The Effect of Early Versus Late Onset of Temporal Lobe Epilepsy on Hemispheric Memory Laterality: An Intracarotid Amobarbital Procedure Study

Thirty-three temporal lobe epilepsy (TLE) patients, 19 left TLE and 14 right TLE, underwent an intracarotid amobarbital procedure. For each patient, hemispheric memory laterality was determined by measuring the relative magnitude of recognition memory following left versus right hemisphere injection of sodium amobarbital. The patients were divided into early and late seizure onset groups, based on the median age (13 yrs) of seizure onset of the total sample. Early-onset left TLE was associated with a greater tendency toward right hemispheric representation of both verbal and visual memory compared with late-onset left TLE. Early-onset right TLE was associated with a greater tendency toward left hemispheric representation of visual, but not verbal, memory compared with late-onset right TLE. These findings indicate that interhemispheric plasticity for memory is greater in early than in late life, bidirectional, and at least partially material-specific. ***(JKMS 1997; 12: 559~63)***

Key Words : *Epilepsy, Temporal lobe; Dominance, Cerebral; Amobarbital*

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INTRODUCTION

Wada (1) introduced the intracarotid amobarbital procedure (IAP), also known as the Wada test, as a technique for determining hemispheric language dominance. This procedure involves injection of 100-200 mg of sodium amobarbital, a short acting anesthetic, into the left or right internal carotid artery through a transfemoral catheter. Language functions during the period of temporary inactivation of the injected hemisphere, usually lasting 2-3 minutes, may reflect the opposite, noninjected hemisphere. The IAP has proven to be a reliable method of determining hemispheric language dominance, and it is now a standard part of presurgical examination for medically intractable temporal lobe and other focal epilepsy patients.

Use of the IAP with focal epilepsy surgery candidates has shown that a substantial proportion of these patients shows atypical (i.e., right or mixed) patterns of language dominance. The incidence of atypical language dominance is particularly high in those patients with early left brain injury (2, 3, 4). Thus, in a well-known IAP study involving a large number of focal epilepsy patients (n=396), Rasmussen and Milner (2) reported that atypical language dominance was found in 55% of those patients with clinical evidence of early left brain injury but in only 9% of those without the evidence. The elevated incidence of atypical language dominance in patients with early than late left brain injury is thought to reflect greater interhemispheric plasticity for language in the immature, developing brain. Supporting evidence for greater interhemispheric plasticity for language in early age includes relatively normal development of language following early left hemispherectomy (5) and good prognosis for childhood aphasics (6).

Milner et al. (7) adapted the IAP to include assessment of hemispheric memory function. The memory procedure involves presentation of stimuli during the period of amobarbital effects and testing memory of the stimuli after full recovery of functions. Temporal lobe epilepsy (TLE) is commonly associated with pathological changes in hippocampal formation (8), a region known to be critical in memory. Previous IAP studies of TLE patients (9, 10, 11) have found a significant association between hemispheric memory laterality and side of seizure onset. The majority of left TLE patients have better right than left hemispheric memory and the majority of right TLE patients show the reverse, i.e., better left than right hemispheric memory. Further, IAP memory asymmetries in TLE patients are significantly correlated with their

MRI hippocampal volume asymmetries (10) or hippocampal cell density (12). These findings indicate that an epileptic, pathological hippocampal formation supports memory less well than its more healthy, nonepileptic counterpart.

Although the effect of early versus late brain injury on hemispheric language lateralization has received much attention, little attention has been given to the effect of early versus late brain injury on hemispheric memory lateralization. With this issue in mind, the present study investigated the effect of early versus late onset of TLE upon hemispheric memory laterality. Early-onset left TLE is associated with a high incidence of atypical language dominance (13), presumably reflecting greater interhemispheric plasticity for language in early than in late life. Given the close linkage between TLE and mesial temporal lobe pathology, early-onset left or right TLE may have a more direct effect upon hemispheric memory lateralization than on hemispheric language lateralization. Thus, on the hypothesis that interhemispheric plasticity for memory is greater in early than in late life, early-onset left TLE should be associated with a greater tendency toward right hemispheric memory representation compared with late-onset left TLE; early-onset right TLE should be associated with a greater tendency toward left hemispheric memory representation compared with late-onset right TLE.

