# Alteration of functional neuroanatomy of simple object memory in medial temporal lobe epilepsy patients

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Received 28 October 2002; accepted 29 October 2002

DOI: 10.1097/01.wnr.0000047682.08940.1e

Using $H_2{}^{15}O$ PET, we examined the neuroanatomy associated with a simple form of episodic memory in patients with right or left medial temporal lobe epilepsy and normal healthy controls. When line drawings of common objects were memorized and tested after a 30 min delay, no behavioral difference was found between the patient groups and the controls. However, the patients with epilepsy showed greater cortical activations than the control group on the side ipsilateral to the epileptic focus. rCBF in the anterior thalamic region was enhanced in patients relative to the control group. The results showed that long-term dysfunction of the medial temporal lobe might reinforce alternative memory pathways and recruit a distributed cortical network ipsilateral to their epilepsy focus. *NeuroReport* 13:2475–2481 © 2002 Lippincott Williams & Wilkins.

**Key words**: Hippocampus; Memory; PET; Temporal lobe epilepsy; Thalamus; Plasticity

## INTRODUCTION

Functional brain imaging techniques such as PET and fMRI have been used to examine memory systems in normal people. Data consistently indicate that left prefrontal regions are involved in encoding of episodic memory in spite of differences in material types (verbal/non-verbal) [1,2] or information processing stages (encoding *vs* recall) [3,4]. Less consistently, data have suggested that the medial temporal lobe, including the hippocampus, also plays an important role depending on encoding processing (e.g. association) or materials (e.g. novelty) [5,6]. The level of activities in these regions also seemed to be associated with subsequent recall [7–9]. However, it is not clear how this functional network would change if one of those structures fails to function normally.

In this study we focused on the functional network of the individuals with dysfunction of the medial temporal lobe due to epilepsy. In accordance with the hypothesis that the medial temporal lobe is important to episodic memory, patients who have medial temporal lobe epilepsy (mTLE) often show memory impairments in some, but not all, memory tasks [10–12]. However, forming episodic memory seems to be mediated not only by the medial temporal lobe, but also by various other brain regions as was shown in functional brain imaging research in normal individuals. The medial temporal lobe may not be involved in relatively simple memory tasks, and even patients with mTLE and animals with hippocampal lesions may show normal performance [13,14]. It is possible that long-term lesion in one of the memory-related structures, such as the medial temporal lobe, might alter the functional network of episodic memory in mTLE patients [15]. It is equally possible that patients may use cognitive strategies different from those of healthy individuals. The use of alternative pathways involved in episodic memory, either due to functional reorganization or different cognitive strategy, would allow patients with mTLE to achieve a normal level of memory performance in spite of damage to the medial temporal lobe. If this was the case, the patients with mTLE would show brain activation patterns different from those of normal healthy individuals during episodic memory tasks. If there were changes in memory related functional neuroanatomy or strategy following medial temporal lobe pathology, the pressures for the changes could also differ depending on the side of the affected medial temporal lobe. For example, if the left medial temporal lobe is more critical for episodic memory than the right side one, then two patient groups might show different activation patterns not only from the normal subjects, but also from each other.

The purpose of this study was to examine differences in memory related functional neuroanatomy between normal adults and epileptic patients in order to delineate the brain regions involved in episodic memory in epileptic patients.

$H_2{}^{15}O$ PET was used to measure changes in regional cerebral blood flow (rCBF) during encoding and retrieval of episodic memory, relative to a fixation or a response control tasks. Any differences in brain activation patterns found in patients with left or right mTLE, relative to the normal controls, will extend the current understanding of the dynamic patterns of pathologically triggered neuronal reorganization in mTLE patients.

## MATERIALS AND METHODS

***Subjects:*** Informed consent was obtained from all 18 participants. Handedness of the participants was assessed based on a simplified version of Edinburgh handedness questionnaire during clinical or pre-scan interview and only those who confirmed to all the questions as right-handed (6.0/6.0) were included in this study.

