling and less easy to demonstrate, using a method which is not transferable to the clinical environment. This study, like the study we present here, did not address the issue of whether a change in memory test scores is reflected by a subjective change in memory ability which is symptomatic for the patient.

A second study, reported in abstract form, also included a mixed group of eight left and three right MTLE patients (Casasanto *et al*., 2001). These subjects underwent a task requiring explicit encoding of visual scenes presented in a block design, with a repeated 'scrambled' image as the baseline condition; this design does not allow subsequent memory effects to be revealed. However, the authors undertook a recognition memory test following scanning; a similar visual scene encoding and recognition memory test was also undertaken following subsequent anterior temporal lobe resection. Asymmetry of activation between ipsilateral and contralateral sides in a region of interest (ROI) at the boundary between the hippocampal formation and the lingual gyrus was determined. This asymmetry was strongly correlated with change in recognition memory score between the pre-operative and post-operative assessments. This study therefore also primarily addressed non-verbal memory. In it, memory improvement was seen following surgery in several patients, emphasizing the non-disabling nature of non-verbal memory change in many such patients. In the same group of patients, asymmetry of fMRI activity in the same ROI showed similar efficiency to the IAP for determining seizure outcome (Killgore *et al*., 1999).

Functional MRI is now a widely used methodology in basic neuroscience, but has yet to show it can provide information useful in clinical settings. Pre-operative localization of motor function is regularly undertaken in some centres to aid neurosurgery in the vicinity of the motor cortex. Although it is often asserted that such an approach provides for a better outcome, there are few supportive data. There is evidence that fMRI of motor function correlates with the sites of motor function determined using electrical stimulation of the cortex during surgery, but the correlation is often imperfect, subject to artefacts in fMRI data, difficult to integrate with other imaging during surgery and possibly requiring subjective interpretation (Stapleton *et al*., 1997; Krings *et al*., 2001, 2002; Roux *et al*., 2001; Liu *et al*., 2003).

In particular, many brain regions may be activated, especially in patients with lesions, and there is no means to determine which of a number of brain regions activated during an fMRI study is necessary and sufficient for normal function (Krings *et al*., 2002; Baciu *et al*., 2003). One study showed a strong prediction from pre-operative data of an immediate post-operative motor deficit following resection of medial frontal lesions if tissue activated in the medial frontal cortex during fMRI was resected, but there was no correlation with outcome a few weeks or months later (Krainik *et al*., 2001).

Mapping cortex responsible for language function in patients has shown a very strong correlation with IAP findings in the same subjects (Binder *et al*., 1996; Benson *et al*., 1999; Springer *et al*., 1999; Lehericy *et al*., 2000), although single subject studies are insufficiently sensitive to do more than lateralize language to one hemisphere and more detailed localization has been uncertain. The optimal choice of language task during fMRI remains unclear. An alternative may be to identify the sum total of all regions activated across a range of language tasks (Rutten *et al*., 2002). In a similar patient group to that presented here, fMRI of a language task showed a predictive value of similar magnitude to the IAP for confrontation naming deficit following left temporal lobe resection (Sabsevitz *et al*., 2003), but the authors did not present data to show that fMRI was a significantly better predictor of naming outcome compared with IAP.

Our findings have immediate relevance in the evaluation of MTLE patients for possible left anterior temporal lobe resection. There are important further avenues to explore, particularly patients with bilateral pathology and pathology other than hippocampal sclerosis, in whom prediction of verbal memory decline may be difficult. We anticipate that the robust prognostic data provided by our fMRI approach will stimulate the development of further valuable clinical tools utilizing fMRI.

Acknowledgements

We wish to thank Mr William Harkness, neurosurgeon, Dr Maria Thom, histopathologist, and the radiographers of the National Society for Epilepsy MRI Unit for their contributions to this study. We also wish to thank Dr Sanjay Sisodiya and Professor Ley Sander for referring patients. M.P.R. is supported by the Medical Research Council, J.S.D. by the National Society for Epilepsy and R.J.D. by the Wellcome Trust.

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