Epilepsia, **45**(6):632–640, 2004
Blackwell Publishing, Inc.

Correlation between ^{1}H MRS and Memory before and after Surgery in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis

*Lütfü Hanoğlu, †Ciğdem Özkara, ‡Cahit Keskinkiliç, ‡Ümmühan Altin, §Mustafa Uzan, §Saffet Tuzgen, ‖Alp Dinçer, and §Emin Özyurt

**Bakirköy Neurology Center; †Department of Neurology, Istanbul University, Cerrahpaşa Medical Faculty; ‡Bakirköy State Hospital for Psychiatric and Neurological Diseases; §Department of Neurosurgery, Istanbul University, Cerrahpaşa Medical Faculty; and ‖Radyomar Radiodiagnostics Laboratory, Istanbul, Turkey*

Summary: *Purpose:* Proton magnetic resonance spectroscopy (^{1}H MRS), which can demonstrate neuronal loss and gliosis, may be used as a sensitive tool for lateralization of temporal lobe epilepsy (TLE). Although the correlation between the memory functions and ^{1}H MRS has been investigated, its predictive value after surgery has not been studied previously. This study evaluated memory and ^{1}H MRS values of medically intractable patients with mesial TLE and hippocampal sclerosis (MTLE-HS) before and after selective amygdalohippocampectomy (SAH).

Methods: Twenty-two patients underwent memory tests and ^{1}H MRS investigation before and 6 months after SAH and were compared with nine control subjects.

Results: The ^{1}H MRS scores were found to be significantly low on the pathological side of the patients. Both right-sided ^{1}H MRS of right TLE and left-sided ^{1}H MRS values of left TLE patients were correlated only with verbal memory scores. Statistical analysis did not reveal any significance for nonverbal memory scores for both TLE groups on either side, which showed no significant correlation between material specificity and ^{1}H MRS findings. Conversely, regression analyses demonstrated that high right- and low left-sided ^{1}H MRS values obtained before surgery may predict a decline in verbal learning scores after surgery.

Conclusions: ^{1}H MRS can be considered as a useful tool to determine the lateralization in patients with MTLE-HS before the surgery. Although only a weak relation exists between the MRS values and memory scores, presurgical MRS scores may be predictive for a possible deterioration in verbal memory after surgery. However, further studies with higher numbers of cases are needed for confirmation of the results. **Key Words:** ^{1}H MRS—Memory—Temporal lobe epilepsy—Hippocampal sclerosis—Surgery.

Hippocampal sclerosis (HS) is characterized by certain pathologic features including selective neuronal loss, reorganization, and reactive gliosis and composes the majority of the pathologic substrate in mesial temporal lobe epilepsy (MTLE) (1). Many patients in this group have medically intractable seizures and progressive memory deficits and highly benefit from epilepsy surgery (2).

Single-voxel proton magnetic resonance spectroscopy (^{1}H MRS) is a sensitive noninvasive tool for presurgical evaluation of epilepsy patients in lateralization of MTLE-HS. The technique can provide information about metabolic changes based on signals from *N*-acetyl aspartate (NAA) and creatine + phosphocreatine (Cr) and choline (Cho)-containing compounds. NAA is exclusively located in neurons, whereas Cho is primarily a membrane-bound constituent of neuroglial cells (3). Altered concentrations of NAA and/or Cho and Cr can be detected by abnormal signals of NAA, Cr, and Cho in the proton spectra of the investigated brain region. It is generally assumed that selective loss of pyramidal cells in hippocampus results in a decrease in NAA concentration, whereas reactive gliosis of astrocytes leads to an increase in Cho and Cr concentrations. Thus the NAA/Cho+Cr signal ratio can be used as a sensitive indicator of neuronal loss/astrocytosis (4).

The decrease in NAA is often interpreted as a sign of irreversible neuronal loss; however, recent studies revealed improvement toward normal ratios in patients after surgery on the same side as surgery (5) and at the contralateral but also abnormal side after surgery, implying that these metabolites may be dynamic markers of both local and

Accepted February 6, 2004.
Address correspondence and reprint requests to Dr. C. Ozkara at Department Neurology, Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey. E-mail: cigdemoz@anet.net.tr, cigdemoz@istanbul.edu.tr

remote physiologic dysfunction (6,7). Demonstration of neuronal dysfunction rather than neuronal loss with ^{1}H MRS measurements evoked curiosity about the interesting relationship between cognition and this functional investigation method. This neuronal dysfunction may give rise to variable cognitive disorders related to the region of interest (i.e., mesial temporal lobe in this study). The presence of memory problems is a well-known phenomenon in MTLE-HS, and the relations between the presurgical (NAA/Cr+Cho) ratios and neuropsychological tests were previously investigated (4,8–10). However, changes in memory functions in relation to ^{1}H MRS results after surgery have not been studied, although such information will enable us not only to determine the place of MRS in the prediction of memory status after surgery but also to understand the relation between so-called normalization of MRS and memory functions, if any. Therefore we performed this study to determine whether any correlation exists between ^{1}H MRS abnormalities and memory functions before and after surgery in patients with MTLE-HS.