The healthy adults recruited as normal control subjects (all male, age range 26–28 years; mean age 26.8 years). They had no left-handed family members and no known neurological or psychiatric diseases, including epilepsy. The six patients with right mTLE were five male and one female, age range 17–38 years (mean 24.3 years). Language dominance was confirmed with Wada test as left hemispheric in all patients. No neurological or psychiatric diseases other than epilepsy were diagnosed. The average duration of epilepsy in this group was 12.5 years (range 6–20 years). Six patients with left mTLE comprised four males and two females with an age range 16–41 years (mean 29.3 years). All patients showed left hemispheric language dominance, confirmed by the Wada test. None had been diagnosed with any brain diseases except epilepsy. The average duration of epilepsy was 16.8 years (range 10–22 years).

***Diagnosis of mTLE:*** The diagnosis was made with standard presurgical evaluation at Seoul National University Hospital, consisting of scalp video-EEG monitoring, brain MRI, interictal EEG, ictal and interictal perfusion single photon emission computed tomography (SPECT), FDG-PET, and the Wada test. The relationships of the various diagnostic methods and related issues have been reported elsewhere [16]. Subjects were selected from patients who had both unilateral hippocampal atrophy on the brain MRI and exclusive temporal ictal onset confirmed by the ictal EEG and semiology.

***Wada memory scores in the patient groups:*** The Wada memory test was performed for both hemispheres. In order to compare both hemisphere scores, each score was converted into an asymmetry index using the a formula (left score−right score)/(left score + right score). According to the index, the right mTLE group consistently recorded greater left dominance scores (positive) as expected. The mean of the asymmetry index of the right mTLE patients was 0.437 (range 0.23 to 1.0). However the average group index of the left mTLE was less consistent with what was expected. The group average of the left mTLE patients was −0.29 (range 0.33 to −1.0).

***Behavioral task:*** Four PET scans were obtained from each subject, one scan for each task condition. The order of task scanning was fixation baseline, response control, encoding, and finally retrieval scan. A 30 min interval was given between scans in order to provide enough delay between encoding and recognition tasks. Stimuli were line drawings of common objects, presented via a LCD monitor (Sharp QD-101MM, Japan, 10.4 inch) with dark background and white lines. Line drawings of common objects were presented as stimuli since they were considered to contain both verbal and non-verbal characteristics. The stimuli were presented every four seconds and button press was required only during the response control task and the recognition task.

In the fixation baseline task subjects were asked to fixate a cross, presented in the center of the monitor. No behavioral response was required. During the response control task either upward (50%) or rightward (50%) arrows were presented. The response control task served as a control task for the recognition task where button press response was required. During the response control task the subjects were asked to press a button only when upward arrows were presented. In the encoding task a total of 30 line drawings of common objects were presented. No response was required during the encoding task but the subjects were instructed to memorize them for later memory test. As a recognition task, 15 items previously studied in the encoding task were presented along with 15 new items, in random order. Unlike the encoding task, however, the subjects were required to press a button in response to the old items.

***PET studies:*** PET scans were acquired using an ECAT EXACT 47 (Siemens-CTI, Knoxville, USA) PET scanner (BGO crystal detector, spatial resolution 6.1 mm, axial resolution 4.3 mm, sensitivity 214 kcps/μCi/mi) in two-dimensional mode with a 16.2 cm axial field of view. Following a transmission scan, four emission scans, each of 2 min, were performed (370–925 MBq, 10–25 mCi i.v. bolus injection of $H_2{}^{15}O$ at scan onset). Attenuation-corrected data were reconstructed (back-projection after Shepp low pass filtering, cutoff 0.30 cycles/pixel) and radioactive counts after the peak count were taken over a 60 s interval as a measure of regional cerebral blood flow (rCBF).

