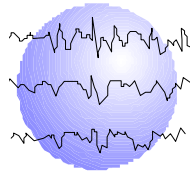


¹H-MRS MESIAL TEMPORAL LOBE ABNORMALITIES AND NEUROPSYCHOLOGICAL FUNCTION IN EPILEPSY PATIENTS

Robert C. Doss, PsyD
John R. Gates, MD
David B. Kispert, MD
Britt Carlson-Emerton, BA



This paper has been prepared specifically for:

American Epilepsy Society Annual Meeting
New Orleans, Louisiana
December 3 - 8, 2004

Please consider this information to be preliminary findings.

Minnesota Epilepsy Group, P.A.[®]
225 Smith Avenue N., Suite 201
St. Paul, MN 55102
Phone: (651) 241-5290
Fax: (651) 241-5248

REVISED ABSTRACT

RATIONALE: Certain neuronal metabolic markers (e.g., NAA & Cr) measured by ¹H magnetic resonance spectroscopy (MRS) have been shown to be highly correlated with EEG abnormalities and degree of atrophy in the brain. A few studies have shown a relationship between MRS brain abnormalities and cognitive performance. This study sought to evaluate the relationship between mesial temporal functional abnormality as measured by MRS and neuropsychological test performance. We hypothesize that epilepsy patients with MRS hippocampal abnormalities will demonstrate worse neuropsychological performance than patients without MRS abnormalities. We further predict that memory function will be disproportionately involved.

METHODS: The sample consisted of 47 epilepsy patients who received both magnetic resonance imaging (MRI) and MRS under an epilepsy imaging protocol. All imaging data were reviewed and interpreted by a neuroradiologist. The region of interest for MRS was the hippocampus on both sides of the brain. All patients were known to, or suspected of having localization-related epilepsy of the temporal lobe. Thirty-five patients showed no abnormality on MRI or MRS (-MRI/-MRS) and 12 had a MRS temporal lobe abnormality (-MRI/+MRS) in the context of a normal MRI. The percentage of patients with left, right, and bilateral MRS abnormality was 42%, 42%, and 16%, respectively. The neuropsychological battery included measures of global cognitive ability, attention-concentration, learning/memory, executive function, speech/language, and information processing speed. The two groups did not differ significantly on education, age of seizure onset, seizure duration, or medications. There were significant differences (both $p < .05$) for age and gender with the -MRI/-MRS group being younger and having a greater proportion of females (69% vs. 33%).

RESULTS: Descriptive statistics revealed a clear trend for the -MRI/+MRS group to perform worse than the -MRI/-MRS group on most measures. Univariate statistical analyses showed the -MRI/+MRS group scored significantly lower than the -MRI/-MRS group on measures of verbal memory ($p < .01$), nonverbal memory ($p < .01$), and general memory ($p < .05$).

CONCLUSION: These data indicate the patients who demonstrate functional mesial temporal lobe abnormality as measured by MRS, perform worse on neuropsychological testing in general, and more specifically on measures of learning/memory than patients without neuroimaging evidence for either a structural or functional lesion. The MRS offers increased sensitivity to detect mesial temporal pathology that is not obvious on structural MRI imaging. The MRS temporal lobe abnormality in isolation appears to correlate with reduced neuropsychological function, particularly learning and memory. The use of MRS in combination with MRI may be valuable in evaluating progression of mesial temporal pathology.

Epilepsia 45 Suppl. 7:173 (Abst. 1.470), 2004

Introduction:

Prior research in epilepsy patients has convincingly demonstrated cognitive impairments associated with metabolic¹⁻² and structural (i.e., gliosis, atrophy)³ changes in the hippocampus as detected by ¹H magnetic resonance spectroscopy (MRS) and conventional MRI, respectively. In MRS neuronal loss or dysfunction is indicated by a decrease in the ratio of N-acetylaspartate (NAA) to choline (CHO) and creatine, which are major metabolites in the brain. These metabolic and structural changes seen in the hippocampus are thought to be pathognomonic for mesial temporal sclerosis (MTS).

A few studies have shown a relationship between MRS brain abnormalities and cognitive performance. This study sought to evaluate the relationship between mesial temporal functional abnormality as measured by MRS and neuropsychological test performance. We hypothesize that epilepsy patients with MRS hippocampal abnormalities will demonstrate worse neuropsychological performance than patients without MRS abnormalities. We further predict that memory function will be disproportionately involved.

Methods:

The subjects were 47 epilepsy patients who underwent diagnostic inpatient evaluation including video-EEG monitoring, MRI of the brain using a thin-cut epilepsy protocol, ¹H-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 2 x 2 x 1cm. All MRI and MRS exams were clinically interpreted by a staff neuroradiologist. All abnormal MRS exams were consistent with MTS.