MATERIALS AND METHODS

Subjects

Thirty-three patients with medically intractable TLE (19 left TLE and 14 right TLE) who were evaluated for epilepsy surgery were investigated. The seizure focus was localized with prolonged interictal and ictal video-EEG recordings from scalp/sphenoidal electrodes. All subjects also underwent magnetic resonance imaging (MRI), interictal single-photon emission computed tomography (SPECT) scanning as part of presurgical workup. When results of scalp/sphenoidal EEG monitoring were inconclusive (n=9), the seizure focus was localized with EEG from chronically implanted bilateral subdural strip electrodes (14). Subjects with extratemporal lobe foci were excluded. Table 1 lists demographic and clinical characteristics of the sample. Twenty were men and 13 were women. Age at time of testing ranged from 11 to 41 years, with the mean of 26.0±7.4. The mean age at seizure onset was 14.6±8.0. Mean Full Scale IQ (FIQ) from the Korean version of the Wechsler Intelligence Scales (K-WAIS; 15) was 80.8±14.5 (available in 29 patients only).

Intracarotid amobarbital procedure (IAP)

All subjects underwent IAP of both left and right hemispheres. All subjects gave their written informed consent as required by Keimyung University Hospital, Taegu, Korea. IAP was conducted, with the patient supine, immediately following angiography. Prior to amobarbital injection, the patient was informed that he or she would be presented with a series of words and pictures. The patient was instructed to concentrate on each word/picture and to remember as many of them as possible for a subsequent memory test. Amobarbital 125 mg in a 10% saline solution was injected into an internal carotid artery using a transfemoral catheter over 4-5 seconds. In most patients, the side considered for resection was injected first. Left and right hemisphere injections were done on the same day with a minimum of 40 minutes between the two injections.

Following demonstration of hemiplegia, the patient was first presented with a series of language tasks. The language tasks tested both expressive (e.g., naming) and comprehensive language functions (e.g., following a command). Patients were then presented with a series of memory stimuli. For most injections, presentation of the memory stimuli was started within 2 minutes of amobarbital injection. A total of 8 memory stimuli was presented : 4 verbal stimuli (2 concrete words, 2 short

Table 1. Demographic and clinical characteristics of patients

Gender distribution	
Male (n)	20
Female (n)	13
Handedness	
Left (n)	3
Right (n)	30
Hemispheric language dominance	
Left (n)	26
Mixed (n)	4
Right (n)	3
Wechsler Full-Scale IQ*	
Mean ± SD	80.8 ± 14.5
Education (yrs)	
Mean ± SD	11.1 ± 2.7
Seizure Onset	
Left temporal lobe (n)	19
Right temporal lobe (n)	14
Age at testing (yrs)	
Mean ± SD	26.0 ± 7.4
Age at first seizure (yrs)	
Mean ± SD	14.6 ± 8.0
Seizure duration (yrs)	
Mean ± SD	12.1 ± 6.6

* This score was available in 29 patients only.

sentences) and 4 visual stimuli (2 line drawings of common objects, 1 geometric figure, and 1 face photograph). Two different matched forms were used, one during each injection, counterbalanced across patients. Each stimulus, both verbal and visual, was mounted on a white sketchboard and presented for 5-10 seconds within the visual field ipsilateral to the hemisphere injected. Follow-up memory testing was performed approximately 15 minutes after injection, after complete resolution of hemiplegia and return of language functions. Free recall was assessed first, followed by recognition testing, using a multiple choice format with three foils per item. Only recognition was analyzed, and free recall was scored as evidence of correct recognition.

Analyses were done separately for verbal and visual stimuli. For each stimulus type, IAP Memory Laterality score (max=4, min=-4) was computed as the number of correct recognition after left hemisphere injection (i.e., when the right hemisphere was active) minus the number of correct recognition after right hemisphere injection (i.e., when the left hemisphere was active). Thus, a positive score indicated better memory when the right hemisphere was active and a negative score indicated superior memory when the left hemisphere was active. To analyze effects of seizure onset age on hemisphere memory lateralization, early and late onset groups were constructed by dividing the patients at the media age (13 yrs) of seizure onset. Four subgroups resulted from this classification: early-onset left TLE (n=9), late-onset left TLE (n=10), early-onset right TLE (n=8), and late-onset right TLE groups (n=6).