***Data analysis:*** Behavioral data from one normal control subject was not included in behavioral data analysis due to failure of data collection. All PET data were analyzed using Statistical Parametric Mapping (SPM 99, University College of London, UK), implanted in the Matlab (Mathworks Inc., USA). Head movement correction, transformation into stereotaxic space (Montreal Neurological Institute coordinates (MNI) as provided by SPM99), and smoothing (Gaussian filter of 16 mm FWHM) were performed. For the within-group analysis, voxel-by-voxel comparison between the encoding scan and the fixation baseline scan was used to find the areas that showed significant increases of rCBF during encoding. Comparison was also made between the recognition scan and the response control scan to find rCBF increases associated with recognition. In the between-

group analysis, the two patient groups were compared with the normal control group to detect areas that showed enhanced or reduced brain activations also for encoding (encoding–fixation baseline) and recognition (recognition–response control). The statistical parametric maps were thresholded at an uncorrected $p < 0.0005$ both for the within-group analysis ($t = 4.78$, $df = 9$) and for the between-group analysis ($t = 3.69$, $df = 27$). In all comparisons we removed clusters $< 12$ voxels ($k = 12$ for 8 mm cube voxels) unless otherwise stated. The local maximum of each significant cluster was reported as MNI coordinate in this study and anatomical locations of significant activation foci were assigned using the Duvernoy atlas [17]. Slightly lenient statistical parametric maps were thresholded at an uncorrected threshold of $p < 0.005$ (extent threshold $k = 200$ voxels) for illustrative purposes in the figures.

## RESULTS

***Behavioral results:*** During the recognition task, no group difference was found ($F(2,14) = 0.906$;. $p = 0.42$), with scores of 100%, 96.67%, and 100% for the controls ($n = 5$), the right mTLE group ($n = 6$), and the left mTLE group ($n = 6$), respectively. The mean correct responses (correct old response–false alarm) were 80%, 85.5%, and 87.6%, respectively. No significant group difference was found in the false alarm response rate ($F(2,14) = 0.382$, $p = 0.68$; 8%, 3.3%, and 7.8%, respectively).

***PET results:*** Results of this PET imaging analyses are summarized for within-group analyses and between-group analyses. In the within-group analyses, significant rCBF increases were found during encoding and recognition, relative to the fixation baseline and the response control conditions respectively. Table 1 indicates the MNI-coordinates of clusters with significant activations ($p < 0.0005$, extent threshold 12 voxels) during encoding or recognition. The normal subjects showed significant rCBF increases in left inferior and middle prefrontal regions during the encoding scan relative to the fixation scan. For the patients with right mTLE, no significant activation was found in the left hemisphere except fusiform gyrus. Instead, the encoding associated activations were found in precentral and inferior parietal gyri in the right hemisphere, which was ipsilateral to the side of epilepsy focus in the patients. The left mTLE patients also showed activations in the cortical regions which were ipsilateral to their epileptic focus, including the left inferior and the superior prefrontal cortices. Only medial brain region such as precuneus showed a significant rCBF increase during encoding. The parametric maps of those analyses are shown on rendered brain templates in Fig. 1 with a slightly lower threshold ($p < 0.005$, extent threshold 200 voxels) for display purpose. The areas with significant brain activations during the recognition were also different within the groups. For example, the control group showed activations in bilateral visual areas including lingual gyrus and fusiform gyrus and in the cerebellum when the normal subjects recognized the previously studied line-drawing figures. Patients with right mTLE showed a significant activation only in the cerebellar region while those with left mTLE showed the recognition-associated activation in various cortical regions. In the left mTLE patients activations were found in inferior prefrontal and middle prefrontal regions in the left hemisphere and in middle prefrontal region in the right hemisphere. Activations were also found in a number of medial brain structures including anterior cingulate gyrus, medial frontal region, cuneus and lingual gyrus.

In the between-group analyses, significant group differences were found for both patient groups compared with the normal healthy control subjects. The results of those analyses are summarized in Table 2, where the coordinates of the brain regions with significant group differences ($p < 0.0005$, extent threshold $= 12$ voxels) are indicated for both encoding (relative to fixation baseline) and recognition (relative to response control condition).

