

THE INTRACAROTID AMOBARBITAL PROCEDURE (WADA TEST) WITH TWO PROTOCOLS COMBINED, MONTREAL AND SEATTLE

PAULO J.M. LEITE*, ROSANA PEREIRA***, DIOGO F. ALMEIDA****, MARCOS C. SANDMANN*,
PAULO GÉSAR SOUZA*****, RONEI SANDRINNI*****, JORGE KANEGUZUKO*****,
PAULO ROBERTO M. DE BITTENCOURT**

ABSTRACT - The intracarotid amobarbital procedure was carried out in 8 male and 7 female candidates to temporal lobectomy, and a female candidate to frontal lesionectomy, aged 18-50 (mean 32.5) years. Language and memory were tested after injection in each hemisphere. Both were measured by the Montreal procedure. In 9 patients language and memory were evaluated with the Seattle procedure too. In 12 patients the left hemisphere was dominant for language; three had bilateral dominance. In 1 patient the Seattle procedure demonstrated the dominant hemisphere by relatively slowness of speech during the drug effect in the left hemisphere. Memory was defined to be in the left hemisphere in 12 patients, in the right in 2, bilateral in 1 and in another lateralization was not possible. In 1 patient memory dominance was determined by the Montreal protocol alone because of lack of cooperation. These early results indicate that the methods may be complementary for determination of language and memory dominance in epilepsy surgery candidates.

KEY WORDS: amobarbital (Wada) test, epilepsy surgery, language, memory.

Procedimentos do amobarbital intracarotídeo (teste de Wada) com dois protocolos combinados, Montreal e Seattle

RESUMO - O teste do amobarbital intracarotídeo foi realizado em 8 homens e 7 mulheres candidatas a lobectomia temporal e em uma mulher candidata a lesionectomia frontal, com idades de 18-50 (média 32,5) anos. Linguagem e memória foram testadas após a injeção do amobarbital em cada hemisfério cerebral. Todos os pacientes foram avaliados pelo método de Montreal e 9 também pelo método de Seattle. Em 12 pacientes o hemisfério cerebral esquerdo foi dominante para linguagem e em 3 pacientes houve dominância bilateral. Em uma paciente a linguagem foi determinada apenas através do método de Seattle, com lentificação relativa da fala, sob ação da droga no hemisfério cerebral esquerdo. Dominância da memória à esquerda foi observada em 12 pacientes, à direita em 2, bilateral em 1 e em outro não foi lateralizada. Dominância da memória foi definida apenas através do método de Montreal em um paciente, devido à pouca cooperação. Estes resultados preliminares indicam que os métodos podem ser complementares para a determinação da dominância da linguagem e memória em especial nos candidatos à lobectomia temporal.

PALAVRAS-CHAVE: teste do amobarbital (Wada), cirurgia de epilepsia, linguagem, memória.

The majority of patients with temporal lobe epilepsy who are refractory to medical treatment and who are submitted to temporal resection have substantial improvement of seizure control¹¹. The possibility that complications related to memory and language may arise due to the surgical procedure must be evaluated before surgery^{4,6,12,13,17}. The intracarotid amobarbital procedure (Wada test) was introduced by Dr. Juhn Wada to determine the side of hemispheric dominance for language^{26,27}. In

*Neurologist, **Head of Neurology and EEG Services, ***Speech Therapist****, *****Medical student, *****Radiologist. Program of Epilepsy Surgery, Hospital Nossa Senhora das Graças, Curitiba: Aceite: 4-fevereiro-1997.

1960 Milner and colleagues attached to the method the evaluation of memory¹⁶. The procedure of the amobarbital test is done in different ways in various epilepsy centers around the world^{1,4,9,11,12,15,19,20}. Recently the amobarbital procedure has been proposed as an additional method for the lateralization of the epileptogenic area in patients with temporal lobe epilepsy^{8,13,21}.

