# Memory and language risk assessment with Wada test in patients' candidates for epilepsy surgery

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**Aim.** To determine post-surgical cognitive risk and associated factors according to lesion location in a sample of patients evaluated for epilepsy surgery with Wada test at the Fundación Instituto Neurológico de Colombia.

**Materials and methods.** An observational, retrospective, analytical study was completed in patients with drug-resistant temporal lobe epilepsy candidates for epilepsy surgery treated from 2001 to 2021, who completed the Wada test as part of the pre-surgical evaluation. A descriptive analysis of sociodemographic, clinical, imaging and neuropsychological variables was completed; a multivariate logistic regression was performed analyzing factors associated with resection risk in patients with left lesions.

**Results.** A total of 369 patients were included, 54.74% of the cases were women, with a median age of seizure onset of 11 years. 92.66% of the cases had lesional epilepsy and 68.56% were secondary to hippocampal sclerosis. Left hemisphere was the most frequently affected (65.68%) being dominant for memory and language in most of the patients with a proportion of 42.82% and 81.3%, respectively. The median functional adequacy was 43.75 (IQR 0-75) and the functional reserve was 75 (IQR 25 -93.75). In 104 patients, the Wada test determined a resection risk. In patients with a left lesion, it was found that functional reserve (PRadjusted 0.99, CI 95% 0.9997-0.9998) and having a right hemispheric dominance for memory (PRadjusted 0.92, CI 95% 0.547-0.999) were protective factors for post-surgical resection risk.

**Conclusion.** Wada test is a useful tool for surgical decision-making in patients with drug-resistant temporal lobe epilepsy. When considering cognitive risk, components such as memory dominance and functional reserve should be considered as protective factors for postsurgical cognitive function preservation in patients with left lesions.

Key words. Cognition. Epilepsy. Intracarotid amobarbital test. Language. Memory. Wada test.

# Introduction

The traditional clinical approach to epilepsy treatment focuses on seizure control using effective anticonvulsant drugs. About 25% of epilepsy patients experience seizure recurrence, with mesial temporal lobe epilepsy being a major cause of treatment resistance, affecting up to 50 to 70% of patients [1]. In such cases, resection of the ictal-onset zone has shown significant success in reducing seizure frequency in 60 to 80% of cases [2].

The temporal lobe is recognized as an eloquent zone, hence epilepsy surgery potentially jeopardizes cognitive abilities, especially language and memory functions in patients with left, right, or bilateral hemispheric involvement [3], Therefore, there is a need to predict post-surgical cognitive risk using different diagnostic tools to determine the location of the epileptogenic and eloquent zones.

The evaluation of the eloquent zone involves functional tests, including neuropsychological as-

sessment, the Wada test (WT), magnetic resonance (MRI), functional magnetic resonance imaging (fMRI) and electroencephalographic video monitoring (video-EEG) [4,5]. The WT is the gold standard for cognitive impairment risk prediction before resection of the epileptogenic zone, through the injection of anesthetics into the arterial circulation simulating transient loss of cognitive function for each anesthetized hemisphere, evaluating the functional reserve, the functional adequacy and contralateral and ipsilateral asymmetries [6].

Despite the decreasing use of the WT due to the emergence of fMRI as a non-invasive alternative [7-9], fMRI may have limitations in memory evaluation, leading to inconclusive results, partly due to technical difficulties such as heterogeneous paradigms or inadequate patient performance during the procedure [10].

Furthermore, it is important to mention that the sensitivity of fMRI memory lateralization varies widely, with reported values ranging from 30% to

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100%, and specificity values from 43% to 100%. In contrast, the sensitivity and specificity of the WT for memory and language lateralization are 79% and 65%, respectively [11]. Additionally, fMRI results may vary depending on memory dominance location. Previous studies have shown that fMRI has a concordance of 78.7% with the WT in patients with unilateral memory representation, whereas in patients with bilateral memory lateralization and temporal lesions, the concordance with the WT drops to 46.8%. This discrepancy may be attributed to laterality index factors and signal thresholds, affecting fMRI's ability to detect unilateral memory lateralization in patients with bilateral memory dominance [12]. The aim of this study was to describe the resection risk assessment with WT in patient's candidates to temporal lobe epilepsy surgery, determining the associated factors to the resection risk findings in WT in patients with left hemispheric lesions.

# **Materials and methods**

# Study design and data collection sources

An observational, retrospective, analytical study was completed based on information collected from medical records, magnetic resonance imaging reports, neuropsychological assessment, and WT reports.

# Sample and study population

Patients with drug-resistant temporal lobe epilepsy candidates for epilepsy surgery treated at the Fundación Instituto Neurológico de Colombia, Medellín, from 2001 to 2021, who completed the WT as part of the pre-surgical evaluation, were included. A convenience sampling was performed taking into account the following eligibility criteria: Patients ≥18 who completed the WT and authorized the use of the data for research. Those with incomplete reports of clinical history, neuropsychological evaluation and neuroimaging were not included.

