Available online at www.sciencedirect.com
ScienceDirect
Epilepsy & Behavior 9 (2006) 579–586
Epilepsy & Behavior
www.elsevier.com/locate/yebeh

Hippocampal memory function as reflected by the intracarotid sodium methohexital Wada test

Fani Andelman [a,*], Svetlana Kipervasser [b,c], Irith I. Reider-Groswasser [c,d], Itzhak Fried [a,c,e], Miri Y. Neufeld [b,c]

[a] Functional Neurosurgery Unit, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
[b] EEG and Epilepsy Unit, Department of Neurology, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
[c] Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel
[d] Section of Neuroradiology, Department of Imaging, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
[e] Division of Neurosurgery, University of California, Los Angeles, Los Angeles, CA, USA

Received 26 May 2006; revised 29 July 2006; accepted 2 August 2006
Available online 30 August 2006

Abstract

The intracarotid amobarbital procedure (IAP) determines lateralization of memory function for predicting the risk of amnesia after epilepsy surgery. Shortages of amobarbital led to its substitution with sodium methohexital in the intracarotid methohexital procedure (IMP). We compared IAP scores (32 patients) with IMP scores (20 patients). Wada ipsilateral and contralateral memory scores were analyzed and compared, as was the relationship of these scores to the results of standard neuropsychological memory tests. There was no significant difference in Wada contralateral memory scores (first injection) between the IAP and IMP. Differences between the IAP and IMP in memory scores for the hemisphere ipsilateral to the epileptogenic focus (second injection) were significant ($P = 0.01$), patients who underwent the IMP manifesting a higher ipsilateral memory reserve. IAP scores related better to standard neuropsychological memory test scores than did IMP scores. The anesthetic drug used in Wada testing may affect lateralized memory assessment and prediction of postsurgical memory changes.

Keywords: Wada test; Methohexital; Amobarbital; Brevital; Epilepsy surgery; Memory

1. Introduction

During the last two decades, surgical resection of epileptogenic brain tissue has become an efficient treatment option for carefully selected patients with intractable seizures of focal origin [1]. About 80% of individuals with complex partial seizure disorder, particularly of temporal origin, either become seizure-free or enjoy a significant reduction in seizure frequency following surgery [1]. Success of surgery depends to a great extent on the selection of appropriate patients, which is based on a comprehensive preoperative evaluation to delineate the epileptogenic zone by means of video/EEG monitoring, structural and functional neuroimaging, neuropsychological assessment, and Wada testing.

The most important use of neuropsychological assessment in the context of epilepsy surgery is as an aid in the lateralization of hemispheric dysfunction that may be associated with the epileptogenic lesion. Because of the association between temporal lobe epilepsy (TLE) and memory deficits, the assessment of memory has become the most important part of the neuropsychological evaluation of surgical candidates who have TLE. The unique contribution made by each temporal lobe to the support of memory function can, however, be difficult to define with the standard neuropsychological assessment. It has been established that the degree of accuracy in predicting the

* Corresponding author. Fax: +9723 697 3992.
E-mail address: fani@hermes.tau.ac.il (F. Andelman).

1525-5050/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.yebeh.2006.08.001

presence of a dysfunction is considerably higher when the results of the standard neuropsychological tests are combined with the findings of the Wada procedure [2–5].

The purposes of the Wada test are to determine cerebral language dominance, assess the memory capacity of each cerebral hemisphere, and assist in determining the laterality of hemispheric dysfunction [5]. The underlying rationale of this procedure, first introduced by Wada in 1949 [6], is that temporary anesthetization of the cerebral hemispheres, one at a time, by injection of an anesthetic agent permits evaluation of the relative contribution made by each temporal lobe to the support of language and memory function. Lateralized memory dysfunction is inferred from the presence of an asymmetry in memory performance after both injections. In addition, intracarotid memory testing should reveal a reversible amnesia if the mesial temporal lobe structures contralateral to the seizure focus are dysfunctional. Since Scoville and Milner reported a case of loss of recent memory after bilateral hippocampal lesions [7], bilateral temporal lobectomy is no longer being performed. Amnesia may occur as a complication of unilateral temporal lobectomy, however, if the contralateral hemisphere is dysfunctional [8]. Despite the controversies and concerns surrounding the Wada procedure [9,10], Wada testing continues to be a standard method for the lateralization of memory function, prediction of postoperative amnesia, and assessment of the magnitude of postsurgical mild to moderate memory decline [11–14].

