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Components of verbal learning and hippocampal damage assessed by T2 relaxometry

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Abstract

We studied a group of 31 temporal lobe epilepsy patients (25 left, 6 right) with unilateral hippocampal sclerosis evident on magnetic resonance imaging. Single slice T2 relaxation times were acquired for the left and right hippocampi. Principal components analysis of preoperative memory data resulted in two factors that reflect a distinction between arbitrary and semantic forms of verbal recall. The former component correlated with left hippocampal T2 relaxation time, while the latter component did not. This study suggests that variation in left hippocampal integrity is more related to the acquisition of arbitrary associates than semantically structured material, and reinforces the possibility that the left temporal lobe is functionally heterogeneous with respect to memory. (*JINS*, 2000, *6*, 529–538.)

Keywords: Memory, Verbal learning, Epilepsy, Temporal lobe, Imaging, Magnetic resonance

INTRODUCTION

Left anterior temporal lobe resection for the treatment of intractable complex partial seizures, which removes mesial temporal and lateral neocortical structures, results in degradation of performance on a wide range of verbal memory tasks (Chelune, 1995; Milner, 1975). These include Logical Memory (LM; Ivnik et al., 1987; Naugle et al., 1993; Novelly et al., 1984; Ojemann & Dodrill, 1985; Powell et al., 1985), the Rey Auditory Verbal Learning Test and its various adaptations (RAVLT; Helmstaedter & Elger, 1996; Ivnik et al., 1987), the selective reminding paradigm (Loring et al., 1991), and Paired Associate Learning (PAL; Goldstein et al., 1988; Ivnik et al., 1987). There is also strong evidence of a relationship between left mesial temporal damage and verbal memory function preoperatively (Miller et al., 1993; Hermann et al., 1997; Saling et al., 1993; Sass et al., 1990). This relationship, however, manifests itself on a more restricted range of measures (Baxendale, 1995; Saling et al., 1993, Sass et al., 1992). For example, Saling et al. (1993) found that LM scores did not differentiate between patients with pathologically confirmed right and left hippocampal sclerosis (HS). Preoperative acquisition of paired associates discriminated clearly between left HS and right HS groups, "hard" pairs explaining more than twice the amount of variance than that explained by "easy" pairs. This pattern has been described by others (Miller et al., 1993; Rausch & Babb, 1993), and suggests that mesial temporal damage exerts task-specific effects on verbal memory (Baxendale, 1995; Saling et al., 1993).

Task-specific effects have also been identified across the stages of RAVLT-type list learning procedures. In essence, the extent of retroactive interference appears to be more sensitive than other RAVLT indices to left mesial temporal sclerosis (Helmstaedter et al., 1997; Hermann et al., 1988; Saling et al., 1995) as well as to the postoperative effects of selective amygdalohippocampectomy (Helmstaedter et al., 1996, 1997). While the total number of words recalled during the acquisition phase (Trials 1–5) of the RAVLT also discriminates between patients with left HS and right HS, it is particularly affected by the additional involvement of anterior, inferior, and lateral aspects of the temporal lobe, as occurs in standard anterior temporal lobe resection (Helmstaedter et al., 1996; Saling et al., 1995). This apparent fractionation of the RAVLT can be accounted for by a differential language contribution to the acquisition phase and retroactive

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interference component (Hermann et al., 1988; Saling et al., 1995). Saling et al. (1995) showed that the total number of words recalled in Trials 1 to 5 of the RAVLT loses its sensitivity to the left–right difference in patients with unilateral hippocampal sclerosis when language competence is partialed out. This applies also to the easy paired associates. The ability of hard paired associates and the retroactive interference index to differentiate left from right HS is unaffected when the effect of language is controlled. This finding strengthens the notion that retroactive interference is a relatively pure measure of mesial temporal damage (Hermann et al., 1988, p. 251) and that the total number of words recalled in Trials 1 to 5 indexes temporal lobe damage more generally. We raise the possibility here that there is more than one dimension underlying verbal memory performance in patients with unilateral HS.

The estimation of hippocampal damage has been facilitated by the recent development of quantitative magnetic resonance imaging (MRI) techniques, including volumetry (Cook et al., 1992; Jack et al., 1989) and T2 relaxometry (Jackson et al., 1993b). In the field of temporal lobe epilepsy (TLE), memory research using MRI techniques has concentrated heavily on LM as the dependent variable and hippocampal volumes as the independent variable (Baxendale et al., 1998; Kälviänian et al., 1997; Lencz et al., 1992; Loring et al., 1993; Trenerry et al., 1993). Preoperatively, left hippocampal volume has been found to correlate with LM immediate (Kälviänian et al., 1997), delayed (Kälviänian et al., 1997; Loring et al., 1993), and percent retention index (Lencz et al., 1992) scores. Trenerry et al. (1993) on the other hand, did not find a relationship between left hippocampal volume and preoperative LM scores.