# **Outcome variable and co-variables**

The outcome variable was the presence of risk of resection determined in the WT. Sociodemographic variables (sex, laterality), clinical characteristics (age at onset of seizures, number of years with the diagnosis of epilepsy, history related to the diagnosis of epilepsy, type of lesion in the structural MRI, hemisphere of the lesion) were evaluated. Neuropsychological evaluation –intelligence quotient (IQ), verbal index, reasoning index, type of alteration in the neuropsychological test–, variables of the WT, baseline neuropsychological characteristics, hemispheric memory dominance, hemispheric language dominance, affected lobe according to dominance, functional reserve (proportion of recognized objects in the contralateral hemisphere to the possible resection focus) and functional adequacy (proportion of recognized objects in the ipsilateral hemisphere to the possible resection focus) and complications of the Wada test.

### Wada test procedure

Initially, a neuropsychologist conducted a cognitive assessment to determine memory and language baseline performance for each patient. Instructions were provided for the WT and the understanding of these instructions by the patient was verified. During the procedure, anesthetics (such as amobarbital, etomidate, or propofol) were administered through the femoral artery into the internal carotid artery blocking temporarily the brain function of each hemisphere.

For each hemisphere, a memory evaluation was performed by presenting and naming 8 objects. After the effects of the anesthetic, an evocation test was conducted, followed by a recognition test with 24 objects, of which 16 had not been presented to the patient previously. Language was assessed through tests of expression, comprehension, naming, repetition, and reading of two sentences, both during and after the effects of the anesthetic. Throughout this process, both the neuropsychologist and the neurologist provided continuous accompaniment and supervision.

## **Data analysis**

The sociodemographic, clinical, imaging, neuropsychological and WT variables were described according to the resection risk. For quantitative variables, measures of central tendency and dispersion were reported according to their normality, and absolute and relative frequencies were presented for qualitative variables. The proportion of patients at resection risk based on the hemispheric lesion location on MRI was also estimated.

Factors associated with resection risk were determined according to the WT in patients with left hemispheric lesions using a binomial logistic regression analysis. In the simple model, those variables with a p-value < 0.25 were selected as candidates for a multivariate analysis. For the quantitative variables, the assumption of linearity was evaluated for the different outcomes and the collinearity between the independent variables was evaluated.

For the construction of the multivariate logistic binomial regression model, the step-by-step method was used with the researcher's criteria, and the most parsimonious model with the Akaike information criterion was chosen. The prevalence ratios were estimated with their 95% confidence interval. The SAS onedemand for academics software was used with the FREQ, UNVIARIATE and GLIMMIX procedures.

# **Ethical publication statement**

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. This research was approved by the ethics committee of Fundación Instituto Neurológico de Colombia on February 22, 2022 with the file number PE8INV5\_PR0108.

## **Results**

# **Characteristics of the study population**

A total of 369 patients with drug-resistant epilepsy candidates for epilepsy surgery who met the eligibility criteria were included. 54.74% (n = 202) of the cases were women, mostly right-handed (90.51%, n = 334), with a median age of seizure onset of 11 years (IQR 3-20 years). A structural epilepsy was found in 20.43% of the cases (n = 66). Similarly, most of the patients had lesional epilepsy in MRI (92.66%, *n* = 34), of which 253 cases had hippocampal sclerosis (68.56%). The left hemisphere was the most frequently affected by these lesions (65.68%, n = 242). In the neuropsychological evaluation, most of the patients had scores <70 (very low) in the IQ with a proportion of 39.46% (n = 118). The sociodemographic, clinical, imaging, and neuropsychological characteristics are described in greater detail in table I.

In the baseline neuropsychological evaluation prior to the WT it was found that 45.65% (n = 168) had memory impairment. In most of the patients the left hemisphere was dominant for memory and language with a proportion of 42.82% and 81.3%, respectively. Similarly, the median functional adequacy was 43.75 (IQR 0-75) and functional reserve

75 (IQR 25 -93.75). The most frequently used anesthetic for the procedure was amobarbital 63.41%(*n* = 234) (Table II).

# Study population characteristics according to the resection risk from the Wada test

In 104 (28.18%) patients a risk of resection was determined, in 232 (62.87%) no risk was determined and in 33 patients (8.94%) the results were inconclusive. It was observed that the proportion of patients with lesions located in the right hemisphere (9.72%) was significantly lower in patients with risk of resection, compared with those without risk (87.50%) and with those with inconclusive risk (2.78%) (p < 0.0001). There were no significant differences in sex, patient's laterality, seizure-onset age, the number of years with epilepsy, the epilepsy etiology and structural MRI findings, intelligence quotient, verbal index and reasoning index between the patients without risk, with risk and with inconclusive risk (Table I).