RESULTS

Effects of seizure onset side

The mean IAP Memory Laterality score for left and right TLE patients are shown in Figure 1. The mean IAP Memory Laterality score for left and right TLE patients were significantly different when scores were based either on verbal stimuli ($t=4.48$, $p<.0001$) or visual stimuli ($t=3.52$, $p<.01$). For either stimulus type, the mean IAP Memory Laterality score of the left TLE group was more positive than that of the right TLE group. Thus, side of seizure onset had a significant effect on hemispheric memory laterality of either stimulus type.

Effects of seizure onset age

The effects of seizure onset age on hemispheric memory laterality were investigated separately for left and right TLE patients. Of left TLE patients, the mean IAP Memory

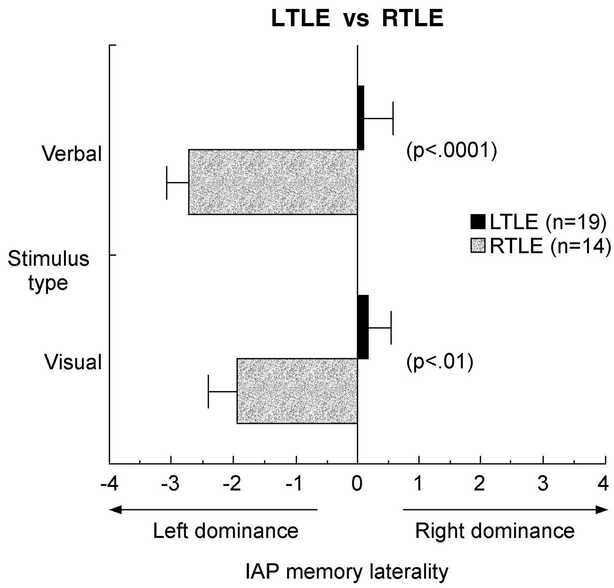

Fig. 1. The mean IAP memory laterality scores for left TLE vs right TLE patients. Error bars represent standard errors.

Laterality scores for early and late onset patients were significantly different when scores were based either on verbal stimuli ($t=2.53$, $p<.05$) or visual stimuli ($t=2.83$, $p<.05$). For either stimulus type, the mean IAP Memory Laterality score of the early onset group was more positive than that of the late onset group (Fig. 2). Thus, early-onset left TLE was associated with a greater tendency toward right hemispheric representation of both verbal and visual memory compared with late-onset left TLE.

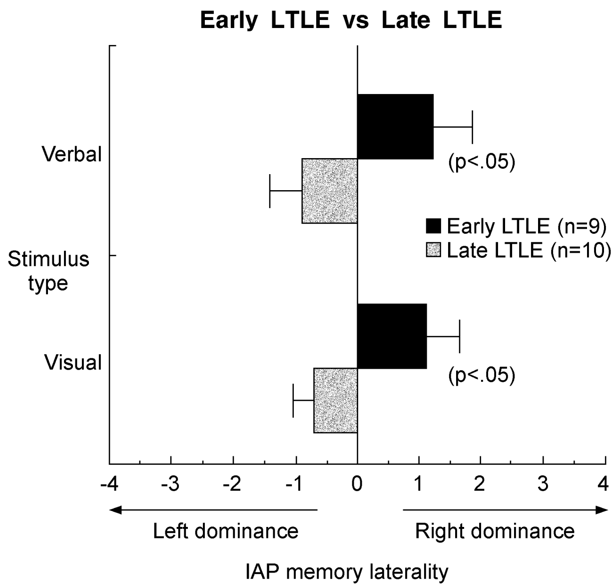

Fig. 2. The mean IAP memory laterality scores for early vs late onset left TLE patients. Error bars represent standard errors.

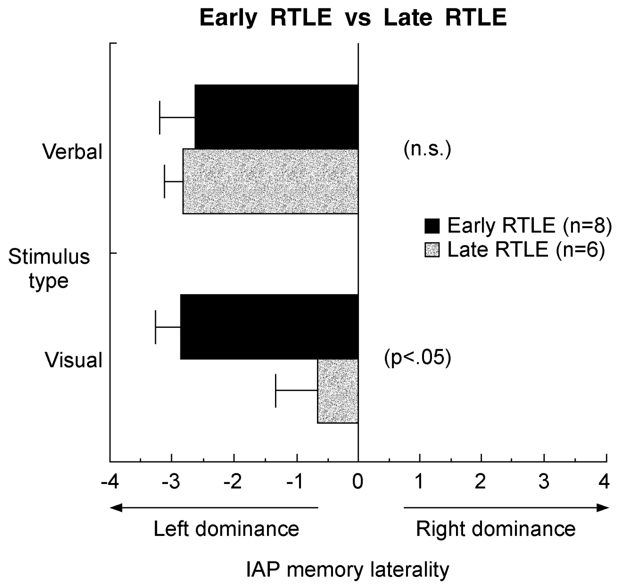

Fig. 3. The mean IAP memory laterality scores for early vs late onset right TLE patients. Error bars represent standard errors.