Relaxometry is a relatively new technique for quantifying T2 signal change. The variable it generates, that is, relaxation time in milliseconds (for example, see Kereiakes, 1989, pp. 3–7), is directly proportional to the logarithmic ratio of glial cells to neurons in the region of interest (Van Paesschen et al., 1997b). The longer the relaxation time, the larger the glial:neuronal ratio. HS is predominantly a condition of neuronal loss in CA1 and CA4 with glial infiltration (Bruton, 1988). T2 relaxometry is, therefore, well suited to detecting the presence of HS and quantifying its severity. Hippocampal volume and relaxation time are highly correlated with volume, accounting for 83% of the variance in relaxation time (Van Paesschen et al., 1995).

T2 relaxometry is a convenient technique for those interested in the relationship between pathology and neuropsychological performance. The data can be acquired rapidly and easily (Jackson, 1995; Van Paesschen et al., 1997a), and the values generated for a given hippocampus appear to be stable over time (Grünewald et al., 1994; Pitkänen et al., 1996). While intra- and interrater reliabilities for T2 relaxation times have not been reported, variation has been described as minimal (Jackson et al., 1993b, p. 1796). Relaxometry is less influenced by neuroanatomic knowledge and skills than is volumetry since measurement is based on a single region of interest (ROI) placed within the boundaries of the hippocampus. T2 relaxation times for normal hippocampi exhibit a very low level of interparticipant variation with no left–right difference.

The aim of this study was to examine the underlying structure of measures of verbal learning in patients with unilateral HS, and to determine the relationship of these measures to hippocampal integrity using T2 relaxometry. More specifically, we hypothesized that hard paired associates and retroactive interference would be highly intercorrelated in patients selected for the presence of unilateral MTS, and would exhibit lower correlations with the total number of words recalled in RAVLT Trials 1 to 5 and easy pairs. Further, we hypothesized that the former set of measures would be related to the degree of left hippocampal damage, while the latter set would not.

METHODS

Research Participants

Data were collected retrospectively for consecutive TLE patients seen in the Comprehensive Epilepsy Program at the Austin and Repatriation Medical Centre between 1994 and 1997. Patients were included in the study if the classic MRI features of unilateral HS were seen on visual inspection (Jackson et al., 1993b), there was no history of head trauma or cerebral infection, pre-operative T2 relaxometry data were available, and if a routine preoperative neuropsychological assessment had been conducted. Further inclusion criteria were a Full Scale IQ greater than 70 and English as a first language. Five cases with previous head injury or encephalitis were excluded because of the high risk of diffuse extratemporal damage. In this series we also encountered four cases with severe left hippocampal damage, entirely normal verbal memory, and profound spatial memory impairments. Like others (Helmstaedter et al., 1994; Seidenberg et al., 1997) we regard this pattern as evidence of reorganization of verbal memory (Wood et al., 1999), suggesting that these cases represent a qualitatively different population.

Using these criteria, the study included 31 patients with unilateral TLE in whom HS was the underlying pathology (6 right, 25 left). The disproportionate number of left- and right-sided patients appears to be a feature of sequential sampling at our center (see, e.g., O'Shea, 1996; Saling et al., 1993, 1995). Diagnosis was based on video-EEG monitoring and neuroimaging (interictal PET, ictal and interictal SPECT, and MRI). Twenty-five patients (80.6%) experienced a febrile convulsion in infancy or early childhood. The incidence of febrile convulsions did not differ between HS groups (Fisher Exact probability = .31). The mean age of habitual seizure onset was 9.65 years ($SD = 6.31$). There was no difference in age of onset between left- and right-sided patients (Mann–Whitney $U = 74.5$, $p = .98$). The average number of years with epilepsy (time between habitual seizure onset and assessment in the CEP) was 23.06 years ($SD = 10.41$, range = 7–43). The number of years with epilepsy for left and right HS patients did not differ significantly (U = 68.0, p = .75). A total of 11 patients were male (3 right HS, 8 left HS) and 20 were female (3 right HS, 17 left HS). There was no significant group difference in sex distribution (Fisher Exact probability = .64). No differences in the distribution of febrile convulsions between male and female participants were observed (Fisher's Exact probability = .99), and there were no sex differences in age at seizure onset (U = 75.5, p = .16).