In addition, amobarbital was the most used anesthetic in patients without risk (68.8%), compared to patients with risk (22.22%) and inconclusive results (8.97%); these differences were significant (p =0.0175). Regarding memory dominance, 83.62% of the patients without risk had a right hemispheric dominancy, compared with the patients with risk (12.93%) and inconclusive risk (3.45%) (*p* < 0.0001). Similarly, the right hemisphere was dominant for language (90.48%) in patients without risk of resection, this difference was significant (p = 0.0003). The median functional adequacy was significantly higher in patients at risk of resection (62.5 IQR: 37.5-87.5; p < 0.0001), while the median functional reserve was significantly lower in this same group of patients (18.75, IQR: 0-50; *p* < 0.0001) (Table II).

# Bivariate and multivariate analysis of binomial logistic regression for patients with left lesion at risk of resection in Wada test

Given that the majority of the study population had a left hemispheric lesion in the MRI, the analysis of the associated factors with the risk of resection findings from the WT was performed in this group of patients. Table III shows the results of the simple binomial logistic regression models of the candidate variables for the multivariate model for patients with risk of resection reported in the WT.

The multivariate logistic regression model that best explained the outcome of patients at risk of resection included the following variables: functional reserve and right hemisphere dominant for memory.

Characteristics	Total (N = 369)	Without risk (n = 232)	With risk ( <i>n</i> = 104)	Inconclusive risk (n = 33)	<i>p</i> -value	
Sociodemographic and clinical characteristi	<i>ics,</i> n (%)					
Gender, women	202 (54.74)	129 (63.86)	53 (26.24)	20 (9.9)	0.5691	
Laterality						
Right-handed	334 (90.51)	206 (61.68)	95 (28.44)	33 (9.88)		
Left-handed	34 (9.21)	26 (76.47)	8 (23.53)	0	0.1227	
Ambidextrous	1 (0.27)	0	1 (100)	0		
Age of seizure onset, years (IQR)	11 (3-20)	9 (3-20)	11 (5-23)	12 (3-20)	0.2399	
Age of seizure onset						
0-6 years	140 (37.94)	97 (69.29)	32 (22.86)	11 (7.86)	-	
7-17 years	101 (27.37)	58 (57.43)	33 (32.67)	10 (9.9)	0.3762	
Greater-equal to 18 years	128 (34.69)	77 (60.16)	39 (30.47)	12 (9.38)	-	
Years with epilepsy (IQR)	22 (11-33)	21 (11-32)	23 (12-36.5)	27 (17-35)	0.1671	
Epilepsy etiology, n (%)						
None	204 (63.16)	122 (59.80)	64 (31.37)	18 (8.82)		
Structural	66 (20.43)	37 (56.06)	21 (31.82)	8 (12.12)	-	
Neuroinfection	49 (15.17)	37 (75.51)	11 (22.45)	1 (2.04)	-	
Genetic	1 (0.31)	1 (100)	0	0	- 0.2546	
Autoinmmune	1 (0.31)	1 (100)	0	0	-	
Toxic-metabolic	2 (0.62)	0	2 (100)	0	-	
Structural MRI findings, n (%)						
Structural MRI lesion	341 (92.66)	215 (63.05)	94 (27.57)	32 (9.38)	0.4165	
Lesion type						
Hippocampal sclerosis	253 (68.56)	160 (63.24)	68 (26.88)	25 (9.88)	0.5227	
Neoplasm	20 (5.42)	15 (75)	4 (20)	1 (5)	0.5054	
Dysplasia	6 (1.63)	3 (50)	3 (50)	0	0.4198	
Malacia	29 (7.84)	17 (58.62)	9 (31.03)	3 (10.34)	0.8823	
Gliosis	23 (6.23)	15 (65.22)	7 (30.43)	1 (4.35)	0.7244	
Infarct	3 (0.81)	3 (100)	0	0	0.4094	
Dual	5 (1.36)	3 (60)	2 (40)	0	0.7008	

Table I. Sociodemographic, clinical, imaging and neuropsychological characteristics of patients according to the resection risk from the Wada test.

Table I. Sociodemographic, clinical, imaging and neuropsychological characteristics of patients according to the resection risk from the Wada test (cont.).

