MEMORY DEFICITS ASSOCIATED WITH ^{1}H-MRS HIPPOCAMPAL ABNORMALITIES IN PATIENTS WITH NORMAL MRI: A PRELIMINARY REPORT

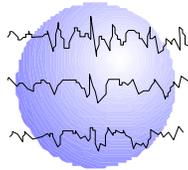Gail L. Risse, PhD

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REVISED ABSTRACT

RATIONALE: Previous research has described cognitive impairments associated with metabolic changes in the hippocampus detected with ^{1}H-MRS. These defects are also presumed to correspond to structural change in the mesial temporal lobes visible on MRI. This study examined the possibility that ^{1}H-MRS may be associated with neuropsychological deficits in the absence of positive findings on MRI.

METHODS: The neuropsychological profiles of seven temporal lobe epilepsy patients (5L; 2R) with negative MRI but positive ^{1}H-MRS were reviewed. A total of 11 memory scores derived from the Weschler Memory Scale III, Buschke Verbal Selective Reminding Test, Nonverbal Selective Reminding Test and Rey Osterrieth Complex Figure were compiled for each patient. Scores falling 1 SD or more below the mean for each measure were considered impaired. Scores on measures of general intellectual ability, naming, verbal fluency, judgement and planning, and spatial judgement were also examined using similar performance criteria.

RESULTS: Full scale IQ was within the average range for all seven patients. However, all seven were impaired on one or more of the 11 memory measures (mean number of memory scores in impaired range = 4.3 per patient). Four of the five left temporal patients also demonstrated impaired performance on visual confrontation naming and/or verbal fluency. No other deficits were identified.

CONCLUSION: Metabolic abnormalities in the hippocampus identified on ^{1}H-MRS are associated with impaired memory performance even in the absence of structural change on MRI. The increased sensitivity of ^{1}H-MRS should improve the diagnosis and treatment of patients with temporal lobe epilepsy.

INTRODUCTION
The identification of mesial temporal sclerosis (MTS) in patients with chronic epilepsy, has traditionally been based on left-right asymmetry or decreased volume of the hippocampus, apparent on MRI. The relationship between MTS and temporal lobe epilepsy and between MTS and material specific memory deficits has been well established. In particular, verbal memory impairment has consistently been reported with unilateral hippocampal atrophy in the dominant hemisphere.

More recently the presence of MTS has been suggested based on metabolic function of the hippocampus using proton magnetic resonance spectroscopy (^{1}H-MRS). In this procedure neuronal loss is inferred by a decrease in the ratio of N-acetylaspartate (NAA) to choline (CHO) and creatine. Previous studies have reported neuropsychological impairment associated with abnormal 1H-MRS of the mesial temporal region. However, for most of these patients, it is assumed that the MRI is also positive for structural change. This study examined the possibility that 1H-MRS may be associated with neuropsychological deficits in the absence of positive findings of MRI.

METHODS
The subjects were seven temporal lobe epilepsy patients who underwent diagnostic inpatient evaluation including video EEG monitoring, MRI of the brain, ^{1}H-MRS of the temporal lobes and comprehensive neuropsychological assessment. MRI was performed with a 1.5 Tesla GE system. The imaging sequence through the temporal lobes incorporated flair coronal 5mm interleaved cuts, fast T2 coronal oblique cuts 3/0.5mm skip and SPGR 3D volume 1.6mm images. Single proton MR spectrum was obtained using a single voxel PRESS TE 35 with voxel volume of 2x2x1cm. None of the patients had undergone epilepsy surgery prior to this evaluation. Patients were selected for inclusion in the study only if their MRIs were negative for temporal lobe abnormality while ^{1}H-MRS was positive for unilateral MTS as indicated by a decrease in N-acetylaspartate to choline and creatine (NAA/Cho+Cr) ratio. Patient characteristics are listed in Table 1.