The Wada procedure has traditionally been performed with amobarbital. Because of the frequent interruptions in the supply of amobarbital during recent years, alternative drugs, such as etomidate, propofol, and methohexital (Brevital), are increasingly being used as transient anesthetic agents for temporary suspension of hemispheric functioning [15–20].

The purpose of the present study was to examine the results of Wada individual memory scores obtained by intracarotid injection of methohexital (intracarotid methohexital procedure (IMP)) and compare them with the results of the intracarotid amobarbital procedure (IAP), and to compare all these results with those of standard neuropsychological memory testing.

2. Methods

2.1. Subjects

Twenty patients with focal epilepsy underwent the IMP and Wada testing between the years 2003 and 2005 at the Tel-Aviv Sourasky Medical Center. They were all diagnosed as having TLE with complex partial seizures with or without secondary generalization and were candidates for epilepsy surgery as treatment of their intractable epilepsy. Each underwent Wada testing to determine cerebral language dominance and unilateral memory potential. The methohexital group included 14 patients with left TLE and 6 patients with right TLE. Their data were compared with historical data on 32 patients with TLE who had undergone IAP and Wada testing between the years 2000 and 2003 at the same center. These data were published elsewhere [21]. There were no statistically significant differences between the two groups in terms of age, gender, age at onset of epilepsy, proportion of patients with secondary generalization, proportion of patients with suspected mesial temporal sclerosis as seen on magnetic resonance imaging (MRI), proportion of anterior cerebral artery cross-flow, and proportion of cerebral language laterality (Table 1).

Table 1
Demographic data for the amobarbital and methohexital patient groups

	Methohexital	Amobarbital
Mean (SD) age	30.45 (6.63)	30.70 (7.45)
Male/female	9/11	18/14
Handedness, R/L	11/9	25/7
Mean (SD) age at onset	8.99 (5.67)	11.14 (5.57)
Proportion of GTCS[a]	11/9	17/5
Proportion of MTS	16/4	24/8
Proportion of cross-flow, yes/no	9/11	13/19
Language laterality, left/right/bilateral	14/4/2	26/6
Hemispheric side of seizure onset, left/right	14/6	19/13

[a] GTCS, generalized tonic–clonic seizures; MTS, mesial temporal sclerosis.

The selection criteria for both groups included a unilateral epileptogenic zone, no history of primary psychiatric diagnosis, and no mental retardation. All patients had undergone technically valid Wada testing. The laterality of the epileptogenic focus was determined by concordance of results of video/EEG monitoring, brain MRI, and, in selected patients, functional imaging such as positron emission tomography (PET). The entire study cohort underwent an extensive neuropsychological examination that included measures of general intelligence, memory, perception, language, motor, and executive functions. Characteristics of the patients who received methohexital are listed in Table 2; and those of the patients given amobarbital, reprinted from [21], in Table 3.

2.2. Intracarotid methohexital procedure

The IMP is based partially on the protocol developed at the University of Florida [15] and partially on the protocol of the Montreal Neurological Institute [22]. Diagnostic angiography including a vascular anatomy examination of the internal carotid artery distribution was performed before Wada testing. A catheter was placed in the internal carotid artery via a transfemoral approach. Intracarotid artery injection of 3 mg methohexital (Table 4) dissolved in a solution of 1 mg in 1 ml was administered via the catheter. Each hemisphere was injected twice: the purpose of the first injection was to determine cerebral language dominance, and the purpose of the second injection was to assess the memory potential of each hemisphere separately. All patients had undergone baseline language and memory testing the day before the procedure. The hemisphere ipsilateral to the epileptogenic lesion was injected first. Four patients did not receive both doses in the right hemisphere: one patient was obtunded, and in the other three patients, the length of hemiparesis was relatively long (range: 165–300 seconds), allowing both language testing and presentation of memory items on a single injection.