Language deficits have been described after temporal resection^{5,25}, but memory is the critical issue, to which more attention has been given^{4,8,14,19,20,23,28}. Global amnesia has been reported after temporal lobectomies in only a few cases in the history of epilepsy surgery^{4,19}. But selective deficits of certain aspects of memory are known to take place more commonly and they have been extensively discussed in the literature^{4,12,17,19,23,28}. When surgery in the dominant hemisphere involves the posterior part of the temporal lobe, certain frontal or parietal regions, cortical language mapping techniques may be indicated^{3,5,18}.

The objective of this study was to compare the clinical use of two routines of the amobarbital (Wada) test. We used the protocols used in Montreal⁷ and in Seattle⁴. These protocols were designed to lateralize memory, language and epileptogenic area in patients with temporal lobe epilepsy who are candidates to temporal resection. This study was designed to analyse the value of the combination of Montreal and Seattle IAP protocols for the lateralization of memory and language dominance, and has been published as an abstract¹⁰.

METHODS

This study was carried out in patients evaluated by Hospital Nossa Senhora das Graças Epilepsy Surgery Program²¹. Patients were asked to undergo the amobarbital (Wada) test when a presurgical investigation indicated that they were good candidates for surgery involving eloquent cerebral regions. All patients underwent a structured investigation including medical, neurological, psychiatric and neuropsychological evaluation. Prolonged monitoring with digital videoelectroencephalography was carried out with the objective of recording enough ictal and interictal material to locate the epileptogenic area. Sphenoidal electrodes were used in all patients with suspected temporal lobe epilepsy²². Patients who at the end of this investigation still needed additional invasive investigation, including subdural plates and electrocorticography, were placed on a waiting list for the time when these procedures are fully established in our center.

Specialised imaging procedures including CT and MR were used in all cases. Hippocampal volumes were determined in all cases of possible temporal lobe epilepsy and in many others too, as part of a control group in a separate research project^{3,21}. Ictal and interictal SPECT were carried out in selected cases.

The Curitiba amobarbital procedure

A brief evaluation was carried out before the test, to establish the patient's normal pattern of memory and language. The opportunity was used to familiarize patients with the technique, and to find out how the patients dealt with the less demanding test situation at his hospital room. Any parts of the test, including objects or cards, were excluded from the actual test situation if the patient had difficulties with it. The test procedure was carried out in a digital angiography room, by a team used to complex vascular procedures including embolization of cerebral vascular or tumoral lesions and intracerebral navigation techniques. The patient was fitted with silver/silver chlorided electrodes for continuous monitoring of the EEG, carried out in a portable 8-channel analog machine. Patterns of slowing of the EEG activity ipsilateral to the injection were used to define the timing of the tests. A 4-vessel angiogram was carried out to assess the intracranial vasculature. The transfemoral Seldinger technique was used, and specific attention was given to possible side-to-side shunting of the cerebral circulation. Material and equipment were at hand in case selective catheterization of cerebral vessels was warranted during the test situation.

Each patient underwent catheterization of the internal carotid artery. The amount of amobarbital to be injected was 112 mg for males and 100 mg for females. The solution was prepared by diluting amobarbital (250 mg) in 5 ml of saline. The side of surgical interest was injected first, and after at least 30 minutes, the other side underwent the same procedure. The Montreal⁷ and the Seattle⁴ procedures were done simultaneously. The Montreal items were shown during the Seattle procedure.

The Montreal procedure consists of the presentation of 5 visual items during the effect of amobarbital, as defined by the lateralization of the slowing observed in the EEG and by the clinical situation of the patient. After the effect of the drug has disappeared the patient is asked to recognize those items which were presented during the effect of the drug. We considered 4 or more items correct "passing" and fewer than 4 as "failing". The

hemisphere dominance for memory is defined as the side in which injection induces the patients to make 2 or more errors in the post injection recognition of the 5 items⁷.