Between-group analyses for the mTLE patients in comparison to the normal control group confirmed increases of brain activity in the cortical regions ipsilateral to the epileptic focus, especially during encoding. For example, the right mTLE group showed the greater prefrontal activation in the right hemisphere and the left mTLE group showed greater middle temporal activation in the left hemisphere compared with normal healthy controls. Brain activations in several midline structures including anterior thalamus (indicated with yellow arrows in Fig. 2) also seemed to be enhanced in both patient groups during encoding. In the left mTLE group, rCBF increases in the anterior thalamus were significantly ($T = 5.30$) greater than in the control group. Hyperactivity ($T = 3.63$) of the anterior thalamic region was also observed in the patients with right mTLE, relative to the normal controls when a slightly lower threshold ($p < 0.005$, extent threshold $= 50$) was applied. Increased brain activations in the cortical regions ipsilateral to the epileptic focus were observed also during recognition (Fig. 2a, right panel). Compared with normal controls, the right mTLE patients showed greater rCBF increases in the middle occipital and in the inferior parietal regions of the right hemisphere in association with recognition. The left mTLE patients also showed the increases in various cortical regions of the left hemisphere, including the middle frontal cortices and the inferior parietal region. However, increased brain activations were also found in the various medial regions including medial prefrontal, anterior cingulate, precuneus, and cuneus. Lastly, we found that activity of right parahippocampal region was significantly reduced during recognition in the right mTLE patients in comparison with the normal healthy subjects. The hypoactivity in the right parahippocampal region (indicated by a green arrow at the right panel of Fig. 2a) in this patent group was consistent with the known pathology of the right mTLE patients. However, it is noteworthy that the significant group difference was observed only during the recognition but not during encoding.

## DISCUSSION

Localization of memory related brain structures of the presurgical patients with mTLE hold great significance for the brain surgery as well as localization of epileptic focus. Here in this study, we utilized a simple form of episodic memory task as similar as possible to the Wada memory test (intracarotid amobarbital) which is most commonly used to localize memory and language areas in epilepsy patients.