Language testing was begun immediately on the occurrence of complete hemiplegia (0/5) after the first methohexital injection. The language test included repetition of single words and sentences, comprehension of instructions, and object naming. Speech arrest, disruption in expressive language tasks, and literal or verbal paraphasias on recovery were used as signs of cerebral language lateralization. After grip strength returned to normal (5/5), the second injection was performed in the same hemisphere for the purpose of memory testing. Immediately on occurrence of hemiplegia, eight objects were presented for memorization over a 60- to 90-second interval during the hemiplegia, with the degree of hemiplegia monitored by the neurologist every 15 seconds. Real objects rather than pictures or written words were chosen for memory testing to avoid, as much as possible, the confounding effects of language on the assessment

Table 2
Characteristics of patients given methohexital

Patient	Age	Age at onset	Gender	Handedness	Full scale IQ	Years of education	Side of seizure onset	Language lateralization
1	29	2	F	Left	100	12	Left	Left
2	31	.75	M	Left	74	8	Left	Right
3	36	8	F	Right	75	10	Left	Left
4	43	2	F	Left	90	12	Left	Left
5	32	5	M	Right	100	12	Left	Left
6	32	14	F	Right	80	10	Right	Left
7	24	15	F	Left	100	10	Left	Bilateral
8	29	3	M	Right	100	12	Right	Left
9	46	31	M	Right	90	10	Left	Left
10	22	13	F	Left	83	8	Right	Left
11	46	1	M	Right	80	11	Right	Left
12	20	15	M	Left	90	12	Left	Right
13	30	4	F	Right	80	12	Left	Left
14	32	18	F	Left	90	15	Right	Right
15	33	11	F	Left	100	12	Right	Right
16	17	5	M	Right	80	8	Left	Left
17	25	7	M	Right	70	9	Left	Left
18	26	19	F	Left	100	14	Left	Left
19	40	27	M	Right	90	12	Left	Left
20	16	1	F	Right	95	11	Left	Bilateral

Table 3
Characteristics of patients given amobarbital

Patient	Gender	Age	Handedness	Years of education	Side of focus	Age at onset	Full scale IQ	Language lateralization
1	M	27	Left	10	Left	4	73	Right
2	F	27	Left	15	Left	5	85	Right
3	F	45	Right	12	Left	23	86	Left
4	F	37	Right	14	Left	8	100	Left
5	M	41	Left	12	Left	21	109	Left
6	F	38	Right	14	Left	19	104	Left
7	M	31	Right	10	Left	15	80	Left
8	M	30	Left	12	Left	.25	90	Right
9	F	30	Right	12	Left	20	90	Left
10	F	39	Right	10	Left	11	80	Left
11	M	16	Right	10	Left	8	85	Left
12	F	36	Right	9	Left	16	82	Left
13	F	48	Right	12	Left	22	83	Left
14	M	23	Right	12	Left	9	94	Left
15	F	22	Right	14	Left	8	96	Left
16	F	22	Right	13	Left	3	82	Left
17	M	33	Left	12	Left	4	73	Left
18	M	19	Right	12	Left	14	100	Left
19	M	17	Right	12	Left	7	107	Left
20	F	47	Right	10	Right	1	84	Left
21	M	34	Right	15	Right	2	100	Left
22	F	26	Right	12	Right	8	100	Left
23	M	27	Right	8	Right	7	81	Left
24	F	25	Right	12	Right	.75	74	Left
25	M	43	Right	11	Right	.5	85	Left
26	F	24	Left	12	Right	12	91	Right
27	M	36	Right	12	Right	16	77	Right
28	M	25	Right	11	Right	5	88	Left
29	M	14	Left	8	Right	.75	110	Left
30	M	26	Right	12	Right	8	80	Right
31	M	24	Right	10	Right	17	86	Left
32	M	19	Right	12	Right	9	87	Left

Source. Reprinted, with permission, from Andelman et al. [21].

of memory as a reflection of mesial temporal lobe function [23]. Memory testing started immediately after complete recovery of motor and language functions. The recognition memory score, assessed by identification of the target stimulus among an array of two foils, was used as an index of memory function [24]. An identical procedure with another set of objects was used to test the other hemisphere immediately on placement of the catheter

Table 4
Length of hemiparesis and methohexital dosage

	Right hemisphere	Left hemisphere
Length of hemiparesis (sec)		
First injection	183.72 (93.57)[a]	174.76 (67.37)
Second injection	199.55 (93.52)	189.07 (53.95)
Dosage (mg)		
First injection	3.12 (0.33)	3.16 (0.51)
Second injection	3.13 (0.81)	3.29 (0.9)

[a] Mean (SD).

in the other hemisphere. Two Wada memory scores were computed for each patient: percentage of memory items recognized on the first, ipsilateral injection (i.e., the contralateral memory score), and percentage of memory items recognized on the second, contralateral injection (i.e., the ipsilateral memory score).