The Seattle procedure involves 3 steps: naming of objects, reading phrases and testings of immediate memory. There are 20 different items which are shown continuously over a period of time. Basically the test is carried out continuously during the effect of amobarbital. The result is quantitative, the patient receiving a mark of 0-100%. Error rates of 0 to 49% are considered "passing" and those "failing" are 50% or more. The clinical effect of the amobarbital is contralateral hemiplegia and speech dysfunction if this is the speech dominant hemisphere, occurring immediately upon right injection of the drug. The EEG shows a diffuse slowing followed by a lateralization of delta waves in the ipsilateral hemisphere. When the effect of amobarbital has waned, usually some 15 minutes after the injection, the visual items are presented to the patient together with other items. The patient is then asked to choose the items that had been shown during the effect of amobarbital⁶. In both procedures language dominance is evaluated during the test of memory, by the observation of errors in naming, speech blockade and receptive and expressive dysphasia.

RESULTS

We evaluated 16 patients in the period between February 1994 and February 1996. There were 8 males and 7 females with refractory temporal lobe epilepsy and 1 female with refractory frontal lobe epilepsy secondary to trauma. They were aged 18-50 years (Table 1). Seven of those patients were submitted only to the Montreal procedure, and nine to both protocols. Twelve of the patients were shown to be left hemisphere dominant for language and three had bilateral language dominance. In one patient language dominance could be determined in a definitive manner by the Seattle procedure only. The patient did not have a dysphasia or speech blockage, only slowness of speech during testing when was compared to the non-dominant hemisphere.

Table 1. Results of the intracarotid amobarbital (Wada) procedure.

Patient	Age	Sex	IQ	Speech dominance (M/S)	Memory dominance (M/S)
RMK	43	f	95	left/-	left/-
RTM	33	f	97	none/left	left/left
AA	30	f	89	left/-	left/-
LCS	32	m	117	left/-	right/-
VH	18	m	104	bilateral/-	right/-
RAP	32	f	82	left/left	left/left
OBD	30	m	67	bilateral/bilateral	left/none
CGF	37	f	102	left/left	left/none
MAB	38	f	95	left/-	left/-
ES	23	f	94	bilateral/bilateral	bilateral/bilateral
OB	50	m	93	left/-	left/-
HCC	32	f	88	left/left	left/left
JDF	21	m	75	left/left	none/none
AR	34	m	94	left/-	left/-
VHM	29	m	106	left/left	left/left
NM	38	m	105	left/left	left/left

Memory dominance was determined to be in the left hemisphere in 12 patients, in the right hemisphere in two and bilateral in one patient. In one patient (n.1, Table 1) memory dominance was determined by the Montreal procedure alone. In another patient memory lateralization was not possible with either method. This particular patient was submitted to a left temporal lobectomy without any relevant changes in memory after surgery. One of the bilateral dominant patients had suffered trauma early in life. In one patient with borderline IQ, memory dominance was determined by the Montreal procedure alone, because cooperation was not compatible with the performance needed for the Seattle procedure.

Lateralization of the epileptogenic area by the amobarbital procedure was correlated with EEG and MRI in 11 of 15 patients. Four patients were submitted to temporal lobectomy on the dominant hemisphere. In one surgery did not improve seizure control. Two have had greater than 80% improvement in seizure frequency; 6 patients are seizure free. Two are scheduled to have invasive monitoring before their epileptogenic area can be resected.

Follow-up of the patients submitted to surgery is 2-24 (mean 12.7) months. Two of the patients have complained of neurological or psychiatric deficits after the temporal lobectomy. In one case the patient had a major depressive episode after surgery; the other patient developed a resersible hemiparesis contralateral to a right temporal lobectomy. In another case the patient reported a worsening of her preoperative memory deficit. She, as well as the others, have not had deficits demonstrated on clinical or specific testing, when pre and post-operative testing with the WAIS and Weschler memory scales was compared. In one case memory and speech were determined to be on the same side of the epileptogenic region, the left temporal lobe. The patient underwent a resection of the more medial aspects of the left temporal lobe, rather than en-bloc resection. The patient has been seizure free for 12 months. In another case of left temporal lobectomy with bilateral dominance for memory (patient n. 13, Table 1) no significant deficit was documented after surgery.