Of right TLE patients, the mean IAP Memory Laterality scores for early and late onset patients were significantly different when scores were calculated from visual stimuli ($t=3.00$, $p<.05$), but similar when they were obtained from verbal stimuli ($t=.29$, $p>.70$). For visual stimuli, the mean IAP Memory Laterality score of the early onset group was more negative than that of the late onset group (Fig. 3). Thus, early-onset right TLE was associated with a greater tendency toward left hemispheric memory representation of visual, but not verbal, memory compared with late-onset right TLE.

DISCUSSION

The present results show that patterns of hemispheric memory laterality for left and right TLE patients are significantly different. These findings are consistent with existing evidence that side of seizure onset is a significant determinant of hemispheric memory laterality (9, 10, 11). More importantly, the present results indicate that age of seizure onset also has a significant effect on hemispheric memory laterality. Thus, early-onset left TLE was associated with a greater tendency toward right hemispheric representation of both verbal and visual memory compared with late-onset left TLE. Early-onset right TLE was associated with a greater tendency toward left hemispheric representation of visual, but not verbal, memory compared with late-onset right TLE. These findings lend support to the hypothesis that interhemispheric plasticity for memory is greater in early life and decreases with age. The findings also suggest that interhemispheric plasticity for memory may be bidirectional, proceeding from left to right when left temporal lobe is injured, and processing from right to left when right temporal lobe is injured.

A comparison of the effects of left and right unilateral temporal lobectomy has revealed certain material-specific hemispheric specialization for memory function (16): the left mesial temporal structures for the learning and retention of verbal material, and the right mesial temporal structures for the learning and retention of nonverbal, visual material. According to this view, interhemispheric reorganization of memory following early brain injury may also be material-specific. Thus, early left temporal lesion may result in interhemispheric reorganization of verbal, but not visual, memory; early right temporal lesion may result in interhemispheric reorganization of visual, but not verbal, memory. In the present study, the effects of early-onset right TLE, but not early-onset left TLE, on hemispheric memory laterality was material-specific. In our view, the effects of early-onset left TLE on visual memory laterality are best attributed to easily verbalizable nature of most present visual stimuli (e.g., drawings of common objects). With more purely visual versus verbal stimuli, the effects of early-onset left TLE on hemispheric memory laterality may be found to be material-specific.

Although we interpret the differential patterns of hemispheric memory laterality for early versus late onset patients as reflecting greater interhemispheric plasticity in early age, alternative interpretations are, of course, possible. For example, it may be suggested that the present findings reflect greater structural destruction associated with early- than late-onset TLE. Lack of MRI volumetry data does not allow us to directly address this question. However, it is relevant that IAP Total Memory score, defined as left injection score plus right injection score, was not different for early- versus late-onset patients ($t=.67$, $p>.50$). If early-onset TLE is, in fact, associated with greater structural destruction and the present findings reflect this factor only, overall IAP memory capacity may be significantly lower for early than late onset patients. Thus, even if early-onset TLE is associated with greater structural destruction compared with late-onset TLE, it may not solely account for the differential patterns of hemispheric memory laterality for early versus late onset patients.

Another alternative interpretation for the present patterns of findings concerns the possible confounding of hemispheric memory laterality with hemispheric language dominance. In the present sample, 44% (4/9) of early-onset left TLE patients, but only 20% (2/10) of late-onset left TLE patients had atypical language dominance. It may be suggested that the differential patterns of hemispheric memory laterality for early- versus late-onset left TLE patients are due to the differential incidence of atypical language dominance. However, an elevated incidence of atypical language dominance is part of the phenomenon associated with early-onset left TLE (13). Thus, exclusion of patients with atypical language dominance from the present sample would have systematically distorted the present results. Thus, any linkage between memory versus language lateralization, whether coincidental or causal, may not undermine the present conclusion that early-onset left TLE is associated with a greater tendency toward right hemispheric memory representation compared with late-onset left TLE.