2.3. Neuropsychological memory tests

The presurgical neuropsychological assessment included testing of memory function. Results of the Rey Auditory Verbal Learning Test (RAVLT) [25] and Rey Complex Figure (RCF) [26] were chosen for analysis because these tests have been standardized for the Hebrew language. Scores for total learning of 15 words (RAVLT-T, representing the sum of the first five trials), scores for best learning (RAVLT-5, fifth trial score), and scores for delayed recall (RAVLT-8, eighth trial score), as well as long-term recall of the RCF, were used as learning and memory indices.

2.4. Statistical analysis

Univariate statistical analysis examined group differences on a variety of demographic variables. χ^2 analysis was used to examine group differences in hand dominance, gender, generalized tonic–clonic seizures mesial temporal sclerosis, cross-flow, and language dominance. The t test and Mann–Whitney test were used to examine group differences in age, age at onset of epilepsy, IQ, and neuropsychological memory test results. A series of two-way analyses of variance (ANOVAs) were used to determine the effects of group and the variables lesion lateralization, hand dominance, cerebral language dominance, and side of lesion/language, as well as interactions of these variables, on the ipsilateral and contralateral Wada memory scores. This analysis was followed by the Mann–Whitney test to examine each group separately. Finally, the Pearson correlation coefficient was used to examine relationships between the two Wada memory measures and standard neuropsychological memory measures in all patients together and in each patient group separately. This study was approved by the local ethics committee.

3. Results

The results of the univariate analysis revealed no statistically significant demographic differences between the two patient groups. In addition, there were no statistically significant group differences with respect to hand dominance, cerebral language dominance, laterality of epileptogenic focus, or number of patients with mesial temporal sclerosis or generalized tonic–clonic seizures. A t test used to compare the results of the standard neuropsychological tests in the two patient groups, without reference to Wada performance, revealed no statistically significant difference in memory performance (Table 5). Methohexital Wada test results for individual patients are summarized in Table 6. Amobarbital and methohexital group mean memory results are summarized in Table 7.

The results of the two-way ANOVA revealed no statistical difference in Wada contralateral memory (i.e., memory ability of the healthy hemisphere) scores between the methohexital group and the amobarbital group. On the other hand, there was a significant difference between the two groups in Wada ipsilateral memory scores ($P = 0.01$), with the methohexital group demonstrating a significantly higher level of memory functioning in the hemisphere ipsilateral to the epileptogenic focus. No effects of lesion lateralization, language, hand dominance, or interactions were observed.

The relationship between Wada memory test performance and results of the standard neuropsychological memory tests was examined using the Pearson correlation coefficient analysis in all 52 patients and for each of the two patient groups. Results of the entire cohort analysis revealed a significant relationship between Wada ipsilateral memory scores and performance on standard neuropsychological tests: the better the patients' performance on standard neuropsychological tests, the higher were their ipsilateral Wada memory scores (delayed recall of RCF: $P = 0.03$, RAVLT-5: $P = 0.02$, RAVLT-T: $P = 0.02$, RAVLT-8: $P = 0.02$). The relationship between contralateral memory scores and neuropsychological test results was not statistically significant (Table 8).

Table 5
Neuropsychological memory test results[a]

	RAVLT-5	RAVLT-T	RAVLT-8	RCF-LTM
Amobarbital				
LH patients ($n = 19$)	10.90(0.68)	45.05(2.04)	7.21(0.64)	11.87(2.24)
RH patients ($n = 13$)	11.39(0.98)	44.92(2.36)	7.00(1.13)	8.92(2.23)
Methohexital				
LH patients ($n = 14$)	9.91(0.39)	42.36(1.99)	6.73(0.45)	11.27(1.70)
RH patients ($n = 6$)	11.17(0.79)	46.67(4.24)	8.67(0.84)	10.08(2.61)

[a] Numbers represent raw data and are group means (SD) of the number of items correctly recalled in each memory test: RCF-LTM, long-term recall of the Rey Complex Figure (out of 36); RAVLT-5, best learning trial of the Rey Auditory Verbal Learning Test (out of 15); RAVLT-T, total learning of the Rey Auditory Verbal Learning Test (out of 75); RAVLT-8, delayed recall trial of the Rey Auditory Learning Test (out of 15). LH patients, patients with left hemisphere epileptic onset; RH patients, patients with right hemisphere epileptic onset.