METHODS

Subjects

Twenty-two consecutive patients, 10 men and 12 women, with a mean age of 27.4 ± 7.48 years (range, 15–45 years) were investigated. They were all diagnosed with medically intractable MTLE-HS and underwent surgery for their epilepsy. Their mean age at seizure onset was 8.95 ± 6.2 years (range, 1–20 years), and clinical history revealed the presence of febrile seizures in 18, an anoxic event in one, and infection in one patient. The epileptic focus was identified by video-EEG monitoring of habitual seizures with sphenoidal electrodes, including interictal and ictal EEG analyses. All patients demonstrated interictal anterior temporal spike focus and ictal fast theta or alpha rhythm localized to right or left sphenoidal and anterior temporal leads. Psychiatric and neuropsychological investigations were other essential elements of our presurgical evaluation protocol. HS was detected by magnetic resonance imaging (MRI) scan with atrophy on T_1W and signal increase on T_2W images, as well as loss of internal structure of the hippocampal formation. Pathological examination confirmed the diagnosis in all cases. Follow-up ^{1}H MRSI and neuropsychological examinations were performed 6 months after surgery as well as awake and sleep EEG recordings.

The surgical technique was selective amygdalohippocampectomy (SAH). The approach was transylvian, as described by Yasargil et al. (11). The hippocampus and the parahippocampal gyrus were usually resected en bloc, and the resection reached at least the middle cerebral peduncle at the widest diameter. The amygdala was resected totally, except the central medial part, in 11 left (L)- and 11 right (R)-sided resections. Seizure outcome was assessed according to Engel's classification, and it was favorable, with 77% seizure-free patients 6 months after surgery (12).

TABLE 1. *Clinical and demographic data of the patient groups and control subjects*

	LTLE (n = 11)	RTLE (n = 11)	C (n = 9)
Male/female	4 M/7 F	6 M/5 F	5 M/4 F
Age (yr)	26.18 (6.83)	28.63 (8.22)	25.33 (4.44)
Education (yr)	10.16	7.12	9.86
Duration of seizures (yr)	18.16	14.75	—
Full-Scale IQ	94.3 (17.67)	95.5 (12.76)	98.0 (10.83)
Outcome after surgery	Class I, 8 Class II, 1 Class III, 2	Class I, 9 Class II, 2	—

LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; C, control subjects.

Patient groups were compared with control group by using the previously mentioned parameters by two-tailed *t* test, and no significant difference was found.

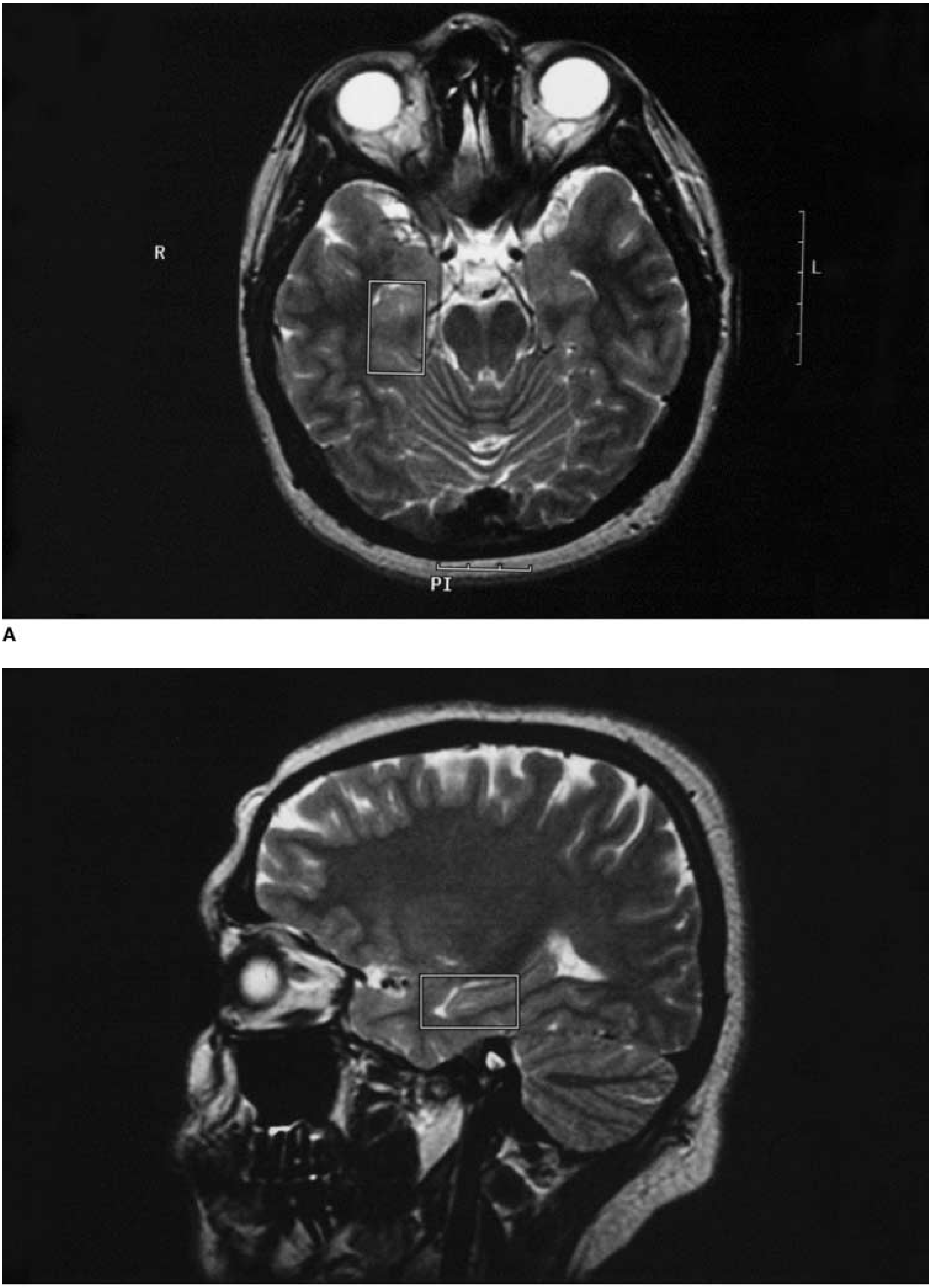
The control group consisted of nine healthy volunteers who had both MRS and neuropsychometric evaluations with the same protocol used for patients. Groups did not differ in clinical characteristics (Table 1), and these parameters were not taken into account during the statistical analysis.