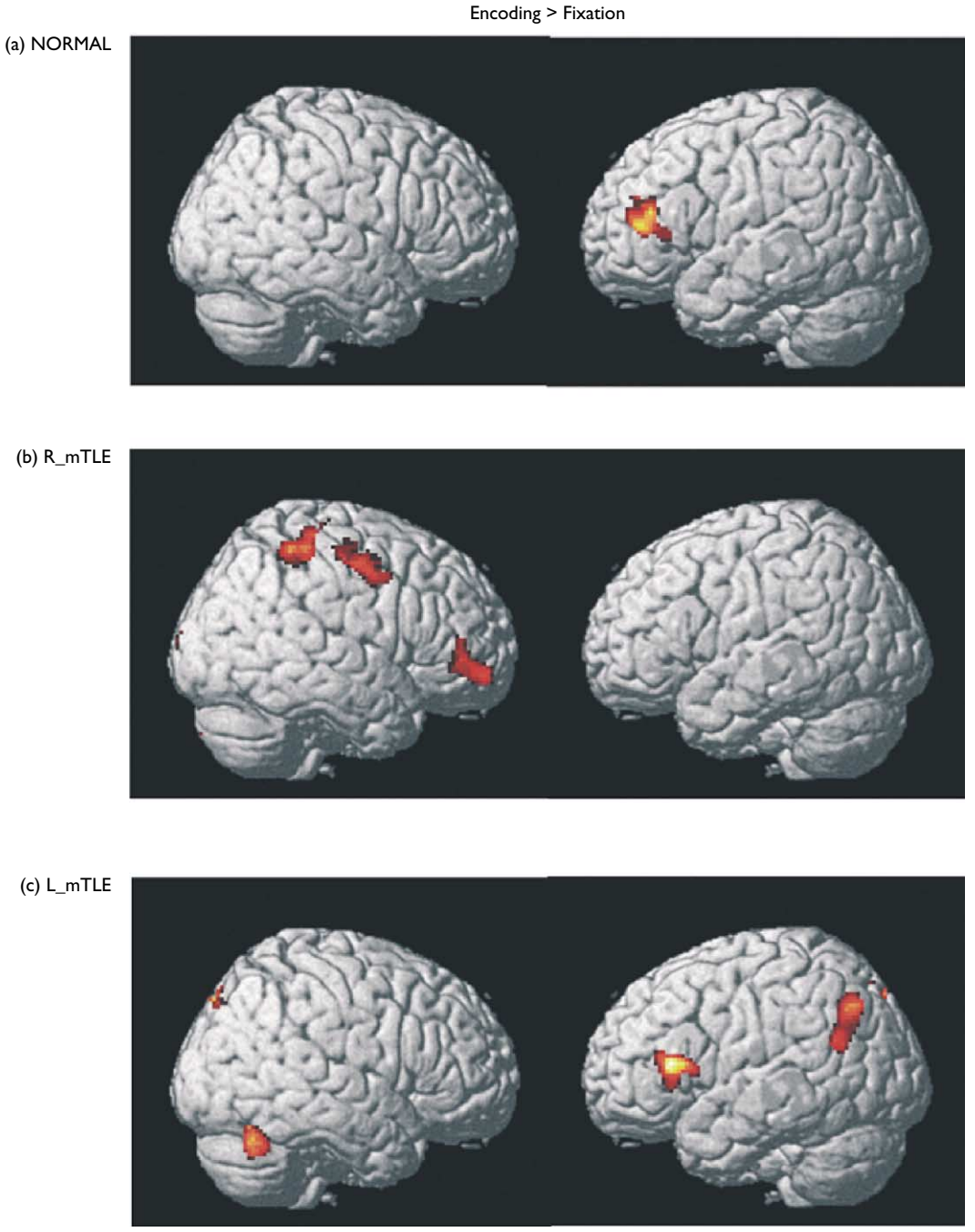


**Fig. 1.** Brain activation during encoding of line drawings in comparison to fixation baseline. (**a**) Normal control subjects; (**b**) Patients with right medial temporal lobe epilepsy; (**c**) Patients with left temporal lobe epilepsy, (uncorrected $p < 0.005$ at voxel level, extent threshold $k = 200$).

The behavioral results suggested that the episodic memory task for line-drawing objects was simple enough so that memory impairment was not found in the epilepsy patients. The PET results, however, indicated that the episodic memory function might have been re-allocated and that the neural pathway for episodic memory was reorganized in the mTLE patients. Rather than inter-hemispheric transfer, the pathologically induced reallocation of memory function seemed to take place within a hemisphere or in the subcortical limbic structures in epilepsy patients. The alternative pathways might include ipsilateral cortical regions, contralateral medial cortical region, or anterior thalamic regions. The alternative pathways for episodic memory could have been developed due to long-term dysfunction in the medial temporal lobe. However, it is also possible that the differences in activation patterns in each patient group compared to the normal healthy subjects might be a consequence of possible neural tissue damage as

**Table 1.** Activated regions during encoding and recognition.

| | Encoding | | | | | Recognition | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Talairach coordinates | | | | | Talairach coordinates | | | |
| Group | Region | x | y | z | Tscore* | Region | x | y | z | Tscore* |
| Normal | L Inferior frontal gyrus | −58 | 24 | −8 | 8.30 | L Posterior cerebellum | −28 | −86 | −28 | 8.29 |
| | L Middle frontal gyrus | −24 | 40 | 22 | 7.78 | L Lingual gyrus | −24 | −74 | −6 | 7.04 |
| | | | | | | R Fusiform gyrus | 32 | −44 | −18 | 7.30 |
| Right mTLE | L Fusiform gyrus | −44 | −76 | −18 | 5.41 | M Anterior cerebellum | 2 | −56 | −36 | 6.21 |
| | R Precentral gyrus | 62 | 2 | 46 | 6.13 | | | | | |
| | R Inferior parietal gyrus | 36 | −44 | 56 | 5.39 | | | | | |
| Left mTLE | L Superior temporal gyrus | −50 | 8 | −18 | 6.04 | L Inferior frontal gyrus | −34 | 24 | −8 | 8.12 |
| | L Inferior frontal gyrus | −48 | 20 | 12 | 5.88 | L Middle frontal gyrus | −30 | 50 | −6 | 5.85 |
| | M Precuneus | 8 | −80 | 44 | 5.96 | R Middle frontal gyrus | 40 | 48 | −18 | 6.52 |
| | | | | | | M Anterior cingulate | 10 | 50 | 4 | 11.84 |
| | | | | | | M Medial frontal gyrus | 6 | 34 | 38 | 7.68 |
| | | | | | | M Cuneus | 12 | −100 | 10 | 11.12 |
| | | | | | | M Cuneus | −8 | −108 | −4 | 10.42 |
| | | | | | | M Lingual gyrus | 6 | −84 | −4 | 10.77 |

*$p < 0.0005$ (T = 4.78) uncorrected, cluster size > 12 voxels.