Table 6
Methohexital Wada test results for individual patients

Patient	Language lateralization	% Memory left[a]	% Memory right[b]	ACA crossflow	Consciousness		Injection dosage (mg)			
					Left injection	Right injection	First left	Second left	First right	Second right
1	Left	25	100	Mild	Alert	Alert	3	2	3	2
2	Right	0	100	None	Alert	Obtunded	3	2	4	—
3	Left	12.5	75	Mild	Alert	Alert	5	4	4	3
4	Left	75	62.5	None	Alert	Alert	3	5	3	2
5	Left	0	100	Moderate	Alert	Alert	3	5	3	3
6	Left	100	—	None	—	Alert	—	—	3.5	—
7	Bilateral	62.5	100	Moderate	Alert	Alert	3	3	3	3
8	Left	75	75	Mild	Alert	Alert	3	3	3	3
9	Left	87.5	87.5	None	Drowsy	Alert	3	2.5	3	3
10	Left	75	37.5	Mild	Alert	Alert	5	—	6	—
11	Left	87.5	25	Mild	Alert	Alert	3	4	3	4
12	Right	100	100	None	Alert	Alert	3	3	3	—
13	Left	100	87.5	None	Alert	Alert	3	3	3	3
14	Right	75	100	None	Alert	Alert	3	3	3	3
15	Right	100	62.5	None	Alert	Alert	3	3	3	3
16	Left	62.5	87.5	None	Alert	Alert	3	3	3	3
17	Left	12.5	62.5	None	Drowsy	Drowsy	3	3	3	3
18	Left	37.5	75	Mild	Alert	Alert	4	3	3	3
19	Left	100	75	Mild	Alert	Alert	3	3	3	3
20	Bilateral	75	75	None	Drowsy	Drowsy	3	3	3	3

[a] Percentage of items recognized by the left hemisphere on right injection.
[b] Percentage of items recognized by the right hemisphere on left injection.

Table 7
Summary of amobarbital versus methohexital Wada memory scores by patient group[a]

	Ipsilateral memory	Contralateral memory
Methohexital		
All patients ($n = 20$)	55.26 (35.43)	84.91 (13.19)
LH patients ($n = 14$)	53.60 (29.80)	84.7 (12.3)
RH patients ($n = 6$)	60 (29.8)	85.4 (12.2)
Amobarbital		
All patients ($n = 32$)	30.74 (30.62)	81.17 (11.44)
LH patients ($n = 19$)	32.87 (33.04)	80.35 (11.14)
RH patients ($n = 13$)	27.63 (27.69)	82.37 (12.23)

[a] Numbers are group means (SD) of the percentage correct recognition. LH patients, patients with left hemisphere epileptic onset; RH patients, patients with right hemisphere epileptic onset.

Table 8
Correlations between Wada memory scores and neuropsychological test results for all patients ($n = 52$)[a]

	RCF-LTM	RAVLT-5	RAVLT-T	RAVLT-8
Contralateral memory score				
r	0.12	0.25	0.09	0.2
P	0.42	0.07	0.51	0.16
Ipsilateral memory score				
r	0.32	0.32	0.32	0.35
P	0.03	0.02	0.02	0.02

[a] RCF-LTM, long-term recall of the Rey Complex Figure; RAVLT-5, best learning trial of the Rey Auditory Verbal Learning Test; RAVLT-T, total learning of the Rey Auditory Verbal Learning Test; RAVLT-8, delayed recall trial of the Rey Auditory Learning Test.

Analysis of the correlation for each patient group separately revealed that the relationship between ipsilateral Wada memory performance and most standard neuropsychological memory test scores was higher for the patients who underwent the amobarbital Wada test than for those who had the methohexital Wada test (RAVLT-5: $P = 0.02$, RAVLT-T: $P = 0.04$, RAVLT-8: $P = 0.04$) (Table 9). No patients had postoperative amnesia.