For purposes of this study the neuropsychological measures extracted from the comprehensive battery included IQ, 11 verbal and nonverbal memory measures, and selected tests of other specific verbal and nonverbal functions. Six of the seven patients were tested on all 11 memory measures. One patient (a 12-year old boy) could not be assessed using the WMS III due to age and was therefore tested on a total of 6 measures. This was the only pediatric patient included in the sample.

Performance on each individual test was considered impaired if a patient's score fell more than one standard deviation below the mean. For measures without standard score equivalents, conservative clinical criteria were used to determine impairment including a delayed recall raw score below 14 on the Rey Osterrieth Complex Figure and a total raw score below 50 on the Boston Naming Test.

RESULTS

Table 2 presents the number of memory measures on which performance was impaired for each of the patients evaluated. Every patient with MTS identified by ^{1}H-MRS alone was impaired on at least one memory test. Note that none of these patients had a full scale IQ below the average range. Yet six of the seven had three or more impaired memory scores, and four of the seven had at least four impaired scores.

Figures 1 and 2 illustrate the number of left and right temporal patients impaired on each individual memory measure. The generally higher incidence of impaired performance on verbal memory tasks reflects in part the disproportionate number of left temporal patients in the sample. In contrast to the high incidence of memory impairment, the number of patients impaired on other cognitive measures is limited and reflects specific naming and verbal fluency deficits in some of the left temporal cases (Figure 3).

Group performance for the five left temporal patients is presented in Table 3. The group mean clearly falls in the impaired range for verbal subtests of the WMS III including the delayed recall conditions of Logical Memory and Paired Associate Learning and the delayed recall condition of the Verbal Selective Reminding Test.

CONCLUSIONS

- Metabolic abnormalities in the hippocampus identified on ^{1}H-MRS are associated with impaired memory performance even in the absence of structural change visible on MRI.

- Patients with left (dominant) MTS identified by ^{1}H-MRS alone demonstrate neuropsychological profiles similar to other chronic left temporal lobe seizure patients.
- The increased sensitivity of ^{1}H-MRS suggests this test may be especially useful when the MRI fails to detect structural change in the hippocampus in patients with EEG data and neuropsychological test findings suggestive of temporal lobe abnormality.

Table 1   Patient Characteristics

N	7 Epilepsy patients
MRI	No evidence of MTS in 7/7 patients
^{1}H-MRS	Evidence of unilateral MTS in 7/7 patients
Side of SeizureOnset	5 L, 2 R
Sex	6 M, 1 F
	Mean (s.d.)
Age	29.4 (11.9)
Age at Onset	15.8 (4.8)
Education	13 (3.5)
FSIQ	97.3 (12)

Table 2   Frequency of Impaired Memory Performance

Pt. #	Side of ^{1}H-MRS Abnormality	FSIQ	Number of memory measures impaired
1	L	89	7/11
2	L	112	3/6
3	R	113	4/11
4	L	85	6/11
5	R	85	3/11
6	L	89	6/11
7	L	108	1/11

Table 3   Memory Performance of Left Temporal Patients (n=5)

	Group Mean	s.d.	Score Type
WMS III			
Logical Memory Delay	6.0	(2.9)	Scaled Score
Paired Associates Delay	5.2	(3.6)	Scaled Score
Faces Delay	8.2	(2.5)	Scaled Score
Family Pictures Delay	9.0	(3.2)	Scaled Score
General Memory	80.0	(12.7)	Standard Score
Verbal Selective Reminding			
CLTR	78.2	(14.2)	Standard Score
Best Recall	93.4	(9.7)	% Correct
Delayed Recall	53.4	(20.0)	% Correct
Nonverbal Selective Reminding			
CTRL	94.6	(18.9)	Standard Score
Delayed Recall	81.6	(18.5)	% Correct
Rey-Osterrieth Complex Figure			
Delayed Recall	13.8	(3.4)	Raw Score

Figure 1 — Verbal Memory

Figure 2 — Nonverbal Memory

Figure 3 — Cognitive Measures