Assessment of memory functions

Our standard neuropsychological examination consists of hand preference, attention, executive functions, language, visuospatial perception, and memory tests for pre- and postsurgical evaluation. The results of verbal learning and memory [evaluated with Rey Auditory verbal learning test (AVLT) adapted to Turkish (13)] and nonverbal learning and memory [evaluated with Wechsler memory scale (WMS) visual reproduction subtest (14)] tests were analyzed.

Magnetic resonance spectroscopy

Examinations were performed with single-voxel ^{1}H MRS, and NAA/Cho+Cr ratios in temporal lobes were calculated before and 6 months after the SAH operation. Single-voxel proton spectroscopy studies were obtained by using a 1.5-T clinical scanner with PROBE software (GE, Milwaukee, WI, U.S.A.), which permitted automated shimming, water suppression, and data processing. T_2-weighted axial images, which were obtained parallel along the long axis of the hippocampus, were used to locate the voxel in the mesiotemporal lobe, including the head, body, and tail of the hippocampus proper, while excluding neighboring tissues as much as possible to minimize voxel contamination. Average voxel size was ~9 cc. The width, length, and thickness of the voxels were 2, 3, and 1.5 cm, respectively (Figs. 1A and B). In all patients, long-TE spectra were obtained by using point-resolved spectroscopy (PRESS; TR, 1,500 ms; TE, 144 ms; 96



A

B

FIG. 1. **A:** T_2W axial image. **B:** T_2W sagittal image showing the placement of voxel at the position of hippocampus.