4. Discussion

The main result of this study is the demonstration of a significant difference in ipsilateral memory function during Wada testing when it is performed with sodium amobarbital versus sodium methohexital. As none of our patients underwent both the IAP and IMP, a direct comparison of the action of the two drugs could not be made, and so, the results of this study are correlative in nature. Patients who underwent the IMP exhibited a higher memory capacity in the hemisphere ipsilateral to their epileptogenic focus. This effect was not observed for the memory capacity of the contralateral, healthy hemisphere. These results were not associated with laterality of the epileptogenic focus, cerebral language laterality, or any demographic or angiography procedure variables. They were, however, associated with the results of standard neuropsychological tests in all patients: the higher the patients' scores on standard memory tests, the higher were their ipsilateral Wada memory scores, particularly in the amobarbital group.

These results support the findings of earlier studies that the methohexital Wada procedure can yield important presurgical information on the risk of postsurgical amnesia [15–17]. The results of our study, however, suggest that

Table 9
Correlations between amobarbital versus methohexital Wada memory scores and neuropsychological test results[a]

		RCF-LTM	RAVLT-5	RAVLT-T	RAVLT-8
Contralateral memory	Amobarbital[b]				
	r	0.11	0.25	0.08	0.14
	P	ns	ns	ns	ns
	Methohexital[c]				
	r	0.16	0.44	0.56	0.41
	P	ns	*0.08*	0.02	ns
Ipsilateral memory	Amobarbital[b]				
	r	0.37	0.42	0.33	0.35
	P	*0.09*	0.02	0.04	0.04
	Methohexital[c]				
	r	0.36	0.45	0.17	0.39
	P	ns	0.08	ns	ns

[a] RCF-LTM, long-term recall of the Rey Complex Figure; RAVLT-5, best learning trial of the Rey Auditory Verbal Learning Test; RAVLT-T, total learning of the Rey Auditory Verbal Learning Test; RAVLT-8, delayed recall trial of the Rey Auditory Learning Test.
[b] $n = 32$.
[c] $n = 20$.

the inferred Wada memory function of the hemisphere ipsilateral to the epileptogenic lesion depends on the anesthetic drug used. Moreover, although ipsilateral Wada memory scores correlated with the results of standard neuropsychological memory tests in both patient groups, these correlations were significantly higher for the amobarbital than for the methohexital group. These results raise the question of the depth and variability of distribution of the anesthetic effect of different drugs on the epileptogenic hemisphere during the Wada procedure, the results affecting neuropsychological interpretations.

Methohexital is an ultrashort-acting barbiturate with an onset of action of <1 minute and duration of action of <10 minutes. Methohexital was used in the past to activate epileptogenic foci at low doses (<100 mg) and to suppress excitatory synaptic transmission at high doses [27,28]. It has also been used as an anesthetic in the Wada test in much smaller dosages [15–17]. Isnard et al. [16] reported their 12 years of experience using methohexital for Wada testing in 75 patients, 19 of whom had their memory tested as well. A single dose of 4 mg methohexital diluted with 10 ml saline solution was injected over 10 seconds. The authors suggest that the clinical manifestations induced by methohexital are similar to those observed with amobarbital. They consider that there are two major advantages of methohexital over amobarbital: the first is a short hemispheric narcosis, which makes it possible to explore the two carotid arteries during the same session and limits the risk of drug diffusion to the two hemispheres, and the second is the rare occurrence of vigilance troubles, such as the drowsiness frequently observed during amobarbital testing.

Buchtel et al. [15] reported that methohexital could be successfully used as an anesthetic in Wada testing. Their procedure involved the use of 5 mg methohexital administered in two consecutive injections on each side of 20 epilepsy surgery patients. The authors concluded that the results of language and memory testing in the Wada test are equivalent for both anesthetics. In contrast to Buchtel and colleagues' impressions, the results of our study suggest different memory functioning of the hemisphere ipsilateral to the epileptogenic focus under methohexital versus amobarbital, as measured by the memory tests.

High ipsilateral methohexital Wada memory scores relative to amobarbital scores in our study may result from the short action and different diffusion of the former drug. As noted by Jones-Gotman et al. [20], because methohexital is an ultrashort-acting barbiturate, it requires either very brief tests or re-injection. In the case of re-injection, the effect of the drug may have waned during testing, resulting in an unpredictable level of anesthesia during the administration of cognitive tests.