The average age at the time of neuropsychological assessment was 32.72 years (SD = 7.98; range = 17–50). Of the patients for whom information regarding educational attainment was available (n = 26), 57.7% had begun secondary education, 23.1% had completed secondary education, and 19.2% had embarked upon tertiary education. Educational attainment did not differ across HS groups [$\chi^2(2)$ = 1.96, p = .37]. Sex differences were not observed for age at testing (U = 72.5, p = .12) or for the distribution of educational attainment [$\chi^2(2)$ = .67, p = .72]. FSIQ was determined by means of the Reynold's short form of the Wechsler Adult Intelligence Scale–Revised (WAIS–R; Reynolds et al., 1983). Average FSIQ did not differ between left (M = 91.9, SD = 9.55) and right (M = 93.5, SD = 13.35) HS patients (U = 73.5, p = .94).

Materials and Procedures

Memory measures

The total number of hard (maximum = 12) and easy (maximum = 18) word pairs correctly acquired over three learning trials was derived from the Wechsler Memory Scale (Form 1) (Wechsler, 1945). The RAVLT (Lezak, 1995, pp. 438–445) measures used were the total number of words correctly recalled on Trials 1 to 5 (RAVLT total) and recall of List A (Trial 6) following an interference condition (List B). The change in recall between Trials 5 and 6 was quantified as [(Trial 5 − Trial 6)/Trial 5] × 100. We follow neuropsychological convention (for example, Hermann et al., 1988) and refer to this as a retroactive interference index. All data for the present study were obtained preoperatively.

Relaxometry

Single coronal T2 maps were acquired during routine MRI examination (Jackson et al., 1993b). All MR imaging was performed on a 1.5T Siemens Magnetom. Multiple sagittal scout images were acquired and the hippocampus located. Oblique coronal images perpendicular to the long axis of the hippocampus were acquired. A single oblique coronal T2 map was centerd on a line crossing the pons at the anterior border of the brainstem. T2 maps were calculated using a Carr–Purcell–Meiboom–Gill (CPMG) sequence, which produced 16 images at varying echo times (22–247 ms). Slice thickness was 8 mm and an inferior saturation pulse was used to minimize pulsation artifacts from the carotid arteries. T2 maps were generated by a computer program that fitted a single exponential to signal-intensity values of corresponding pixels from each image. The program applied a gray scale to the pixel map, resulting in an image where pixel intensity represented the T2 relaxation time. Measurement of T2 relaxation times was achieved by placing a circular region of interest within the anatomical boundaries of the structures to be measured, avoiding boundaries between structures and CSF where partial voluming may occur. At our center, a cut-off value of 109 ms has been established on the basis of data from 50 normal controls (see Briellman et al., 1998). Values greater than the cut-off are considered abnormal (Briellman et al., 1998; Jackson et al., 1993b).

RESULTS

Mean relaxation times for the left and right hippocampi across all HS individuals are given in Table 1. In order to facilitate interpretation of the substantive findings, the relationship between left and right hippocampal T2 relaxation times was explored at the outset. Within the left HS group there was suggestion of a moderate positive relationship, but this failed to reach significance (r = .32, p = .12). In the right HS group a nonsignificant correlation between left and right hippocampal relaxation times of .26 (p = .62) was obtained. Across all HS patients there was a significant negative correlation between left and right T2 relaxation times ($r = -.36$, $p < .05$) attributable to the *a priori* classification of cases into left and right HS groups (see Figure 1). The relaxation times for the left hippocampi ranged between 91 and 155, comparable to the range for the right hippocampi (93–142). Relaxation time in the contralateral (nonsclerotic) hippocampus was in the normal range in all cases. In one left HS patient the left hippocampal T2 value was 101 ms, and it was 108 ms in two left HS patients. It is worth noting that the presence of hippocampal sclerosis increases the variability in relaxation time (see Table 1). A classification analysis, with group (left HS *vs.* right HS) as

Table 1. Mean left and right T2 relaxation times for hippocampal sclerosis groups

	Left HS			Right HS		
Relaxation time	*M*	*SD*	Range	*M*	*SD*	Range
Left T2 relaxation time	121.4	12.56	101–155	101.5	5.47	91–107
Right T2 relaxation time	101.84	4.01	93–108	122.17	10.23	115–142