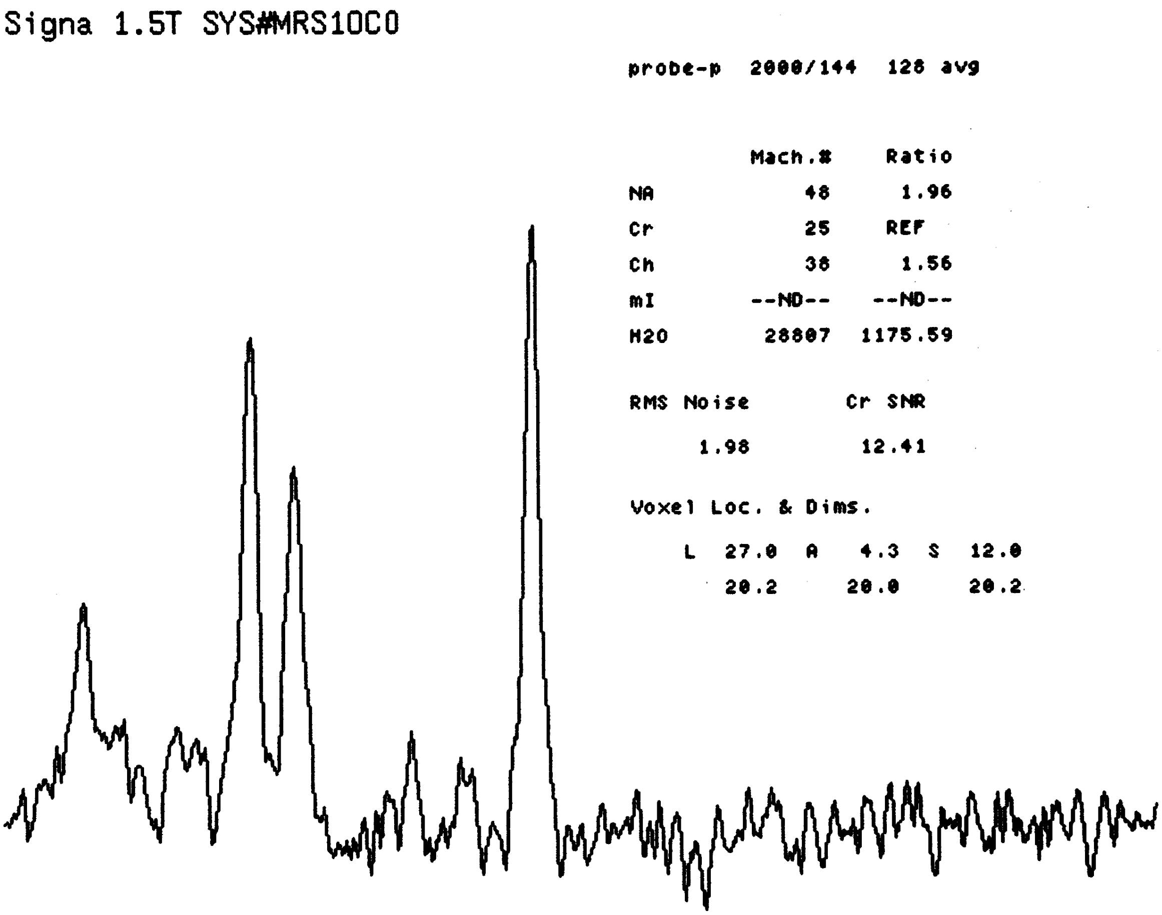


FIG. 2. ^{1}H magnetic resonance spectra obtained from the hippocampal area from a normal control.

acquisitions). After immediate automatic processing of the raw data, spectra were evaluated qualitatively. Then NAA/Cr, Cho/Cr, and NAA/Cr+Cho ratios were calculated by square measurement under the peaks at 2, 3, and 3.2 ppm, respectively (Fig. 2).

Statistical analyses

To search for the relation between the MRS and the lateralization of TLE; the presurgical NAA/Cho+Cr ratios measured from the affected sides of patient groups were compared with the similar side of normal controls, and the ratios measured from the contralateral (nonaffected) side were again compared with the similar sides of controls (i.e., R side of LTLE with R side of control) by the Mann–Whitney *U* test. The presurgical memory test scores were compared with Kruskal–Wallis one-way analysis of variance (ANOVA) in patient groups and normal controls.

Wilcoxon matched-pairs test was performed to demonstrate the change in cognitive performance within the group, analyzing pre- and postsurgical memory scores of R and LTLE patients.

Pearson correlation analysis was used to evaluate the correlation between MRS values and material-specific memory functions. In the patient group, NAA/Cho+Cr ratios obtained from both sides before surgery and from the nonaffected side after surgery were compared with verbal and nonverbal pre- and postsurgical scores by the Pearson correlation method. This analysis was applied for both patient groups and also for control group separately.

Parameters used for memory assessment in this study were total learning, delayed recall, and recognition for verbal memory and immediate recall and delayed recall for nonverbal memory.

Individual changes in memory performance

The test–retest data of 11 patients with TLE with HS waiting for the surgery was used to indicate the significance of individual postoperative changes. The mean retest interval was 23 months (SD, 8.25); mean age, 21.64 years (SD, 5.64 years). The 90% confidence interval for the before and after difference scores were calculated according to the previous proposals in the literature (15,16), based on retest reliabilities of the group waiting for the surgery and correcting for the retest effects. In the patient group who had surgery, the individual memory changes were classified as being worse, improved, or unchanged (if they were within this confidence interval).

Multiple-regression analysis was performed to see whether [1]H MRS values measured before surgery can predict the possible change in memory scores obtained after surgery. Postoperative memory scores were taken as dependent; preoperative [1]H MRS values measured from both L and R hippocampal regions, age, gender, seizure outcome, side of surgery, and preoperative memory scores were taken as independent variables. The patient group was not split into two groups as L and R; all values were calculated altogether instead.

RESULTS

Analyses of [1]H MRS values

NAA/Cho+Cr values before and after surgery are shown in Table 2. When [1]H MRS scores of the same side of control subjects were compared with those of the operated-on side of patients by using the Mann–Whitney *U* test, the scores were significantly lower in the patient group for both R and LTLE ($z = -3.0516$, $p = 0.0023$; and $z = -1.9790$, $p = 0.0478$, respectively). But when the ratios of the contralateral (nonaffected) sides of patient groups were compared with the same sides of controls (i.e., R side of LTLE with right side of control) by the same statistical analyses, no statistically significant difference was detected for L side of RTLE and L side of control ($z = -0.419$, $p = 0.6752$) and for R side of LTLE and R side of control ($z = -1.1066$, $p = 0.2685$).

Analyses of memory tests

Verbal and nonverbal memory test scores of control and patient groups before and 6 months after surgery are shown in Table 3. The comparison of presurgical (verbal and nonverbal) memory scores of patients with normal controls by Kruskal–Wallis one-way ANOVA revealed a statistically significant difference in only the total learning subtest of the AVLT ($\chi^2 = 14.07$, $p = 0.0009$). Multiple comparison analyses by Dunn test showed lower test scores in both left and right TLE patients compared with normal controls ($p < 0.01$).

TABLE 2. *MRS values of control group and patients before and 6 months after surgery*

	NAA/Cho+Cr			
	Before surgery		After surgery	
Groups	Left	Right	Left	Right
LTLE	0.62 (0.21)[a]	0.72 (0.13)	Not measured	0.73 (0.10)
RTLE	0.73 (0.11)	0.54 (0.08)[b]	0.68 (0.10)	Not measured
C	0.73 (0.09)	0.68 (0.07)		

MRS, magnetic resonance spectroscopy; L, left; R, right; TLE, temporal lobe epilepsy; C, control subjects; NAA, *N*-acetylacetate; Cho, choline; Cr, creatinine.