**Table 2.** Brain activations in mTLE groups and normal controls.

| | | | Talairach coordinates | | | |
|---|---|---|---|---|---|---|
| Group | | Region | x | y | z | Tscore* |
| ENCODING | | | | | | |
| Right mTLE | Increases | L Claustrum | −34 | −10 | −4 | 4.44 |
| | | R Middle frontal gyrus | 38 | 44 | −4 | 4.31 |
| | | M — | −6 | 0 | 20 | 4.35 |
| | | *Anterior thalamus* | 0 | 2 | 2 | 3.63+ |
| | | M Cerebellum | −4 | −84 | −38 | 4.02 |
| | Decreases | L Superior temporal gyrus | −60 | −2 | 6 | 4.69 |
| | | L Middle frontal gyrus | −24 | 40 | 18 | 4.20 |
| | | R Cerebellum | 52 | −76 | −44 | 4.26 |
| Left mTLE | Increases | L Middle temporal gyrus | −56 | −10 | −20 | 4.27 |
| | | M Anterior thalamus | 6 | −2 | 12 | 5.30 |
| | | M Precuneus | 6 | −78 | 44 | 4.76 |
| | | M Cerebellum | 2 | −68 | −36 | 4.03 |
| | Decreases | L Orbitofrontal gyrus | −20 | 52 | −24 | 4.06 |
| | | R Superior frontal gyrus | 2 | 68 | −4 | 4.23 |
| RECOGNITION | | | | | | |
| Right mTLE | Increases | R Middle occipital gyrus | 52 | −84 | 18 | 4.31 |
| | | R Inferior parietal gyrus | 50 | −42 | 38 | 4.07 |
| | Decreases | R Parahippocampal gyrus | 16 | −34 | −10 | 3.88 |
| Left mTLE | Increases | L Middle frontal gyrus | −34 | 26 | 26 | 4.74 |
| | | L Middle frontal gyrus | −34 | 12 | 64 | 4.43 |
| | | L Inferior parietal gyrus | −36 | −42 | 42 | 6.06 |
| | | R Superior temporal gyrus | 48 | −42 | 18 | 4.31 |
| | | M Medial frontal gyrus | 10 | 38 | 46 | 5.17 |
| | | M Anterior cingulate gyrus | 0 | 0 | 32 | 4.02 |
| | | M Precuneus | 14 | −86 | 54 | 5.41 |
| | | M Cuneus | 16 | −102 | 20 | 4.67 |
| | Decreases | L Posterior central gyrus | −16 | −40 | 78 | 4.82 |
| | | L Fusiform gyrus | −46 | −76 | −22 | 4.58 |
| | | R Anterior cerebellum | 30 | −48 | −26 | 4.96 |
| | | R Lateral cerebellum | 56 | −38 | −32 | 4.31 |
| | | R Posterior cerebellum | 54 | −72 | −36 | 4.45 |

*$p < 0.0005$ (T = 3.69) uncorrected, cluster size > 12 voxels; +$p < 0.005$ (T = 2.77) uncorrected, cluster size > 50 voxels.

well as dysfunction due to epileptic seizures in memory-related brain regions. The documented patient profiles indicated a likelihood of long-term pathology such as hippocampal sclerosis (one exception in each group) in most patients and/or > 10 years of epileptic history (only one exception in the right mTLE group). Alternatively, the activation pattern in episodic memory encoding might suggest a possibility that the patients have utilized