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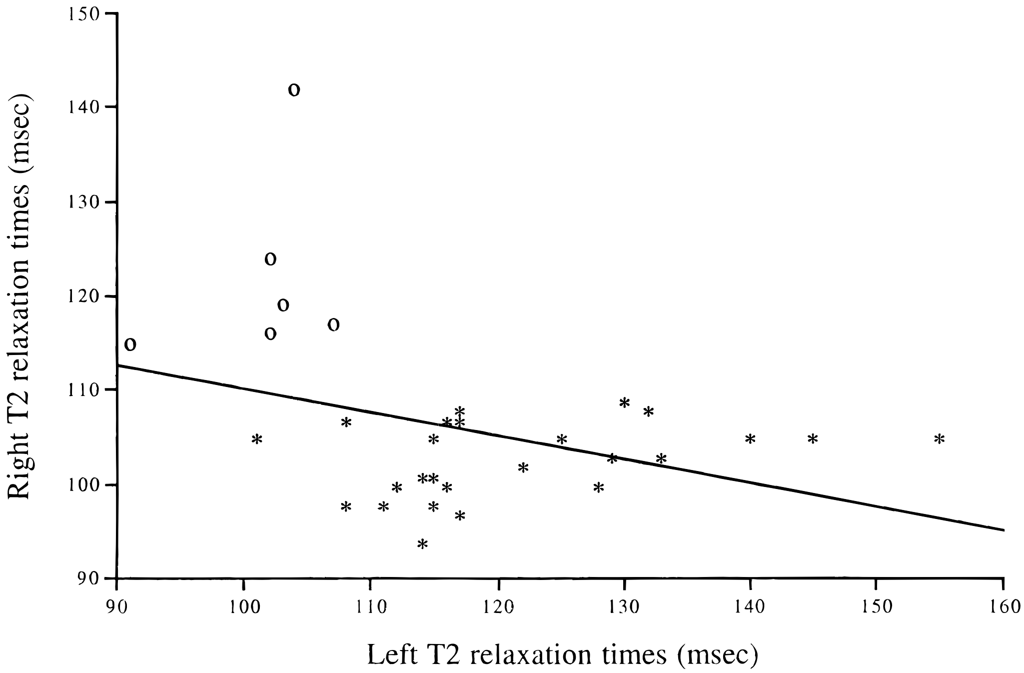

Fig. 1. Relationship between right and left T2 relaxation times. Legend: * = left TLE, o = right TLE.

the criterion and relaxation times (left *vs*. right hippocampus) as the predictors, correctly classified all cases on the basis of a single discriminant function; its canonical correlation with groups was .88 (Wilks's $\lambda = .23$; $\chi^2 = 41.71$, $p < .0005$).

There was no significant relationship between the number of years with epilepsy and either left ($r = -.12$, $p = .57$) or right ($r = -.15$, $p = .44$) T2 relaxation times. Similarly, age at assessment did not correlate with left ($r = -.01$, $p = .94$) or right ($r = -.30$, $p = .10$) T2 relaxation times.

Performance on each of the verbal memory measures is shown in Table 2. The left HS groups acquired fewer hard pairs ($M = 3.80$) than did the right HS group ($M = 7.50$; $U = 27.0$, $p = .01$). There were no group differences on easy PAL ($U = 52.5$, $p = .27$) or on the total number of words acquired during the first five trials of the RAVLT ($U = 64.5$, $p = .61$). There was a numerically larger retroactive interference effect in the left HS group, but this failed to reach statistical significance ($U = 43.5$, $p = .12$); in this respect it should be noted that the variances associated with the retroactive interference means are comparatively large. Performance by male and female participants did not differ significantly on the total number of hard ($U = 79.0$, $p = .21$) or easy ($U = 106.5$, $p = .89$) word pairs or on RAVLT total ($U = 79.5$, $p = .21$) or retroactive interference ($U = 100.0$, $p = .70$).

Retroactive interference, RAVLT total, and the two PAL scores for the combined groups were subjected to a principal components analysis with varimax rotation. The first two components met Kaiser's criterion, accounting for 48.8% and 28.7% of the variance respectively. The varimax rotated components are shown in Table 3. The first component (I) received its highest loadings from hard PAL (.907) and retroactive interference of the RAVLT (−.843). The second component (II) received its highest loadings from easy PAL (.864) and RAVLT total (.843). In general, this solution is characterized by adequate simple structure. Nevertheless, it is worth noting that the two RAVLT variables show a marginally greater tendency to load on their respective minor components (I in the case of RAVLT total, and II in the case of RAVLT retroactive interference) than did the paired associate variables.