Values expressed as mean (SD) and show significant difference compared with NAA/Cho+Cr values of same side of controls with Mann–Whitney U test.

[a] $p = 0.0478$; $z = -1.9790$.

[b] $p = 0.0023$; $z = -3.0516$, 5.

To search for the changes in memory performance within the groups, pre- and postsurgical test scores were analyzed with the Wilcoxon matched-pairs test, and a significant worsening was detected only in AVLT total learning scores of left TLE patients after surgery ($z = -2.1915$, $p = 0.0284$).

Individual memory changes after surgery are demonstrated in Table 4. Both verbal and nonverbal memory were impaired in all patients, whereas only 10% of RTLE patients showed some improvement in both verbal and nonverbal memory, and the unchanged group again consisted of 10–20% of both the R and LTLE group verbal memory.

Relation between [1]H MRS and memory scores

The correlations between the memory scores and values of control subjects and patients before and after SAH were analyzed. Neither right nor left NAA/Cho+Cr ratios showed any correlation with verbal or nonverbal memory parameters in the control group.

Right TLE group

Presurgical right-side NAA/Cho+Cr scores were found to be significantly correlated with presurgical AVLT delayed recall ($r = 0.74$, $p = 0.015$) and AVLT recognition ($r = -0.72$, $p = 0.018$) and postsurgical AVLT total learning scores ($r = 0.81$, $p = 0.008$). Neither pre- nor postsurgical contralateral (left) side NAA/Cho+Cr scores revealed any significant correlation with pre- and postsurgical memory parameters.

Left TLE group

Presurgical left-side NAA/Cho+Cr scores were found to be significantly correlated with AVLT delayed recall ($r = 0.65$, $p = 0.041$) and AVLT recognition ($r = -0.74$, $p = 0.015$) and postsurgical AVLT recognition ($r = -0.67$, $p = 0.034$) values. Neither pre- nor postsurgical contralateral (right) side NAA/Cho+Cr scores revealed any significant correlation with pre- and postsurgical memory parameters.

The relation between presurgical MRS values and memory test scores is demonstrated in Table 5, and between the presurgical MRS values and postsurgical memory test scores in Table 6. No significant finding was related to presurgical MRS ratios and memory performance.

Prediction of the change in memory scores by using the preoperative [1]H MRS values after surgery

The significant findings of regression analyses are demonstrated in Table 7. For nonverbal memory parameters (i.e., immediate and delayed recall), no relation was found in both sided [1]H MRS values measured before surgery in terms of prediction. However, for verbal memory total learning scores both preoperative right and left [1]HMRS values were demonstrated to be predictive for a change in within 5% confidence interval. When

TABLE 3. *Memory test scores of control group and patients before and 6 months after surgery*

Memory tests		LTLE Presurgical	LTLE Postsurgical	RTLE Presurgical	RTLE Postsurgical	Control
AVLT	Total Learning	99.70 (25.23)[a]	83.80 (19.03)[b]	103.90 (22.18)[a]	104.22 (23.54)	132.33 (7.91)
	Delayed Recall	9.10 (3.38)	8.20 (3.05)	10.70 (3.37)	10.90 (3.35)	12.78 (1.64)
	Recognition	5.30 (3.06)	5.20 (2.15)	3.20 (1.99)	3.80 (2.74)	2.86 (1.21)
WMS	Immediate Recall	11.00 (3.80)	10.20 (3.39)	9.90 (3.48)	10.30 (3.43)	11.78 (4.09)
	Delayed Recall	9.60 (4.03)	7.90 (3.38)	8.50 (3.63)	8.60 (3.78)	11.44 (4.28)

L, left; R, right; TLE, temporal lobe epilepsy; C, control subjects; AVLT, Auditory verbal learning test; WMS, Wechsler memory scale.
[a]Values showing a significant difference compared with controls by Kruskal–Wallis one-way analysis of variance ($p < 0.01$).
[b]Values showing significant worsening after surgery compared with the presurgical same test scores by Wilcoxon matched pairs ($z = -2.1915$; $p = 0.0284$).

recognition was taken into consideration it was found to be related to the left preoperative MRS values. In another words, preoperative right ^{1}HMRS values if they were high and preoperative left ^{1}HMRS values, if they were low, were found to be predictive for a decrease in verbal learning scores; whereas preoperative left ^{1}H MRS values, if they were low, were found to be predictive for a decrease in verbal recognition scores after surgery.

Conversely, left-sided SAH also was found to be predictive of a decrease in total learning scores obtained after surgery. The analyses also indicated that the preoperative total learning and recognition scores of verbal memory and delayed recall scores of nonverbal memory may be predictive of the postoperative scores of the same tests.