DISCUSSION

The objective of this paper was to evaluate the efficacy of two different protocols of the Wada (amobarbital) test in the determination of language and memory dominance in candidates to temporal lobectomy. Our experience suggest that there may be critical differences between the two methods. In the Seattle⁴ procedure memory performance is evaluated during the effect of the drug. Consequently it gives a more comprehensive report of the state of memory and language during the test session. The Seattle procedure is complex for patients and for those carrying out the tests, and some patients are not able to perform well enough in the test environment and cannot complete the procedure. The Montreal⁷ procedure is simple, fast, and relatively easy for patients and for those carrying out the test.

Language function is assessed more comprehensively by the Seattle procedure⁴. In one of our cases a rare situation occurred: we could only lateralize language because of a relative slowing of speech during the effect of the amobarbital in the left hemisphere. In this particular case the patient had no dysphasia or naming error during the drug effect in the left hemisphere. In two patients lateralization of memory was only possible with the Montreal⁷ procedure. The patient with borderline IQ did not collaborate enough for the Seattle procedure; another patient had no demonstrable memory deficit with the Seattle procedure with injection in either hemisphere.

The amobarbital (Wada) test^{16,26,27} has been incorporated in our surgical program as one of its most important components, as in many other epilepsy surgery programmes^{4,7,8,11,19,23,24}. It is decisive for assuring patients and physicians that resection of the epileptogenic region will not lead to significant memory or language deficits. Our data may support the concept that the Wada test may be one more factor to indicate the laterality of the epileptogenic region, once it has been shown to be in one of the temporal lobes. Our results may indicate that the methods are complementary for determination of

language and memory dominance in candidates to temporal lobectomies. We intend to continue using the procedure as specified here, with the following specifications: routine bilateral injections into the internal carotids; assessment of effect of amobarbital by EEG and clinical evaluation of hemiplegia and alertness; use of the Montreal and Seattle procedures concomitantly.

Acknowledgment - The authors wish to thank Dr Carl B Dodrill (Seattle, USA) for the advice he has continuously given to the team of the Program for Epilepsy Surgery of Hospital Nossa Senhora das Graças.