Table 2. Scores obtained by left and right HS patients for the verbal memory measures

	Left HS				Right HS			
Score	*M*	*SD*	*N*	Range	*M*	*SD*	*N*	Range
Hard PAL	3.80	2.97	25	0–9	7.50	3.08	6	2–10
Easy PAL	16.56	1.29	25	13–18	15.50	2.35	6	11–17
RAVLT total	45.48	7.37	25	29–57	46.83	7.52	6	31–55
RAVLT retroactive interference	35.69	26.05	25	0–100.00	19.09	16.64	6	0–38.46

Table 3. Factor loadings from the principal components analysis of verbal memory measures

	Component	
Measure	I	II
Hard paired associates	*.907*	.017
RAVLT retroactive interference	−*.843*	−.275
RAVLT total	.180	*.843*
Easy paired associates	.040	*.864*

Note. The italicized values are the loadings which best define each factor.

The number of years with epilepsy was not significantly related to either Component I ($r = -.14$, $p = .46$) or Component II ($r = .03$, $p = .88$) scores. There was also no significant correlation between age at assessment and either Component I ($r = -.24$, $p = .19$) or Component II ($r = .04$, $p = .81$).

There is a negative linear relationship between left T2 relaxation time and Component I scores ($r = -.39$, $p < .02$, one-tailed; Figure 2a), suggesting that increasing left hippocampal damage is associated with poorer hard PAL and resistance to the effects of retroactive interference. On the other hand, there is a *positive* linear relationship between right T2 relaxation time and Component I scores ($r = .37$, $p = .02$, one-tailed). A stepwise multiple regression showed that right T2 relaxation time did not increase Component I variation already explained by left T2 relaxation time to a significant extent [$R^2_{ch} = .06$; $F(1,28) = 2.16$, $p = .15$]. Further exploration of the relationship between Component I and left T2 relaxation time revealed a significant quadratic trend that accounted for 23.9% of the variance [$F(2,28) = 4.39$, $p = .02$; see Figure 2b]. This finding suggests that severe hippocampal damage is not necessarily associated with the worst levels of verbal memory performance.

Left T2 relaxation time did not predict Component II scores ($r = -.12$, $p = .26$, one-tailed). A box plot identified two outliers on Component II with Z scores of -3.20 and -2.06 (see Figure 3). When these outliers were removed the correlation with left T2 relaxation times increased marginally but remained nonsignificant ($r = -.23$, $p = .22$). A quadratic model also failed to reach significance [$r = .16$; $F(2,28) = .38$, $p = .69$]. There was no significant relationship between Component II and right T2 relaxation times ($r = -.20$, $p = .14$, one-tailed). Again, a quadratic model was not significant [$r = .25$; $F(2,28) = .92$, $p = .41$).

DISCUSSION

The measures of verbal memory used in this study might not reflect a single underlying dimension. Our findings suggest that they are better characterized by at least two orthogonal components. The size of the sample in this study is smaller than that usually encountered in factor analytic work, and replication of the solution is desirable. Nevertheless, this two-component structure is consistent with previously described fractionations in RAVLT (Helmstaedter et al., 1996, 1997; Hermann et al., 1988; Murphy, 1998) and PAL (Saling et al., 1993, 1995) provoked by left mesial temporal sclerosis and temporal lobe resection. It also converges on the previously described differential relationship between RAVLT and PAL measures and general language competence (Hermann et al., 1988; Saling et al., 1995): Measures that in this study form Component II do not discriminate between left and right HS in the presence of a language covariate, while the sensitivity to left HS of measures that here form Component I is not affected when language is partialed out (Saling et al., 1995). In the present study, the comparatively small number of RHS patients places some limitation on the interpretation of between group variation. This, however, is not germane to the main aim of the study, namely the exploration of underlying structure.

Hippocampal Relaxation Times

Before discussing the relationship between the memory component scores and hippocampal damage, the relationship between left and right hippocampal relaxation times deserves some mention. Within each HS group there was a discernible (albeit nonsignificant) positive relationship between left and right T2 relaxation times, suggesting that increasingly severe damage on one side raises the probability of incipient sclerosis on the contralateral side. This possibility has been articulated in the recent hypothesis of Briellman et al. (1998, p. 1180), which includes the notion of epileptogenic priming of the contralateral hippocampus, making it more vulnerable to subsequent seizure-related damage. Nevertheless, all of our cases had asymmetrical hippocampi, and the hippocampus with the higher T2 value was always ipsilateral to the epileptogenic focus; in no case was T2 relaxation time in the nonepileptogenic hippocampus in the abnormal range. Across the HS group as a whole, the correlation between left and right T2 relaxation time was significant but negative. This appears to be a consequence of the *a priori* classification of cases into left and right HS groups.