Thirty-five patients showed no evidence for MTS on MRI or MRS (-MRI/-MRS; see Figure 1) and 12 had a negative MRI but positive MRS (-MRI/+MRS; see Figure 2). None of the patients had undergone epilepsy surgery prior to this evaluation. Patient characteristics are listed in Table 1.

The two groups did not significantly differ with respect to education, age of seizure onset, duration of seizures, and number of antiepileptic drugs. There were significant group differences for age and gender (both $p < .05$).

Results

Table 2 shows the neuropsychological test descriptive statistics by group.

We compared cognitive performance among those subjects with MRS evidence of MTS (-MRI/+MRS) and without (-MRI/-MRS). Table 2 shows that the -MRI/+MRS group scored lower than the -MRI/-MRS group on nearly all cognitive tests but the differences were significant only for learning/memory measures.

Figure 3 illustrates the two groups' performance on specific WAIS-III/WMS-III measures.

Conclusions:

- Patients with functional mesial temporal lobe abnormality by MRS perform worse on neuropsychological testing in general, and more specifically on measures of learning/memory than patients with normal MRI and MRS.
- Metabolic temporal lobe abnormalities suggestive of MTS are associated with greater cognitive morbidity consistent with prior research.
- The MRS offers increased sensitivity to detect mesial temporal pathology that is not obvious on structural MRI imaging.
- The increased sensitivity of MRS suggests this test may be especially useful when the MRI fails to detect structural change in the hippocampus of patients with temporal lobe epilepsy.
- The use of MRS in combination with MRI may be valuable in evaluating progression of mesial temporal pathology.

References:

1. Martin, R.C., Sawrie, S., Hugg, J., Gilliam, F. Faught, E., & Kuzniecky, R. (1999). Cognitive correlates of ¹H MRSI-detected hippocampal abnormalities in temporal lobe epilepsy. *Neurology*, *53*, 2052-2058.
2. Sawrie, S.M., Martin, R.C., Gilliam, F.G., Faught, R.E., Maton, B., Hugg, J.W., Bush, N., Sinclair, K. & Kuzniecky, R.I. (2000). Visual confrontational naming and hippocampal function: A neural network study using quantitative ¹H magnetic resonance spectroscopy. *Brain*, *123*, 770-780.
3. Hermann, B.P., Seidenberg, M., Schoenfeld, J., & Davies, K. (1997). Neuropsychological characteristics of the syndrome of mesial temporal lobe epilepsy. *Archives of Neurology*, *54*, 369-376.