Characteristics	Total ( <i>N</i> = 369)	Without risk (n = 232)	With risk ( <i>n</i> = 104)	Inconclusive risk (n = 33)	<i>p</i> -value
Hemisphere of the lesion					
Right	72 (19.51)	63 (87.50)	7 (9.72)	2 (2.78)	
Left	242 (65.68)	143 (59.09)	72 (29.75)	27 (11.16)	<0.0001
Bilateral	25 (6.78)	10 (40)	14 (56)	1 (4)	-
Lesion lobe					
Extratemporal	60 (16.39)	35 (58.33)	17 (28.33)	8 (13.33)	0.4171
Neuropsychological evaluation, n (%)					
Intelligence quotient					
Normal-high (110-119)	6 (2.01)	5 (83.33)	1 (16.67)	0	
Normal (90-109)	48 (16.05)	34 (70.83)	11 (22.92)	3 (6.25)	_
Normal-low (80-89)	50 (16.72)	33 (66)	16 (32)	1 (2)	0.5056
Borderline (71-79)	77 (25.75)	46 (59.74)	22 (28.57)	9 (11.69)	_
Very low (≤70)	118 (39.46)	79 (66.95)	27 (22.88)	12 (10.17)	_
Verbal quotient					
Superior (≥120)	3 (1.16)	3 (100)	0	0	
Normal-high (110-119)	7 (2.71)	6 (85.71)	1 (14.29)	0	-
Normal (90-109)	46 (17.83)	32 (69.57)	11 (23.91)	3 (6.52)	0.0070
Normal-low (80-89)	56 (21.71)	36 (64.29)	15 (26.79)	5 (8.93)	- 0.6879
Borderline (71-79)	66 (25.58)	36 (54.55)	22 (33.33)	8 (12.12)	_
Very low (≤70)	80 (31.05)	55 (68.75)	18 (22.50)	7 (8.75)	_
Reasoning index					
Normal-high (110-119)	3 (1.18)	1 (33.33)	1 (33.33)	1 (33.33)	
Normal (90-109)	34 (13.39)	25 (73.53)	7 (20.59)	2 (5.88)	
Normal-low (80-89)	39 (15.35)	26 (66.67)	11(28.21)	2 (5.13)	0.5594
Borderline (71-79)	73 (28.74)	46 (63.01)	22 (30.14)	5 (6.85)	
Very low (≤70)	105 (41.34)	67 (63.81)	25 (23.81)	13 (12.38)	_
Alteration in neuropsychological test					
None	26 (8)	18 (69.23)	6 (23.08)	2 (7.69)	
Mnesic	46 (14.15)	31 (67.39)	13 (28.26)	2 (4.35)	
Linguistic	22 (6.77)	12 (54.55)	8 (36.36)	2 (9.09)	0.9495
Mixed	128 (39.38)	84 (65.63)	34 (26.56)	10 (7.81)	_
Generalized	95 (29.23)	59 (62.11)	26 (27.37)	10 (10.53)	-
IQR: interquartile range; MRI: magnetic resona	nce image.				

Characteristics	Total ( <i>N</i> = 369)	Without risk (n = 232)	With risk ( <i>n</i> = 104)	Inconclusive risk (n = 33)	<i>p</i> -value
Baseline compromise, n (%)					
Comprehension	8 (2.2)	4 (50)	3 (37.50)	1 (12.50)	0.7352
Nomination	153 (42.03)	100 (65.36)	40 (26.14)	13 (8.50)	0.6574
Repetition	110 (29.97)	73 (66.36)	28 (25.45)	9 (8.18)	0.6321
Reading	39 (10.6)	27 (69.23)	10 (23.81)	7 (5.13)	0.3590
Dysarthria	13 (3.55)	9 (69.23)	1 (7.69)	3 (23.08)	0.0834
Evocation	259 (70.38)	162 (62.55)	73 (28.19)	24 (9.27)	0.6188
Recognition	29 (7.88)	16 (55.17)	8 (27.59)	5 (17.24)	0.2595
Type of baseline compromise, n (%)	1				
None	44 (11.99)	26 (59.09)	16 (36.36)	2 (4.55)	
Mnesic	168 (45.65)	103 (61.31)	49 (29.17)	16 (9.52)	
Linguistic	17 (4.62)	10 (58.82)	6 (35.29)	1 (5.88)	0.6479
Mixed	139 (37.77)	92 (66.19)	33 (23.74)	14 (10.07)	
Anesthetic, n (%)					
Amobarbital	234 (63.41)	161 (68.8)	52 (22.22)	21 (8.97)	
Etomidate	119 (32.25)	63 (52.94)	45 (37.82)	11 (9.24)	0.0175
Propofol	16 (4.34)	8 (50)	7 (43.75)	1 (6.25)	
Memory dominance, n (%)					
Not defined	37 (10.03)	6 (16.22)	11 (29.73)	20 (54.05)	
Left	158 (42.82)	87 (55.06)	65 (41.14)	6 (3.80)	
Right	116 (31.44)	97 (83.62)	15 (12.93)	4 (3.45)	<0.0001
Bitemporal	58 (15.72)	42 (72.41)	13 (22.41)	3 (5.17)	
Language dominance, n (%)					
Not defined	3 (0.81)	0	1 (33.33)	2 (66.67)	
Left	300 (81.3)	179 (59.67)	95 (31.67)	26 (8.67)	
Right	21 (51.69)	19 (90.48)	1 (4.76)	1 (4.76)	0.0003
Bilateral	45 (12.2)	34 (75.56)	7 (15.56)	4 (8.89)	
Involved lobe according to the num	ber of recognized objec	<i>ts</i> , n (%)			
Extratemporal	31 (13.66)	24 (77.42)	5 (16.13)	2 (6.45)	
Temporal	179 (78.85)	91 (50.84)	74 (41.34)	14 (7.82)	<0.0001
Not defined	16 (7.05)	6 (35.29)	4 (23.53)	7 (41.18)	
Functional adequacy, (IQR)	43.75 (0-75)	31.25 (0-68.75)	62.5 (37.5-87.5)	0 (0-43.72)	<0.0001
Functional reserve, (IQR)	75 (25-93.75)	87.5 (75-100)	18.75(0-50)	18.75 (0-75)	<0.0001
IQR: interquartile range; MRI: magne	tic resonance image.				