In addition to the high memory scores following the second methohexital injection observed in our study, some informal observations during the IMP included a relatively low incidence of paraphasias and a higher incidence of spared language comprehension. Although there was no question about the determination of laterality of cerebral language production in any of our patients, cerebral language comprehension seemed to be bilaterally represented in more patients during methohexital Wada testing than during amobarbital Wada testing. Because of the rare occurrence of obtundation or agitation during methohexital Wada testing, however, these observations may actually be more reflective of lateralized cerebral dominance of language comprehension than they are of expression and may be correlated better with functional MRI results. A formal analysis of these observations is currently underway at our center.

In conclusion, the major finding of this study is the demonstration of a higher memory potential of the hemisphere ipsilateral to the epileptogenic focus during Wada testing performed with methohexital compared with amobarbital. The higher ipsilateral memory scores, resulting in smaller asymmetry values, obtained with the IMP as compared with the IAP raise the question of which of these tests more accurately reflects the extent of lateralized hemispheric memory dysfunction. Although both tests seem to predict postsurgical amnesia, high correlations of IAP memory results with the standard memory test results suggest that the degree of adequacy of lateralized memory assessment is possibly higher with the IAP than with the IMP. The results of our study suggest that the narcotic drug used during Wada testing may be a factor in prediction of postsurgical memory changes, which may be crucial in some cases, particularly in cases of ''reversed asymmetry'' [29].

The results of our previous study conducted on patients who underwent the IAP as well as pre- and postsurgical memory testing [21] supported the view that the risk for memory decrements following mesial temporal lobe surgery is inversely related to the functional adequacy of the tissue to be resected, and supported the functional adequacy model of hippocampal function [11]. As only nine patients in our methohexital patient sample have undergone postsurgical neuropsychological follow-up thus far, we cannot provide any reliable conclusions regarding the relationship between the methohexital Wada memory results and changes in postsurgical memory status. Comparing IAP and IMP results, as well as pre- and postsurgical memory scores, would provide the best answer to the question of the validity of amobarbital versus methohexital Wada testing in predicting patients' postsurgical memory status. Future studies should examine the relationship of methohexital Wada language and memory results to functional imaging results [30–33] and compare them with IAP results.

Acknowledgments

We thank the staff of the Interventional Angiography Unit; Esther Shabtai for statistical analysis; and Esther Eshkol for editorial assistance.