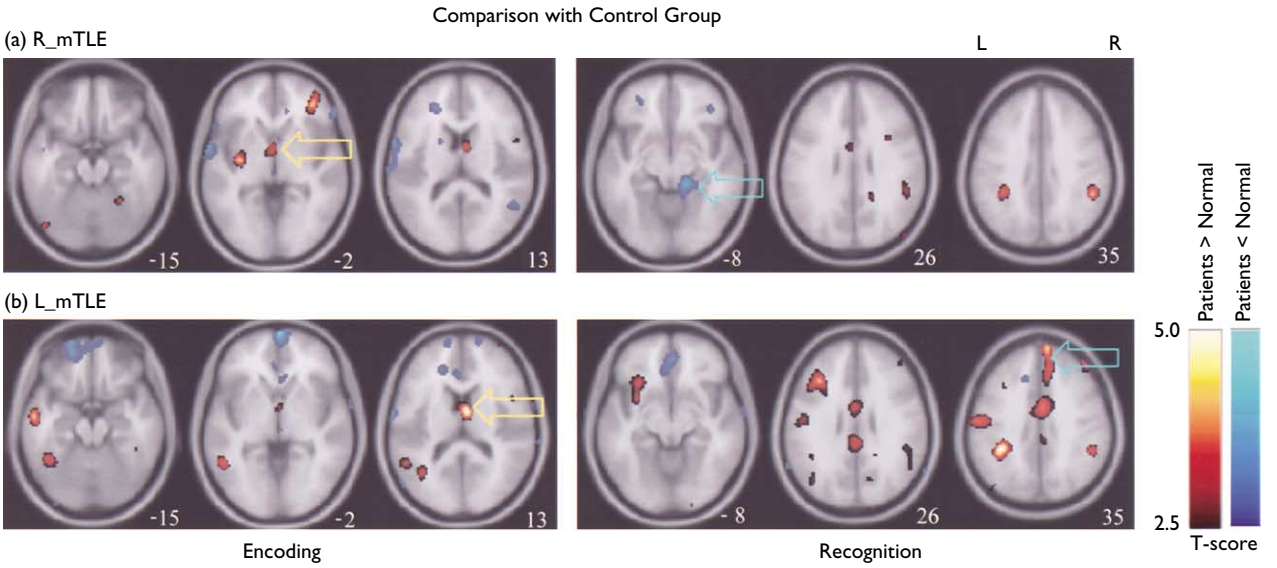


**Fig. 2.** Brain regions with significant group differences both during encoding (left panel) and recognition (right panel). Increased activation or decreased activation of each patient group relative to the normal control subjects was indicated as red and blue respectively. (**a**) Patients with right medial temporal lobe epilepsy; (**b**) Patients with left temporal lobe epilepsy (uncorrected $p < 0.005$ at voxel level, extent threshold $k = 200$).

qualitatively different memory strategies from the normal controls in order to compensate for dysfunction of medial temporal structures. In the normal controls the ventral inferior prefrontal and the middle prefrontal regions in left hemisphere were observed during encoding, which was consistent with the previous findings [1,4]. However, the left inferior prefrontal activation was not detected in the right mTLE patients in association with the encoding with the current threshold ($p < 0.0005$, extent threshold = 12 voxels). Patients with right mTLE showed activations mainly in the right hemisphere. The left mTLE patients, on the contrary, showed extensive left lateralized activations in prefrontal and temporal regions during the encoding. Interestingly, the left prefrontal activation (MNI coordinates −48,20,20) in the patients with mTLE was more dorsal than ventral part of left inferior prefrontal region, unlike the normal healthy control subjects (MNI coordinates −58,24,−8). During recognition, the normal healthy subjects showed the increased rCBF in lateral visual cortices such as left lingual gyrus and right fusiform gyrus but no significant prefrontal activation was detected. The results suggest the involvement of perceptual processing in normal subjects during the recognition of line drawing.

In addition to the cortical activations, the encoding associated group differences were found in the anterior thalamic region in both mTLE groups. The anterior thalamus has been known to be one of the structures that have close anatomical connections with medial temporal structures, either via fornix, or via subiculum and contribute to memory formation both in human and animals [18–20]. The findings of increased brain activations in the patients with epilepsy are consistent with those in a previous animal study, where the learning-related physiological activities of the anterior thalamus or the dorsomedial thalamus were enhanced following lesions of subiculum/posterior cingulate or hippocampus [21]. This animal study suggested an inhibitory modulation from the hippocampus on learning related neural activity in limbic thalamic regions. If the anterior thalamus of the epilepsy patients was disinhibited from a hippocampal inhibitory modulation, the anterior thalamus of the patients could play an important role in the learning and memory of this episodic memory task in comparison with the normal healthy subjects. This indication is supported by a recent quantitative MRI study where fornix atrophy was observed in most medial temporal lobe epilepsy patients [22]. If, in addition to the hippocampus, interrelated limbic structures such as the fornix have developed atrophy, then the inhibitory effect from the hippocampus to the limbic thalamus via the fornix is likely to be reduced and hyperactivity could be observed in these structures during episodic memory. These subcortical limbic structures could then subserve sufficient encoding of episodic memory, if it is simple enough. This might be the case in the patients with mTLE, when single item encoding is required.