 Table II. Wada test findings and according to the resection risk in the total population.

Table III.	Simple binomial	logistic r	regression	analysis of	of the ca	andidate	variables	for the	multivariate	model in	patients with	left le	sion a	at risk of	re
section.															

Characteristics	Total <i>N</i> = 242	Without risk n = 143	With risk n = 72	PR crude (Cl 95%)	<i>p</i> -value
Gender, women	143 (59.09)	89 (62.24)	38 (26.57)	0.744 (0.456-1.139)	0.1853
Number of years with epilepsy	23 (10-33)	20 (9-32)	24.5 (11.5-38)	1.018 (1.001-1.035)	0.0362
MRI finding of dysplasia	5 (2.07)	2 (40)	3 (60)	2.007(0.556-2.584)	0.2269
MRI finding of malacia	19 (7.85)	9 (47.37)	8 (42.11)	1.55 (0.732-2.400)	0.2236
Intelligence quotient					
Borderline (71-79)	47 (24.35)	24 (51.06)	16 (34.04)	1.631 (0.834-2.643)	0.1419
Verbal index					
Borderline (71-79)	38 (23.17)	18 (47.37)	14 (36.84)	2.150(1.01-3.473)	0.0473
Reasoning index					
Normal (90-109)	23 (14.29)	20 (86.96)	2 (8.70)	0.321 (0.067-1.316)	0.1223
Borderline (71-79)	48 (29.81)	26 (54.17)	18 (37.50)	1.686 (0.843-2.739)	0.1295
Anesthetic					
Amobarbital	150 (61.98)	94 (62.67)	39 (26)	0.475 (0.139-1.129)	0.1151
Baseline compromise					
None	29 (11.98)	15 (51.72)	12 (41.38)	1.682 (0.845-2.631)	0.1277
Hemispheric language dominanc	е				
Left	187 (77.27)	100 (53.48)	65 (34.76)	2.319(1.082-3.94)	0.032
Hemispheric memory dominance					
Left	73 (30.17)	25 (34.25)	44 (60.27)	2.511 (1.62-2.98)	0.0006
Right	97 (40.08)	85 (87.63)	10 (10.31)	0.336 (0.136-0.789)	0.0111
Functional adequacy	50 (12.5-81.25)	37.5 (0-75)	62.5 (43.75-87.5)	1.012 (1.004-1.02)	0.0017
Functional reserve	62.5 (25-87.5)	87.5 (62.5-100)	21.87 (0-43.75)	0.999 (0.9996-0.9998)	<0.001
CI 95%: confidence interval; MRI: n	nagnetic resonance ima	ige.			

It was found that in patients with left hemispheric lesion, for each percentage point of the functional reserve, the probability of being a patient with risk of post-surgical resection detected in the WT decreases 0.01 times (PR adjusted 0.99; 95% CI: 0.9997-0.9998). Similarly, having the right hemisphere dominant for memory was a protective factor for

having a risk of post-surgical resection detected in the WT (PR adjusted 0.92; 95% CI: 0.547-0.999).

# Discussion

In the pre-surgical evaluation of patients who are

candidates for epilepsy surgery, the aim is to confirm the presence of the epileptic zone and to determine its extension through the use of multiple diagnostic tools. Once the epileptogenic zone has been identified, the risks of a surgical intervention regarding memory and language function in relation to the affected area and circuit are considered, and its benefits compared to refractory traditional medical treatments are evaluated [13,14].

This study highlights the relevance of neuropsychological evaluation and the determination of lateralization and hemispheric dominance through the WT. Demonstrating that components such as the function of the contralateral hippocampus and the hemispheric memory dominance are essential factors for the resection risk evaluation in the WT.