Although the left T2 values of three left HS patients fell within the normal range as we have defined it (Briellman et al., 1998), two of these fell just 1 ms below the cut-off and a discriminant function analysis correctly classified all patients on the basis of relaxation times. Van Paesschen et al. (1997a) examined hippocampal volume and relaxation time in patients with TLE who were grouped according to hippocampal volume ratio. Within the group that had asymmetric volumes, three patients (6%) had normal T2 relaxation times. Inspection of the *hippocampal volume distribution graphs* (Van Paesschen et al., 1997a) in these cases revealed atrophy restricted to the anterior portion of the hippocampus. The small number of normal T2 relaxation times observed by ourselves and Van Paesschen and colleagues (1997a) accords well with the finding (Quigg et al., 1997; Van Paesschen et al., 1997a) that HS affects the entire long axis of the hippocampus in the majority of cases.

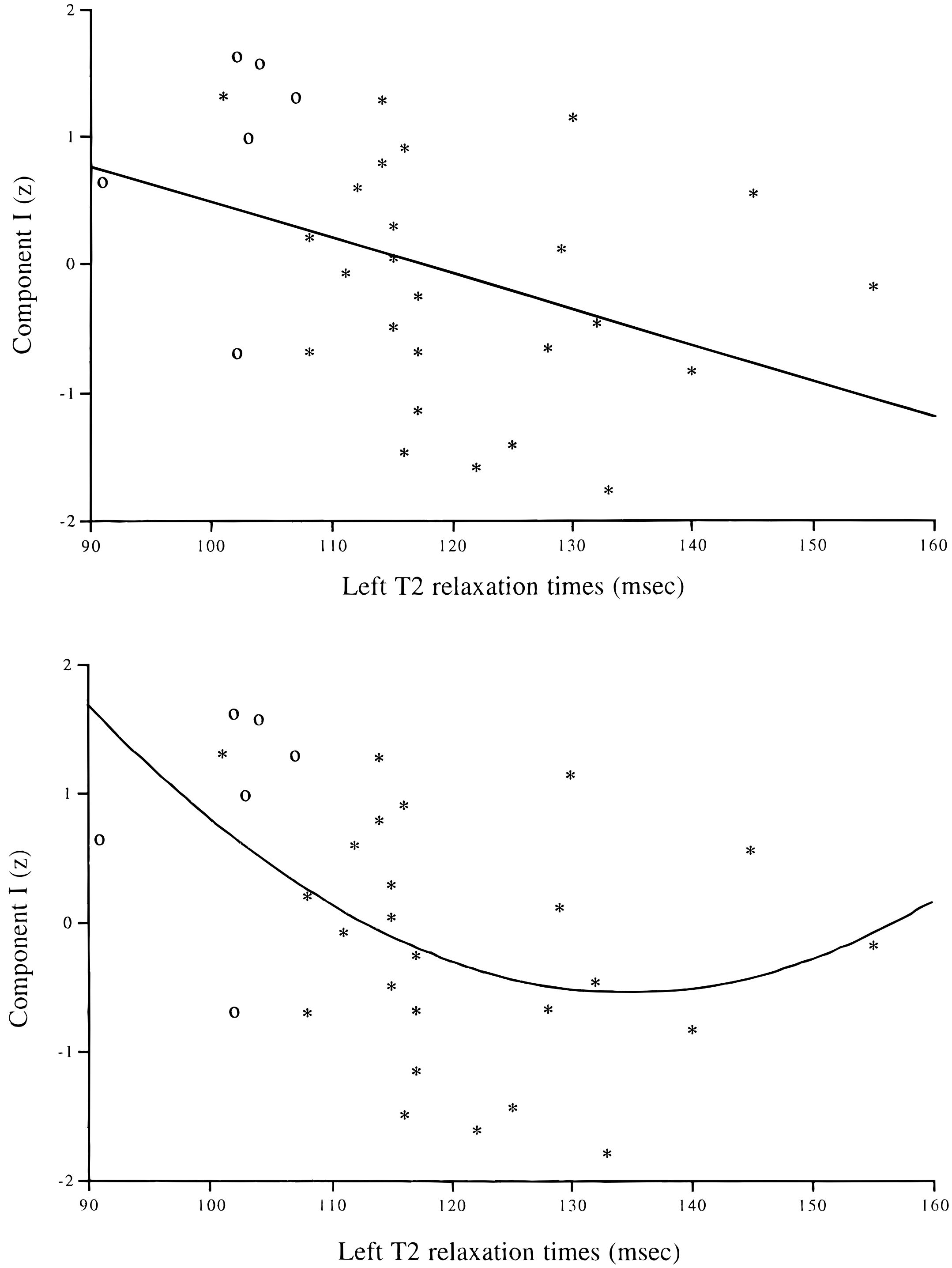

Fig. 2. Relationship between left T2 relaxation times and Component I scores. *Note*: (top) linear trend, $y = -0.028x + 3.278$; (bottom) quadratic trend, $y = .001x^2 - .300x + 19.714$. Legend: * = left TLE, o = right TLE.