DISCUSSION

In this study, the memory test and ^{1}H MRS scores obtained before and after the surgery were evaluated in patients with MTLE-HS. Significant differences were detected only in verbal memory total learning scores between patients (both R and LTLE) and normal controls after statistical analysis, although the results demonstrated marked differences in other parameters (Table 3). Verbal memory scores of the LTLE group were found to be lower than the verbal memory scores of control and RTLE groups. Similarly, nonverbal memory scores of the RLT group were lower than the nonverbal memory scores of control and LTLE groups. Verbal and nonverbal memory scores of RTLE patients did not differ after surgery; however, a decrease at verbal memory scores was detected in LTLE patients. This profile is consistent with the studies reporting disorders in material-specific memory in patients with MTLE before and after surgery (17–24).

When NAA/Cho+Cr values are taken into account, the comparison of values demonstrated lower scores both in R and LTLE patients when compared with the same side of the control group (Table 2). This finding is also in parallel with the literature, and it can be used as an evidence for MRS being a reliable noninvasive technique to determine the pathological side in MTLE-HS (3,25–27).

The results of our presurgical analysis demonstrated that both right-sided NAA/Cho+Cr values of RTLE and left-sided NAA/Cho+Cr values of LTLE patients were correlated only with verbal memory scores. The analysis of presurgical NAA/Cho+Cr values (right side for RTLE and left side for LTLE) and postsurgical memory scores revealed a significant relation with only some verbal memory scores, as indicated in Table 6.

In this study, statistical analysis did not demonstrate any significance for nonverbal memory scores for both TLE groups on either side (Tables 5 and 6), which showed lack of marked correlation between material specificity and ^{1}H MRS findings. Although a correlation between the material-specific memory and ^{1}H MRS values was claimed to be demonstrated in the previous studies, as

TABLE 4. *Individual changes in memory after left and right TLE*

	Loss Left TLE	Loss Right TLE	Unchanged Left TLE	Unchanged Right TLE	Gain Left TLE	Gain Right TLE
AVLT						
Learning	90	78	10	11	–	11
Delayed recall	80	80	20	20	–	–
Recognition	90	90	10	10	–	–
WMS						
Immediate recall	90	90	10	–	–	10
Delayed recall	100	100	–	–	–	–

The data show the percentage of patients in the left and right selective amygdalohippocampectomy (SAH) groups showing a loss, no change, or a gain in their postoperative performance compared with their preoperative performance.
TLE, temporal lobe epilepsy; AVLT, Auditory verbal learning test; WMS, Wechsler memory scale.

TABLE 5. *The relation between the presurgical memory test scores and presurgical magnetic resonance spectroscopy values*

		MRS values (NAA/Cho+Cr)			
		RTLE group		LTLE group	
Memory tests		Right	Left	Right	Left
AVLT	Total Learning	NS	NS	NS	NS
	Delayed Recall	p = 0.015 *r* = 0.74	NS	NS	p = 0.041 *r* = 0.65
	Recognition	p = 0.018 *r* = –0.72	NS	NS	p = 0.015 *r* = –0.74
WMS	Immediate Recall	NS	NS	NS	NS
	Delayed Recall	NS	NS	NS	NS

Pearson correlation analyses were performed.
LTLE, left temporal lobe epilepsy; RTLE, right temporal lobe epilepsy; NS, not significant; NAA, N-acetylacetate; Cho, choline; Cr, creatinine; AVLT, Auditory verbal learning test; WMS, Wechsler memory scale.

discussed later, differences between the memory tests performed and interpretation of the results might account for this contradiction.

Kikuchi et al. (10) performed a wide variety of tests and showed a correlation between right-sided NAA/Cho+Cr values and nonverbal memory and left-sided NAA/Cho+Cr values and verbal memory before surgery. Although other nonverbal memory tests were correlated, the visuo-reproduction subtest of WMS did not reveal any relation with the right-sided ^{1}H MRS; authors claimed that this test was not sensitive enough for nonverbal memory. However, Namer et al. (9) failed to demonstrate any correlation when nonverbal and verbal test scores and ^{1}H MRS values were taken separately, whereas they showed a significant correlation between verbal tests and left-sided and nonverbal tests and right-sided ^{1}H MRS values if T_2 relaxation time measurements were added and analyzed altogether (9).

In another study in which episodic verbal memory and visual reproduction subtests were used for WMS, only left-sided ^{1}H-MRS values were found to be correlated with the WMS episodic verbal memory subtest. No correlation was detected between right MRS scores and the WMS visual reproduction subtest (8). All of these studies confirm a correlation between material-specific memory and ^{1}H MRS values related to left-sided MRS values and verbal memory, similar to our findings. However, the correlation between nonverbal memory and right-sided ^{1}H MRS values is not clear enough. This situation was explained by the use of some test materials (i.e., WMS visual reproduction subtest for both verbal and nonverbal coding). Therefore some authors advised increasing the number of nonverbal memory tests (8,10). To overcome the same problem, Namer et al. (9) added another parameter (i.e., T_2 relaxation time measurements).

The involvement of the other regions in nonverbal memory like parahippocampal gyrus, which was not included in the ^{1}H MRS measurements, may be another explanation for the situation (8). We find this hypothesis more plausible.