Regarding the study population characteristics, although the literature suggests that the age of seizure onset is associated with cognitive alterations in patients with epilepsy and may affect post-surgical cognitive outcomes [15-18]. In this study, the median age of seizure onset was 11 years (IQR: 3-20) and no significant differences were found between patients without risk of resection, at risk, and with inconclusive results.

In the present study, most of the patients had lesional epilepsy, mainly temporally located, and affecting the left hemisphere secondary to hippocampal sclerosis. These findings coincide with previous studies on refractory epilepsy [19-21]. A higher proportion of patients with left hemispheric lesions were observed to be at risk of resection. It is important to note that the WT employs verbal and double-coding stimuli, which serve as indicators of left hemisphere integrity in individuals with leftlanguage dominant temporal lobe epilepsy and significantly predict memory performance in the left hemisphere during the test. Therefore, the results support the utilization of the WT primarily for patients with left-sided lesions [22].

Patient's pre-surgical cognitive baseline influences postoperative cognitive outcomes. It has been observed that patients with high IQ present less postoperative deterioration. However, those with high manipulative IQ might experience cognitive decline [23]. In this study, it's important to emphasize that despite a higher proportion of patients with an IQ below 70, no significant differences in IQ levels were found among patients categorized as atrisk, without-risk, and inconclusively risk based on the WT results. Given the difficulties associated with implementing fMRI paradigms in patients with low IQ, the implementation of the WT is recommended including interrelation and verbal guidance from professionals to the patients before and during the WT.

Numerous studies have identified clinical variables as predictors of a worse postoperative cognitive outcome (mainly in terms of memory), such as resection in the dominant hemisphere for language [13], low functional preoperative memory, lateage seizure onset, low verbal IQ, seizure persistence after surgery, psychiatric comorbidities, and MRI findings other than exclusively unilateral mesial temporal sclerosis [24-26]. In this study, the information from the postoperative neuropsychological evaluation was not available, therefore, it was decided to evaluate the factors associated with the finding of risk of resection in the TW in patients with left lesions.

Previous studies suggest that the duration of epilepsy is not linked to postoperative changes in the IQ [24]. This phenomenon can be explained by the fact that in patients with long-standing epilepsy, uncontrolled electrical discharges toward the affected hippocampus and its contralateral counterpart result in poorer preoperative cognitive performance [27]. Consequently, the resection of less functional areas adjacent to the EZ will have a lesser impact on cognitive performance scores [28,29]. The findings of this study support this hypothesis, as they reveal that the number of years with epilepsy was not significantly associated, in the multivariate model, with the identification of resection risk in the WT.

In the WT, dominance for memory and language are relevant when evaluating the ability of the healthy hemisphere contralateral to the lesion to maintain memory and language functions [30,31]. In patients with left lesions, it was observed that a right hemispheric dominance for memory contralateral to the epileptogenic focus to be resected was a protective factor for the finding of risk of resection in the WT (adjusted PR 0.92; 95% CI 0.547-0.999). These results are similar to other reports in which memory dominance ipsilateral to the lesion is considered as one of the factors associated with postoperative verbal memory compromise [32]. It is considered that the WT continues to be useful when evaluating memory tasks related to the mesial zone, since it allows the characterization of the memory dominance of small areas of the hippocampus [33].

Estimates of functional reserve and functional adequacy are data only obtained through the WT, these cannot be collected with other lateralization diagnostic tools such as fMRI and therefore are key and distinctive data of this procedure [34,35]. In relation to this, there is a debate regarding the model to follow to define post-surgical risk; the first

model suggests that the post-surgical memory deficit depends on the ability of the hippocampus contralateral to the lesion to adequately sustain memory functions after the operation (functional reserve) [3]. The second model of functional adequacy postulates that the post-surgical deficit depends on the functionality of the target hippocampus to be resected [36]. In this regard, most studies suggest that functional adequacy instead of functional reserve is what determines the degree of postoperative decrease [25]. Our study is consistent with the first model, giving greater value to the functional reserve, determining that for each percentage point of function of the hippocampus contralateral to the lesion, the probability of risk of post-surgical cognitive compromise decreases 0.01 times.

The current study is not without limitations, notably the absence of post-surgical follow-up evaluations for patients who completed the WT. Consequently, it remained unfeasible to ascertain the occurrence of memory impairment after surgery for those patients who were predicted to be at cognitive risk. The results and interpretation of this study must be contextualized within the parameters that influence the outcomes of the WT. As part of ongoing research, a subsequent study will be conducted, focusing on patients who have undergone post-surgical neuropsychological assessments.