References

[1] Engel J, Wieser HG, Spencer D. Overview: surgical therapy. In: Engel J, Pedley T, editors. Epilepsy: a comprehensive textbook. New York: Lippincott-Raven; 1997. p. 1673–6.
[2] Wada J, Rasmussen T. Intracarotid injection of sodium amytal for the lateralization of cerebral dominance: experimental and clinical observations. J Neurosurg 1960;17:266–82.
[3] Branch C, Milner B, Rasmussen T. Intracarotid sodium amytal for the lateralization of cerebral speech dominance: observations in 123 patients. J Neurosurg 1964;21:399–405.
[4] Milner B, Branch C, Rasmussen T. Study of short-term memory after intracarotid injection of sodium amytal. Trans Am Neurol Assoc 1962;87:224–6.
[5] Loring DW, Meador KJ, Lee GP, King DW. Amobarbital effects and lateralized brain function. New York: Springer-Verlag; 1992. p. 59–62.
[6] Wada J. A new method for the determination of the side of cerebral speech dominance: a preliminary report of the intracarotid injection of sodium amytal in man. Igaku to Seibutsugaki 1949;14:221–2. [In Japanese].
[7] Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. J Neurol Neurosurg Psychiatry 1957;20:11–21.
[8] Oxbury S, Oxbury J, Renowden S, Squier W, Carpenter K. Severe amnesia: an unusual late complication after temporal lobectomy. Neuropsychologia 1997;35:975–88.
[9] Meador KJ, Loring DW. The Wada test: controversies, concerns, and insight. Neurology 1999;52:1535–6.
[10] Grote CL, Meador K. Has amobarbital expired? Neurology 2005;65:1692–3.
[11] Chelune GJ. Hippocampal adequacy versus functional reserve: predicting memory-functions following temporal lobectomy. Arch Clin Neuropsychol 1995;10:413–32.
[12] Martin RC, Grote CL. Does the Wada test predict memory decline following epilepsy surgery? Epilepsy Behav 2002;3:4–15.
[13] Valton L, Mascott C. Quelle est la place du test de Wada dans le bilan prechirurgical des epilepsies pharmacoresistantes chez l'adulte? Rev Neurol (Paris) 2004;160:4S01–6.
[14] Meador KJ, Loring DW. The Wada test for language and memory lateralization [commentary]. Neurology 2005;65:659.
[15] Buchtel HA, Passaro EA, Selwa LM, Deveikis J, Gomez-Hassan D. Sodium methohexital (brevital) as an anesthetic in the Wada test. Epilepsia 2002;43:1056–61.
[16] Isnard J, Garde P, Fischer C, Duquesnel J, Mauguiere F. Manifestations cliniques et electro-encephalographiques lors du test de Wada par injection intra-carotidienne de methohexital (brietal). Rev Neurol (Paris) 1994;150:266–73.
[17] Bacia T, Bendarzewska-Nawrocka B, Szymanska O, Dowzenko A, Sadowski Z. A comparison of Wada test for cerebral speech dominance by use of amytal or brietal. Neurol Neurochir Pol 1998;32(Suppl. 2):247–61.
[18] Takayama M, Miyamoto S, Ikeda A, et al. Intracarotid propofol test for speech and memory dominance in man. Neurology 2004;63:510–5.
[19] Mikuni N, Takayama M, Satow T, et al. Evaluation of adverse effects in intracarotid propofol injection for Wada test. Neurology 2005;65:1813–6.
[20] Jones-Gotman M, Sziklas V, Djordjevic J, et al. Etomidate speech and memory test (eSAM): a new drug and improved intracarotid procedure. Neurology 2005;65:1723–9.
[21] Andelman F, Kipervasser S, Neufeld M, Kramer U, Fried I. Predictive value of Wada memory scores on postoperative learning and memory abilities in patients with intractable epilepsy. J Neurosurg 2006;104:1–7.
[22] Djordjevic J, Jones-Gotman M. Psychological testing in presurgical evaluation of epilepsy. In: Shorvon S, Perucca E, Fish D, Dodson E, editors. The treatment of epilepsy. Oxford: Blackwell Science; 2004. p. 699–715.
[23] Kirsch HE, Walker JA, Winstanley FS, et al. Limitations of Wada memory asymmetry as a predictor of outcomes after temporal lobectomy. Neurology 2005;65:676–80.
[24] Andelman F, Neufeld M, Reider-Groswasser I, Kramer U, Segev Y, Fried I. Presurgical neuropsychological assessment: the Wada test. Harefua 2000;138:440–4. [In Hebrew].
[25] Vakil E, Blachstein H. Rey auditory verbal learning test: developmental norms for adults and the sensitivity of different memory measures to age. Clin Neuropsychol 1997;11:356–69.
[26] Meyers JE, Meyers KL. Rey Complex Figure Test and recognition trial. Odessa: Psychological Assessment Resources 1995.
[27] Morrell F. Secondary epileptogenesis in man. Arch Neurol 1985;42:318–35.
[28] Morrell F. Varieties of human secondary epileptogenesis. J Clin Neurophysiol 1989;3:227–75.
[29] Sabsevitz DS, Swanson SJ, Morris GL, Mueller WM, Seidenberg M. Memory outcome after left anterior temporal lobectomy in patients

with expected and reversed Wada memory asymmetry scores. Epilepsia 2001;42:1408–15.
[30] Richardson MP, Strange BA, Duncan JS, Dolan RJ. Memory fMRI in left hippocampal sclerosis: optimizing the approach to predicting postsurgical memory. Neurology 2006;66:699–705.
[31] Richardson MP, Strange BA, Thompson PJ, Baxendale SA, Duncan JS, Dolan RJ. Pre-operative verbal memory fMRI predicts post-operative memory decline after left temporal lobe resection. Brain 2004;127:2419–26.
[32] Rabin ML, Narayan VM, Kimberg DY, et al. Functional MRI predicts postsurgical memory following temporal lobectomy. Brain 2004;127:2286–98.
[33] Papanicolaou AC, Simos PG, Castillo EM, et al. Magnetocephalography: a noninvasive alternative to the Wada procedure. J Neurosurg 2004;100:867–76.