Activations in visual cortices were found in lateral occipital regions bilaterally in the healthy normal control subjects only during recognition, as discussed above. In the patients with left mTLE we observed significant rCBF increases in medial visual cortices such as the precueus and cuneus during encoding or recognition (Table 1). The activities of these regions were also significantly greater than in the control group (Table 2). Since these areas have been shown to be activated in various mental imagery or visual memory tasks [23], one could speculate that patients with left medial temporal lobe dysfunction depend on a visual representation/imagery type of strategy during encoding and recognition more than the other groups.

The recognition-associated brain activations of the right mTLE group, however, were observed in a limited area during recognition, relative to the response control condition. The low level of brain activation during recognition in

the right mTLE group could reflect either reduced brain activity during recognition *per se*, or relatively high levels of activation during the response control scan. The latter seemed to be the case according to an additional analysis (data not shown) where the recognition scan was compared with the fixation baseline scan instead of the response control scan. Additional analysis showed that the extent of the recognition-associated brain activations in the right mTLE group was comparable with the other groups. It seems, therefore, that the response control task, where visuo-spatial processing might be required in detecting a particular direction of arrow, might be a greater burden to the patients with right mTLE than to the other two groups.

Our findings of cortical hyperactivation ipsilateral to epileptic focus are contrary to the widely held belief of interhemispheric shift of given function to homologous regions following unilateral damage. Damage to the brain areas responsible for language function with original left hemisphere dominance [24] could result in interhemisphere transfer of its function, but this may not occur in other functions such as memory or motor [15]. A recent finding [25] also supported that notion that epilepsy-induced alteration of neuroanatomy of memory were more as within-hemisphere transfer than between-hemisphere. In this fMRI study, all left mTLE patients showed consistent and extensive left prefrontal activations during all verbal episodic memory tasks, including encoding and retrieval (recall). In spite of the differences in imaging modality (fMRI *vs* PET), material type (word *vs* line-drawing picture), and retrieval test (recall *vs* recognition) between their study and ours, similar findings of the ipsilateral cortical hyperactivity were obtained, at least during the encoding task. However, only our study reported increased brain activation in anterior thalamic regions in the mTLE patients. Considering that the anterior thalamic structure is involved in learning, this may account for the absence of memory deficits in our patients during this simple episodic memory task. However, caution should be exercised in interpreting these results since these different patterns of activations in epilepsy patients might also indicate a possibility that the patients adopted different behavioral strategy in a way to compensate for their medial temporal lobe dysfunction, rather than reorganization of brain network. Only further research will be able to answer this kind of issue. Meanwhile, characterizing pathological changes in brain function should improve the way in which a diagnosis is made for epilepsy. Understanding the pattern of pathologically induced brain reorganization will also extend our knowledge on brain plasticity in compensating for functional brain damage.

## CONCLUSION

We found distinctive patterns of brain activations in patients with mTLE in comparison to normal healthy controls. First, the mTLE patients showed scattered and extensive cortical activations, mostly ipsilateral to the epileptic focus during encoding. Second, during episodic encoding both patient groups showed increased activations in the anterior thalamic regions, which are known to be learning/memory-related subcortical limbic structures. Considering that no behavioral impairments were observed during the memory task used in this study, these results might suggest a neural compensatory mechanism for memory function following epilepsy. Memory-related neural substrates might have been reorganized in the brains of patients with long-term medial temporal lobe dysfunction.

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Acknowledgements: This work has been supported by Korea Science and Engineering Foundation grants 97-0403-0401-3 (S.K.L) and R05-2000-00011 (E.K).