# Conclusions

The WT determines valuable mnesic components and the interpretation helps in decision-making regarding the possibility of surgical resection of the epileptogenic focus. Specifically, the higher the percentage values of the functional reserve, the greater the probability of post-surgical memory preservation. In the same way, the function of the hippocampus to be resected must be taken into account, whose pre-surgical involvement will affect the results of post-surgical memory. In the decision-making of patients with drug-resistant epilepsy, the neuropsychological evaluation completed during the WT plays a relevant role by identifying the hemispheric dominance of cognitive functions, in which it is identified that in patients with a secondary epileptogenic focus to left lesions, the dominance for memory in the right hemisphere is a protective factor.

#### References

 Téllez-Zenteno JF, Hernández-Ronquillo L. A review of the epidemiology of temporal lobe epilepsy. Epilepsy Res Treat 2012; 2012: 630853.

- Cendes F, Sakamoto AC, Spreafico R, Bingaman W, Becker AJ. Epilepsies associated with hippocampal sclerosis. Acta Neuropathol (Berl) 2014; 128: 21-37.
- Parra-Díaz P, García-Casares N. Memory assessment in patients with temporal lobe epilepsy to predict memory impairment after surgery: a systematic review. Neurologia (Engl Ed) 2019; 34: 596-606.
- Marín-Romero B, Tirapu-Ustárroz J, Chiofalo MF. Neuropsychological assessment protocol for adults in epilepsy surgery. Rev Neurol 2020; 70: 341-7.
- Sanjuan A, Villanueva VE, Avila C. Evaluación prequirúrgica del lenguaje y la memoria mediante técnicas de resonancia magnética funcional en pacientes con epilepsia farmacorresistente. Rev Neurol 2008; 46 (Supl 1): S25-8.
- Baxendale S. The Wada test. Curr Opin Neurol 2009; 22: 185-9.
   Bonelli SB, Powell RHW, Yogarajah M, Samson RS, Symms
- MR, Thompson PJ, et al. Imaging memory in temporal lobe epilepsy: predicting the effects of temporal lobe resection. Brain 2010; 133: 1186-99.
- Massot-Tarrús A, White K, Mirsattari SM. Comparing the Wada Test and functional MRI for the presurgical evaluation of memory in temporal lobe epilepsy. Curr Neurol Neurosci Rep 2019; 19: 31.
- Dupont S, Duron E, Samson S, Denos M, Volle E, Delmaire C, et al. Functional MR imaging or Wada Test: which is the better predictor of individual postoperative memory outcome? Radiol J 2010; 255: 128-34.
- Conradi N, Rosenberg F, Knake S, Biermann L, Haag A, Gorny I, et al. Wada test results contribute to the prediction of change in verbal learning and verbal memory function after temporal lobe epilepsy surgery. Sci Rep 2021; 11: 10979.
- Schmid E, Thomschewski A, Taylor A, Zimmermann G, Kirschner M, Kobulashvili T, et al. Diagnostic accuracy of functional magnetic resonance imaging, Wada test, magnetoencephalography, and functional transcranial Doppler sonography for memory and language outcome after epilepsy surgery: a systematic review. Epilepsia 2018; 59: 2305-17.
- Massot-Tarrús A, White KP, Mousavi SR, Hayman-Abello S, Hayman-Abello B, Mirsattari SM. Concordance between fMRI and Wada test for memory lateralization in temporal lobe epilepsy: a meta-analysis and systematic review. Epilepsy Behav 2020; 107: 107065.
- Schulze-Bonhage A, Zentner J. The preoperative evaluation and surgical treatment of epilepsy. Dtsch Ärztebl Int 2014; 111: 313-9.
- Jones-Gotman M, Smith ML, Risse GL, Westerveld M, Swanson SJ, Giovagnoli AR, et al. The contribution of neuropsychology to diagnostic assessment in epilepsy. Epilepsy Behav 2010; 18: 3-12.
- 15. Spencer S, Huh L. Outcomes of epilepsy surgery in adults and children. Lancet Neurol 2008; 7: 525-37.
- 16. Meador KJ. Cognitive outcomes and predictive factors in epilepsy. Neurology 2002; 58 (8 Suppl 5): S21-6.
- Shehata GA, Bateh AE, Aziz M. Cognitive function, mood, behavioral aspects, and personality traits of adult males with idiopathic epilepsy. Epilepsy Behav 2009; 14: 121-4.
- Manno EM, Sperling MR, Ding X, Jaggi J, Alavi A, O'Connor MJ, et al. Predictors of outcome after anterior temporal lobectomy: positron emission tomography. Neurology 1994; 44: 2331-6.
- Asadi-Pooya AA, Stewart GR, Abrams DJ, Sharan A. Prevalence and incidence of drug-resistant mesial temporal lobe epilepsy in the United States. World Neurosurg 2017; 99: 662-6.
- Labate A, Aguglia U, Tripepi G, Mumoli L, Ferlazzo E, Baggetta R, et al. Long-term outcome of mild mesial temporal lobe epilepsy: a prospective longitudinal cohort study. Neurology 2016; 86: 1904-10.
- Mehvari Habibabadi J, Moein H, Jourahmad Z, Ahmadian M, Basiratnia R, Zare M, et al. Outcome of epilepsy surgery in lesional epilepsy: experiences from a developing country. Epilepsy Behav 2021; 122: 108221.