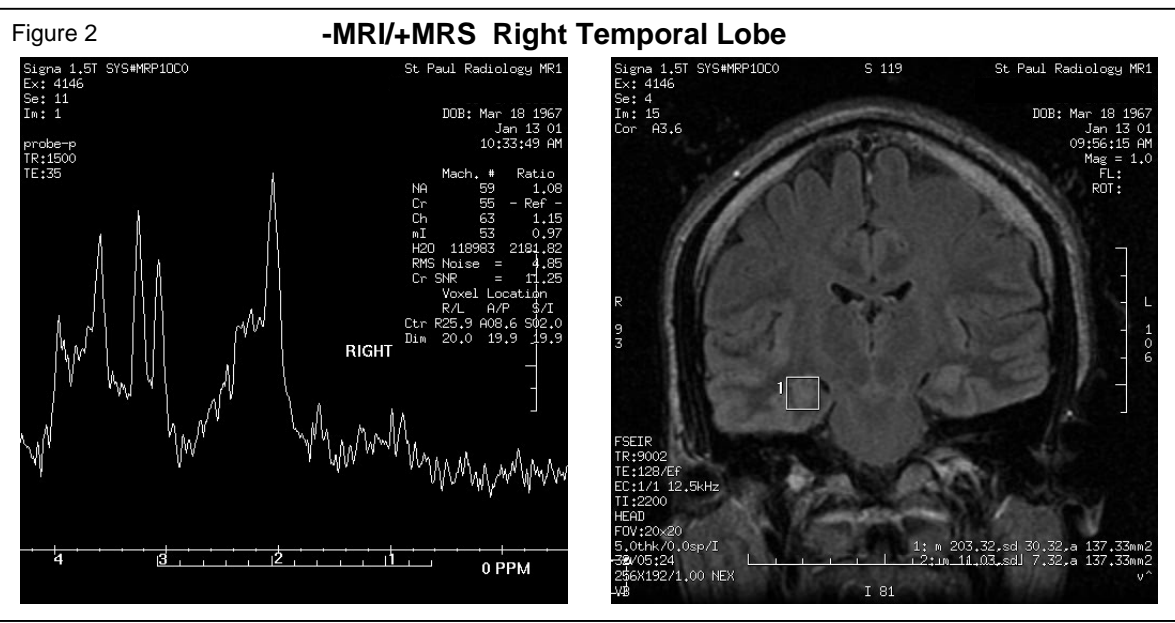
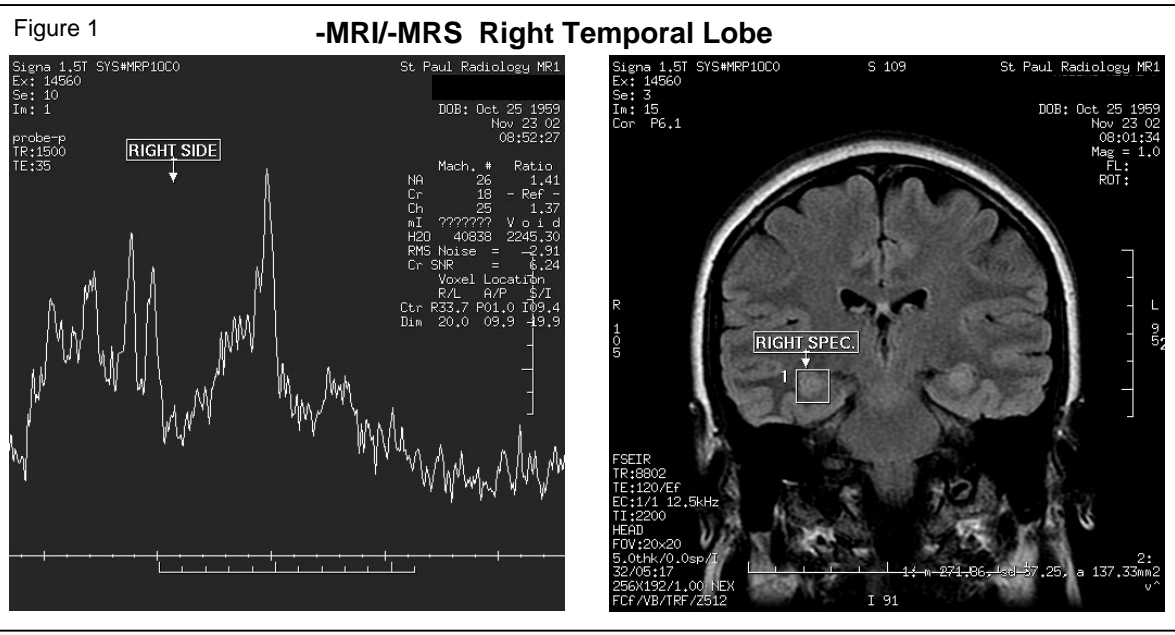


Table 1 Patient Characteristics

	-MRI/-MRS	-MRI/+MRS
<i>n</i>	35	12
MRI/MRS Focus		
Left	0	5
Right	0	5
Bilateral	0	2
Age ¹ *	32.2(10.5)	40.3(10.7)
Gender (% Male)*	31%	67%
Education ¹	13.4(2.9)	14.2(2.7)
Age of Seizure Onset ¹	19.3(13.0)	27.2(13.8)
Duration of Seizures (years) ¹	12.9(11.2)	13.1(13.3)
No of AEDs ¹	1.3(1.0)	.7(.8)

¹ = M(SD)
* *p* < .05

Table 2

Neuropsychological Descriptives

	-MRI/-MRS	-MRI/+MRS
Full Scale IQ (FSIQ) ²	98.5(18.6)	94.2(14.3)
Verbal Comprehension Index (VCI) ²	97.2(17.9)	95.5(15.6)
Perceptual Organization Index (POI) ²	102.0 (17.5)	96.0(14.7)
Processing Speed Index (PSI) ²	97.3(17.9)	91.8(14.8)
Working Memory Index (WMI) ^{1,2}	100.2(17.5)	94.6(12.6)
Wisconsin Card Sort Test Errors ³	27.4(21.0)	32.2(17.7)
Boston Naming Test	49.0(9.6)	50.8(4.9)
RCFT Copy ³	29.9(3.7)	27.1(5.5)
NVSRT LTS ²	94.3(24.3)	89.3(29.0)
Buschke LTS ²	86.15(23.3)	71.6(28.7)
Immediate Memory Index (IMI) ^{2 *}	98.7(14.6)	90.8(9.1)
General Memory Index (GMI) ^{2 *}	102.7(15.5)	91.3(11.0)
Buschke Delayed Recall ^{3 **}	9.8(1.8)	7.6(2.4)
RCFT Immediate Recall ^{3 **}	19.2(6.2)	13.4(6.5)
RCFT Delayed Recall ^{3 *}	17.1(4.8)	13.0(6.2)

¹WMS-III²Standard Score³Raw Score

Figure 3

WAIS-III/WMS-III Performance By Group