Memory Components and Left Hippocampal Damage

The first component seems to represent what may be referred to as relational (Eichenbaum et al., 1994), or nonsemantic, form of verbal learning. It receives its highest contribution from tests that reflect the acquisition of arbitrary cooccurences (hard word pairs) as well as resistance to the effects of interference (RAVLT retroactive interference). Mesial temporal function has been implicated in both of these processes. According to Squire (1992), Cohen and Eichenbaum (1993), and McClelland (1994), the rapid formation of conjunctions between arbitrarily associated events is one of the fundamental mnemonic roles of the hippocam-

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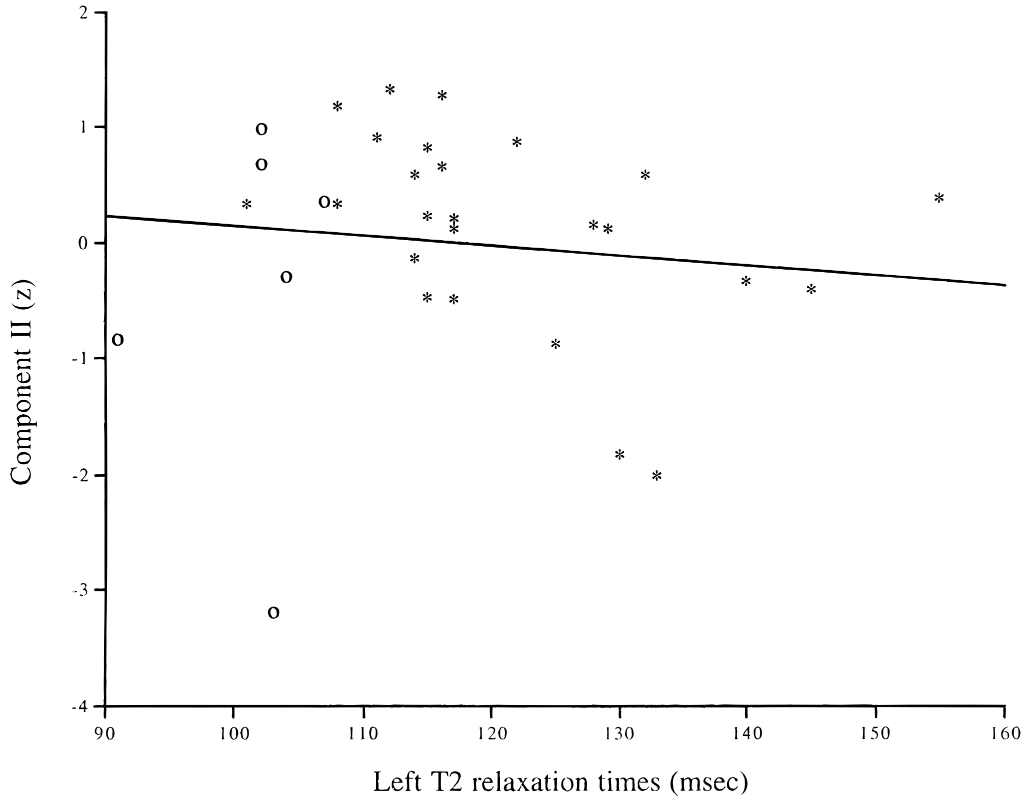

Fig. 3. Relationship between left T2 relaxation times and Component II scores. Legend: * = left TLE, o = right TLE.

pus. At an empirical level, the effects of left HS on verbal paired associates have been described previously (Miller et al., 1993; Rausch & Babb, 1993; Saling et al., 1993) with the magnitude of the effect on hard paired associates (36%) being twice as large as that on easy word pairs (15%; Saling et al., 1993). Resistance to interference (or alternatively, resistance to the effect of delay, during which rehearsal is prevented or limited) is intimately bound up with the notion of consolidation and, indeed, is a necessary precondition for its occurrence (McClelland et al., 1995). This time-limited protection of new memories is primarily attributed to mesial temporal regions (Dudai, 1990; Eichenbaum et al., 1994; Milner, 1970; Squire, 1992; Zola-Morgan & Squire, 1990).

The relational learning component (that is, Component I) exhibited a moderate, significant negative correlation with left T2 relaxation times, explaining 15.21% of the variance. Poorer memory scores were associated with increased left T2 relaxation times. When right T2 relaxation time is correlated with relational learning, the direction of the relationship changes to a positive one. This effect seems to be secondary to the negative relationship between left and right T2 relaxation times in the group as a whole, and lends weight to the argument that left, but not right, hippocampal integrity underlies performance on the specific measures that make up the relational learning component.