In sum, clinical and experimental evidence indicates that neural plasticity is greater in early life and decreases with age. Prior IAP studies (2, 3, 4) indicated that interhemispheric plasticity for language may be greater in early than in late life. The present result provides evidence that interhemispheric plasticity for memory may also be greater in early than in late life. Thus, early-onset left TLE was associated with a greater tendency toward right hemispheric representation of both verbal and visual memory compared with late-onset left TLE. Early-onset right TLE was associated with a greater tendency toward left hemispheric representation of visual, but not verbal, memory compared with late-onset right TLE. These results suggest that interhemispheric reorganization of memory following early brain injury is bidirectional, proceeding from right to left as well as from left to right. The results also indicate that interhemispheric reorganization of memory is at least partially material-specific.

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REFERENCES

1. Wada J. *A new method for determination of the side of cerebral speech dominance : a preliminary report on the intracarotid injection of Sodium Amytal in man. Igaku Seibutsugaku 1949 ; 14 : 221-2.*
2. Rasmussen T, Milner B. *The role of early left-brain injury in determining lateralization of cerebral speech functions. Ann NY Acad Sci 1977 ; 299 : 355-69.*
3. Woods RP, Dodrill CB, Ojemann GA. *Brain injury, handedness, and speech lateralization in a series of amobarbital studies. Ann Neurol 1988 ; 23 : 510-8.*
4. Satz P, Strauss E, Wada J, Orsini DL. *Some correlates of intra- and interhemispheric speech organization after left focal brain injury. Neuropsychologia 1988 ; 26 : 345-50.*
5. Basser LS. *Hemiplegia of early onset and the faculty of speech with special reference to the effects of hemispherectomy. Brain 1962 ; 85 : 427-60.*
6. Vargha-Khadem F, O' Gorman AM, Watters GV. *Aphasia and handedness in relation to hemispheric side, age at injury and severity of cerebral lesion during childhood. Brain 1985 ; 108 : 677-96.*
7. Miner B, Branch C, Rasmussen T. *Study of short-term memory after intracarotid injection of sodium Amytal. Trans Am Neurol Assoc 1962 ; 87 : 224-6.*
8. Babb TL, Brown WJ. *Pathological findings in epilepsy. In : Engel J, ed. Surgical treatment of the epilepsies. New York : Raven Press, 1987 ; 511-40.*
9. Rausch R, Babb TL, Engel JJr, Crandall PH. *Memory following intracarotid amobarbital injection contralateral to hippocampal damage. Arch Neurol 1989 ; 46 : 783-8.*
10. Loring DW, Murro AM, Meador KJ, Lee JP, Gratton CA, Nichols ME, Gallagher BB, King DW, Smith JR. *Wada memory testing and hippocampal volume measurements in the evaluation for temporal lobectomy. Neurology 1993 ; 43 : 1789-93.*
11. Perrine K, Westerveld M, Sass KJ, Devinsky O, Dogali M, Spencer DD, Luciano DJ, Nelson PK. *Wada memory disparities predict seizure laterality and postoperative seizure control. Epilepsia 1995 ; 36 : 851-6.*
12. Sass KJ, Lencz T, Westerveld M, Novelly RA, Spencer DD, Kim JH. *The neural substrate of memory impairment demonstrated by the intracarotid amobarbital procedure. Arch Neurol 1991 ; 48 : 48-52.*
13. Rey M, Dellatolas G, Bancaud J, Talairach J. *Hemispheric lateralization of motor and speech functions after early brain lesion : Study of 73 epileptic patients with intracarotid amytal test. Neuropsychologia 1988 ; 26 : 167-72.*
14. Wyler AR, Ojemann GA, Lettich E, Ward AAJr. *Subdural strip electrodes for localizing epileptogenic foci. J Neurosurg 1988 ; 60 : 1195-2000.*
15. Yeom T, Park Y, Oh K, Kim J, Lee Y. *K-WAIS manual. Korea : Korea Guidance, 1992.*
16. Milner B. *Interhemispheric differences in the localization of psychological processes in man. Br Med Bull 1971; 27: 272-7.*