Memory is a dynamic function and operates within a network system with participation of several anatomic brain structures, including the hippocampus (19,28). This operational system requires the involvement of both hemispheres where laterality or material specificity are known features. Therefore MTL resection will certainly have complex consequences on the memory network that cannot be easily predicted and explained. For that reason, one should not expect to find a clear relation between MRS measurements, results of a test reflecting the

TABLE 6. *Relation between the postsurgical memory test scores and presurgical magnetic resonance spectroscopy values*

		MRS values (NAA/Cho+Cr)			
		RTLE group		LTLE group	
Memory tests		Right	Left	Right	Left
AVLT	Total Learning	p = 0.008 *r* = 0.81	NS	NS	NS
	Delayed Recall	NS	NS	NS	NS
	Recognition	NS	NS	NS	p = 0.034 *r* = −0.67
WMS	Immediate Recall		NS	NS	
	Delayed Recall	NS	NS	NS	NS

Pearson correlation analyses were performed.
L, left; R, right; TLE, temporal lobe epilepsy; C, control subjects; NAA, *N*-acetylacetate; Cho, choline; Cr, creatinine; AVLT, Auditory verbal learning test; WMS, Wechsler memory scale.

TABLE 7. *Predictors of postoperative memory changes*

Dependent variable	Analysis of variance	Predictors	*t*
AVLT			
Total Learning	$F = 8.74$	Preop L MRS	2.092[a]
	$R^2 = 0.813$	Preop R MRS	−2.469[a]
	Sign. 0.0008	Side of operation	− 4.271[b]
		Preop level	5.845[b]
Recognition	$F = 26.02$	Preop L MRS	2.306[a]
	$R^2 = 0.923$	Preop level	11.462[b]
	Sign. 0.0000		
WMS			
Delayed recall	$F = 14.98$	Preop level	6.554[b]
	$R^2 = 0.897$		
	Sign. 0.02		

Pearson correlation analyses were performed.

L, left; R, right; TLE, temporal lobe epilepsy; C, control subjects; NAA, *N*-acetylacetate; Cho, choline; Cr, creatinine; AVLT, Auditory verbal learning test; WMS, Wechsler memory scale.

[a] $p \leq 0.05$.

[b] $p < 0.01$.

cellular metabolism and gliosis in a limited brain region, and memory tests, which evaluate the overall performance of the memory network.

However, although ¹H MRS scores do not demonstrate a direct and close relation to material-specific memory in general, according to our study preoperative, ¹H MRS values can be used for prediction of verbal memory, at least partially, after surgery. The results showed that if NAA/Cho+Cr values obtained before surgery were high at the right and low at the left hippocampus, this may predict a deterioration in verbal learning scores after surgery.

Accordingly, the group that is expected to get worse, in terms of verbal memory after surgery, will be those with high-right and low-left MRS values obtained before surgery. Likewise, low-left MRS values may also be predictive of impairment in recognition after surgery. Incisa della Rocchetta et al. (29) demonstrated an impairment in verbal memory after right-sided temporal lobectomy in patients in whom bilateral abnormality was detected by MRS and T_2 relaxometry studies but not MRI alone before surgery. However, we showed left-sided presurgical MRS abnormality to be an independent predictor for verbal memory after the resection, regardless of the side, by using a different measurement (MRS) in this study. Other studies performed with different techniques revealed somewhat conflicting results indicating a decline in verbal memory after left-sided surgery if an already reserved capacity at the left hippocampus was demonstrated by normal positron emission tomography (PET) and MR volumetry studies (30,31). Although these results seem to be contradictory to ours, one must take into account that a different modality of investigation (MRS) was used to search for the hippocampal function in our study. Conversely, evaluation of whole memory network through a restricted window (i.e., hippocampus) by any tools will not be adequate to generate a precise determination.

In conclusion; ¹H MRS may be taken as a useful adjunctive tool to determine lateralization in patients with MTLE before the surgery. Furthermore, although no direct relation seems to exist between the MRS values and material-specific memory scores, presurgical MRS also can be used as a clinical parameter for the prediction of possible deterioration in verbal memory after surgery.

Obviously, the replication of similar studies in larger patient populations will provide more information about the situation; however, the concept of a network for the memory functions and the limitations of MRS as a technique must be taken into consideration while interpreting the results.

Acknowledgment: We thank Ömer Uysal and to Burç Ülengin for help in statistical analyses.