REFERENCIAS

1. Bittencourt PRM. Epileptogênese, estrutura e função cerebral na epilepsia do lobo temporal: um estudo prospectivo controlado. Thesis for the degree of Professor of Medicine (Neurology), Universidade Federal do Paraná. Curitiba, 1991.
2. Blume WT, Grabow JD, Darley FL, Aronson AE. Intracarotid amobarbital test of language and memory before temporal lobectomy for seizure control. *Neurology* 1973;23:812-819.
3. Davis AE, Wada JA. Speech dominance and handedness in the normal human. *Brain & Language* 1978;5:42-45.
4. Dodrill CB. Preoperative criteria for identifying eloquent brain: intracarotid amyltal for language and memory testing. *Neurosurg Clin North Am* 1993;4:211-215.
5. Herrmann BP, Wyler AR, Somes G. Language function following anterior temporal lobectomy. *J Neurosurg* 1991;74:560-566.
6. Ivnic RJ, Sharbrough FW, Laws ER. Anterior temporal lobectomy for the control of partial complex seizures: information for counseling patients. *Mayo Clin Proc* 1988;63:783-793.
7. Jones-Gotman M. Commentary: psychological evaluation-testing hippocampal function. In J Engel (ed). *Surgical treatment of the epilepsies*. New York: Raven Press, 1987:203-211.
8. Kneebone AC, Chelune GJ, Dinner DS, Naugle RI, Awad IA. Intracarotid amobarbital procedure as predictor of material-specific memory change after anterior temporal lobectomy. *Epilepsia* 1995;36:857-865.
9. Lee GP, Loring DW, Smith JR, Flanigin HF. Intraoperative hippocampal cooling and Wada memory in the evaluation of amnesia risk following anterior temporal lobectomy. *Arch Neurol* 1995;52:857-861.
10. Leite PJM, Pereira R, Sandmann MC, Souza PC, Sandrinini RA, Kaneguzuko J, Bittencourt PRM. Intracarotid amobarbital procedure with the Montreal and Seattle protocols combined. (Abst). 21st International Epilepsy Congress. Sydney, Australia, 1995, Vol 36 (Suppl 3):123.
11. Lesser RP, Dinner DS, Luders H, Morris HH. Memory for objects presented soon after intracarotid amobarbital sodium injections in patients with medically intractable complex partial seizures. *Neurology* 1986;36:895-899.
12. Loring DW, Lee GP, Meador KJ, Flanigin HF, Smith JR, Figueroa RE, Martin RC. The intracarotid amobarbital procedure as a predictor of memory failure following unilateral temporal lobectomy. *Neurology* 1960;40:605-610.
13. Loring DW, Meador KJ, Lee GP, Nichols ME, King DW, Gallagher BB, Murro AM, Smith JR. Wada memory performance predicts seizure outcome following anterior temporal lobectomy. *Neurology* 1994;44:2322-2324.
14. Loring DW, Meador KJ, Lee GP, King DW, Gallagher BB, Murro AM, Smith JR. Stimulus timing effects on Wada memory testing. *Arch Neurol* 1994;51:806-810.
15. Loring DW, Murro AM, Meador KJ, Lee GP, 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;43:1789-1793.
16. Milner B, Brench C, Rasmussen T. Study of short-term memory after intracarotid injection of sodium amyltal. *Trans Am Neurol Assoc* 1962;87:224-226.
17. Ojemann GA, Dodrill CB. Verbal memory deficits after left temporal lobectomy for epilepsy. *J Neurosurg* 1985;62:101-107.
18. Ojemann GA, Ojemann BAJ, Lettich E, Berger M. Cortical language localization in left dominant hemisphere: an electrical stimulation mapping investigation in 117 patients. *J Neurosurg* 1989;71:316-326.
19. Perrine K, Gershengorn J, Brown ER, Choi IS, Luciano DJ, Devinski O. Material-specific memory in the intracarotid amobarbital procedure. *Neurology* 1993;43:706-711.
20. Rausch R, Babb TL, Engel J JR, Crandall PH. Memory following intracarotid amobarbital injection contralateral to hippocampal damage. *Arch Neurol* 1989;39:783-788.
21. Sandmann MC, Leite PJM, Pontes L, Bittencourt PRM. Early results of a new epilepsy surgery program. (Abst). 21st International Epilepsy Congress. Sydney, Australia. 1995. Vol 36 (Suppl 3):259.
22. Sandmann MC, Rogaszeski E, Mazer S, Bittencourt PRM. Lateralização da área epileptogênica através de ressonância magnética na epilepsia do lobo temporal. *Arq Neuropsiquiatr* 1994;52:309-313.
23. Saxe KI, Lenz T, Westerveld M, Novelty RA, Spencer DD, Kim JH. The neural substrate of memory impairment demonstrated by the intracarotid amobarbital procedure. *Arch Neurol* 1991;48:48-52.
24. Sperling MR, Saykin AJ, Glosser G, Moran M, French JA, Brooks M, O'Connor MJ. Predictors of outcome after anterior temporal lobectomy: the intracarotid amobarbital test. *Neurology* 1994;44:2325-2330.
25. Stafiniak P, Saykin AJ, Sperling MR, Kester DB, Robinson LJ, O'Connor MJ, Gur RC. Acute naming deficits following dominant temporal lobectomy: prediction by age at 1st risk for seizures. *Neurology* 1990;40:1509-1512.
26. Wada J. A new method for the determination of the side of cerebral speech dominance: a preliminary report on the intracarotid injection of sodium amyltal in man. *Igaku to Seibutsugaki* 1945;14:221-222.
27. Wada J, Rasmussen T. Intracarotid injection of sodium amyltal for the lateralization of cerebral speech dominance: experimental and clinical observations. *J Neurosurg* 1960;17:266-282.
28. Wyllie E, Naugle R, Awad I, Chelune G, Luders H, Dinner D, Skibinski C, Abl J. Intracarotid amobarbital procedure: prediction of decreased modality-specific memory scores after temporal lobectomy. *Epilepsia* 1991;32:857-864.