Component II scores, on the other hand, did not correlate significantly with either left or right T2 relaxation times, suggesting that the measures that it contains are less dependent upon mesial temporal integrity. The acquisition of word lists is maximized when semantic encoding strategies are used (Hermann et al., 1992) and is predicted by measures of general language competence (Hermann et al., 1988) to a greater extent than are relational forms of learning. In neurological terms, this task is likely to involve lateral neocortex and to depend less heavily on mesial temporal function. In referring to our earlier study (Saling et al., 1993), Bell and Davies (1998) question this notion, suggesting that it "does not appear viable when memory test results are considered across studies measuring preoperative and postoperative performance" (p. 28). Word-list recall, however, worsens after left anterior temporal lobectomy, which includes a neocortical resection (Helmstaedter et al., 1997; Saling et al., 1995), but is relatively unaffected by selective amygdalohippocampectomy (Helmstaedter et al., 1996). Easy paired associates are constructed on a semanticosyntactic basis and cooccurrences of this nature are already well established in neocortical systems.

In view of the small sample size our findings should be treated as preliminary, but the data do seem to support the emerging hypothesis that arbitrary forms of verbal learning might be a more sensitive marker of hippocampal capacity than forms of verbal learning that are facilitated by semanticosyntactic structure. This could be interpreted within the framework of task specificity in verbal memory (Baxendale, 1995; Saling et al., 1993), namely, the specific demands of each verbal memory test will determine the extent to which it is affected by left- or right-sided damage, and the extent to which it is mediated by archicortical or neocortical systems (Dobbins et al., 1998; Helmstaedter et al., 1996, 1997; Saling et al., 1993, 1995).

Our findings point to the importance of clarifying the *nature* of verbal memory impairment in the preoperative evaluation of surgical candidates with TLE. Although the measures of Component II may differentiate between right- and left-sided damage in some samples, their performance is more susceptible to the confounding effects of additional cognitive factors such as language competency (Hermann et al., 1988; Saling et al., 1993, 1995). This limits their capacity to estimate reliably the functional deficit produced by left mesial temporal sclerosis. Measures of the first component are likely to be more sensitive to damage in the left mesial temporal region. The continuous linear relationship between the first component and left T2 relaxation time values suggests that fundamental impairments in these aspects of verbal memory are dependent upon the *degree* of preoperative hippocampal damage.

The notion that the relationship between verbal memory performance and hippocampal integrity is essentially linear is a long-held assumption in TLE-memory research, and one that has found support in a number of studies and reviews of presurgical memory function (Baxendale, 1995; Chelune, 1995; Lencz et al., 1992; Milner, 1970; O'Rourke et al., 1993; Rausch & Babb, 1993; Sass et al., 1990). Inspection of our data suggests that a decline in arbitrary learning scores is most evident in cases with mild to moderate left T2 signal abnormality (see Figure 1), principally between the normative cut-off (109) and 130 ms. When left T2 abnormality is severe ($\geq$130 ms), however, there was a discernible trend towards higher scores on Component I tests, producing a significant quadratic effect. One possible interpretation of this pattern is that it reflects the occurrence of verbal memory compensation in cases in whom damage was more severe at an early age. The emergence of a quadratic trend is somewhat surprising, since we intentionally excluded cases that met criteria for putative memory transfer (Wood et al., 1999). It is possible, however, that memory compensation is a more continuous phenomenon than we have previously suspected. Interestingly, 3 of the 4 excluded cases had a left T2 relaxation time in excess of 130 ms. We present this interpretation tentatively; clearly, further investigation is needed.

To date, memory studies in the field of temporal lobe epilepsy have emphasized the mesial temporal region to the exclusion of neocortical involvement in verbal memory (Chelune, 1995). This has been closely associated with the often implicit assumption that a wide variety of verbal memory measures in clinical use (word lists, passages, and paired associates) are good markers of hippocampal status. A handful of studies, including the present one, now suggest that the structure of verbal memory tasks is relevant to their ability to detect hippocampal damage (Helmstaedter et al, 1997; Ojemann & Dodrill, 1985; Saling et al., 1993). Component II measures may serve as a model for the development of procedures that assay the temporal neocortical contribution to verbal memory more effectively. There is also a suggestion that measures of this type are more likely to reflect *change* in verbal memory after left anterior temporal lobectomy (Helmstaedter et al., 1997; Saling et al., 1995), which generally involves resection of neocortical tissue.

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