REFERENCES

1. Blümcke I, Beck H, Lie AA, et al. Molecular neuropathology of human mesial temporal lobe epilepsy. *Epilepsy Res* 1999;36:205–23.
2. Engel J Jr, Williamson PD, Wieser HG. Mesial temporal lobe epilepsy. In: Engel J Jr, Pedley T, eds. *Epilepsy: a comprehensive textbook*. Philadelphia: Lippincott Raven, 1998:2417.
3. Kuzniecky R, Hugg JW, Hetherington H, et al. Relative utility of 1H spectroscopic imaging and hippocampal volumetry in the lateralization of mesial temporal lobe epilepsy. *Neurology* 1998;51:66–71.
4. Gadian DG, Isaacs EB, Cross HJ, et al. Lateralization of brain function in childhood revealed by magnetic resonance spectroscopy. *Neurology* 1996;46:974–7.
5. Cendes F, Andermann F, Dubeau F, et al. Normalization of neuronal metabolic dysfunction after surgery for temporal lobe epilepsy: evidence for proton MR spectroscopic imaging. *Neurology* 1997;49:1525–33.
6. Hugg JW, Kuzniecky RI, Gilliam FG, et al. Normalization of contralateral metabolic function following temporal lobectomy demonstrated by 1H magnetic resonance spectroscopic imaging. *Ann Neurol* 1996;40:236–9.
7. Veermathen P, Ende G, Laxer KD, et al. Temporal lobectomy for epilepsy: recovery of the contralateral hippocampus measured by 1H MRS. *Neurology* 2002;59:633–6.
8. Martin RC, Sawrie S, Hugg J, et al. Cognitive correlates of H1MRSI-detected hippocampal abnormalities in temporal lobe epilepsy. *Neurology* 1999;53:2052–8.
9. Namer IJ, Bolo NR, Nguyen VH, et al. Combined measurements of hippocampal *N*-acetyl aspartate and T2 relaxation time in the evaluation of mesial temporal lobe epilepsy: correlation with clinical severity and memory performances. *Epilepsia* 1999;40:1424–32.
10. Kikuchi S, Kubota F, Hattori S, et al. A study of the relationship between metabolism using 1H-MRS and function using several neuropsychological tests in temporal lobe epilepsy. *Seizure* 2001;10:188–93.
11. Yaşargil MG, Teddy PJ, Roth P. Selective amygdalo-hippocampectomy: operative anatomy and surgical technique. In: Symon L, Brihaye J, Guidetti B, et al., eds. *Advances and technical standards in neurosurgery*. Vienna: Springer Verlag, 1985:93–123.
12. Engel J Jr. Outcome with respect to epileptic seizures. In: Engel J Jr, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1993:553–71.
13. Öktem Ö. Sözel Bellek Süreçleri Testi (SBST). *Nöropsikiyatri Arşivi* 1992;29:196–206.

14. Karakaş S, Eski R, Başar E. Türk kültürü için standardizasyonu yapilmiş nöropsikolojik testler topluluğu. Istanbul: 32. Ulusal nöroloji Kongre Kitabi, 1996.
15. Hermann BP, Seidenberg M, Schonfeld J, et al. Empirical techniques for determining the reliability, magnitude, and pattern of neuropsychological change after epilepsy surgery. *Epilepsia* 1996;37:942–50.
16. Gleissner U, Helmsteadter C, Schramm J, et al. Memory outcome after selective amygdalohippocampectomy: a study in 140 patients with temporal lobe epilepsy. *Epilepsia* 2002;43:87–95.
17. Rausch R. Psychological evaluation. In: Engel J Jr, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:181–96.
18. Delaney RC, Alexander J, Rosen AJ, et al. Memory function in focal epilepsy: a comparison of nonsurgical, unilateral temporal lobe and frontal lobe samples. *Cortex* 1980;16:103–17.
19. Baxendale SA, van Paesschen W, Thompson PJ, et al. The relationship between quantitative MRI and neuropsychological functioning in temporal lobe epilepsy. *Epilepsia* 1998;39:158–66.
20. Breier JI, Plenger PM, Wheless JW, et al. Memory tests distinguish between patients with focal temporal and extratemporal lobe epilepsy. *Epilepsia* 1996;37:165–70.
21. Herman BP, Seidenberg M, Haltiner A, et al. Relationship of age at onset, chronologic age and adequacy of preoperative performance to verbal memory change after anterior temporal lobectomy. *Epilepsia* 1995;36:137–45.
22. Helmstaedter C, Elger CE. Cognitive consequences of two-thirds anterior temporal lobectomy on verbal memory in 144 patients: a three month follow-up study. *Epilepsia* 1996;37:171–80.
23. Jones-Gotman M. Commentary: psychological evaluation: testing hippocampal function. In: Engel J Jr, ed. *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:68–76.
24. Walton NH, Goodsman C, McCarter R, et al. An analysis of neuropsychological change scores following selective temporal lobe resection of the non-dominant temporal lobe. *Seizure* 1999;8:241–5.
25. Connelly A, Paesschen W, Porter DA, et al. Proton magnetic resonance spectroscopy in MRI-negative temporal lobe epilepsy. *Neurology* 1998;51:61–6.
26. Achten E, Boon P, Van De Kerckhove T, et al. Value of single-voxel proton MR spectroscopy in temporal lobe epilepsy. *Am J Neuroradiol AJNR* 1997;18:1131–9.
27. Cendes F, Caramanos Z, Andermann F, et al. Proton magnetic resonance spectroscopic imaging and magnetic resonance imaging volumetry in the lateralization of temporal lobe epilepsy: a series of 100 patients. *Ann Neurol* 1997;42:737–46.
28. Mesulam MM. Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Ann Neurol* 1990;28:597–613.
29. Incisa della Rocchetta A, Gadian DG, et al. Verbal memory impairment after right temporal lobe surgery: role of contralateral damage as revealed by 1H magnetic resonance spectroscopy and T2 relaxometry. *Neurology* 1995;45:797–802.
30. Griffith HR, Perlman SB, Woodard AR, et al. Preoperative FDG-PET temporal lobe hypometabolism and verbal memory after temporal lobectomy. *Neurology* 2000;14:1161–5.
31. Chelune GJ. Hippocampal adequacy versus functional reserve: predicting memory functions following temporal lobectomy. *Arch Clin Neuropsychol* 1995;10:413–32.