- 22. Vingerhoets G, Miatton M, Vonck K, Seurinck R, Boon P. Memory performance during the intracarotid amobarbital procedure and neuropsychological assessment in medial temporal lobe epilepsy: The limits of material specificity. Epilepsy Behav 2006; 8: 422-8.
- Cano-López I, Vázquez-Costa JF, Gutiérrez A, Villanueva V, González-Bono E. Cognitive reserve as a modulating factor in the impact of surgery on visual memory and naming in temporal lobe epilepsy patients. Rev Neurol 2021; 73: 267-74.
- Yu HY, Shih YH, Su TP, Shan IK, Yiu CH, Lin YY, et al. The Wada memory test and prediction of outcome after anterior temporal lobectomy. J Clin Neurosci Off J Neurosurg Soc Australas 2010; 17: 857-61.
- Dupont S. Imaging memory and predicting postoperative memory decline in temporal lobe epilepsy: Insights from functional imaging. Rev Neurol (Paris) 2015; 171: 307-14.
- Englot DJ, Ouyang D, Garcia PA, Barbaro NM, Chang EF. Epilepsy surgery trends in the United States, 1990-2008. Neurology 2012; 78: 1200-6.
- 27. Helmstaedter C, Kurthen M, Lux S, Reuber M, Elger CE. Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. Ann Neurol 2003; 54: 425-32.
- Shah U, Desai A, Ravat S, Muzumdar D, Godge Y, Sawant N, et al. Memory outcomes in mesial temporal lobe epilepsy surgery. Int J Surg 2016; 36: 448-53.
- D'Orio P, Pelliccia V, Gozzo F, Cardinale F, Castana L, Lo Russo G, et al. Epilepsy surgery in patients older than 50 years: effectiveness, safety, and predictors of outcome. Seizure 2017; 50: 60-6.

- Andelman F, Kipervasser S, Neufeld MY, 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: 20-6.
- Kundu B, Rolston JD, Grandhi R. Mapping language dominance through the lens of the Wada test. Neurosurg Focus 2019; 47: E5.
- 32. Roessler K, Kasper BS, Shawarba J, Walther K, Coras R, Brandner S, et al. Operative variations in temporal lobe epilepsy surgery and seizure and memory outcome in 226 patients suffering from hippocampal sclerosis. Neurol Res 2021; 43: 884-93.
- Htet NN, Pizarro R, Nair VA, Chu DY, Meier T, Tunnell E, et al. Comparison of language and memory lateralization by functional MRI and Wada Test in epilepsy. Front Neurol Neurosci Res 2021; 2: 100009.
- 34. Machado RA, Astencio AG, Guerra JCL, González JAJ, Jiménez ML, Sosa DMA, et al. Evaluación de la reserva funcional de memoria en candidatos a cirugía de la epilepsia en Cuba mediante el test de Wada con propofol: reporte de casos. Rev Mex Neurocienc 2013; 14: 281-5.
- 35. Qadri S, Dave H, Das R, Alick-Lindstrom S. Beyond the Wada: an updated approach to pre-surgical language and memory testing: an updated review of available evaluation techniques and recommended workflow to limit Wada test use to essential clinical cases. Epilepsy Res 2021; 174: 106673.
- Chelune GJ. Hippocampal adequacy versus functional reserve: predicting memory functions following temporal lobectomy. Arch Clin Neuropsychol Off J Natl Acad Neuropsychol 1995; 10: 413-32.

# Evaluación de la memoria y el lenguaje mediante el test de Wada en pacientes candidatos a cirugía de epilepsia

**Objetivo.** Determinar el riesgo cognitivo posquirúrgico y factores asociados según la localización de la lesión en una muestra de pacientes evaluados para cirugía de epilepsia con el test de Wada en la Fundación Instituto Neurológico de Colombia.

**Materiales y métodos.** Se realizó un estudio observacional, retrospectivo y analítico en pacientes con epilepsia farmacorresistente del lóbulo temporal candidatos a cirugía de epilepsia tratados entre 2001 y 2021, que completaron el test de Wada como parte de la evaluación prequirúrgica. Se realizó un análisis descriptivo de variables sociodemográficas, clínicas, imagenológicas y neuropsicológicas. Se realizó una regresión logística multivariada analizando factores asociados al riesgo de resección en pacientes con lesiones izquierdas.

**Resultados.** Se incluyó a 369 pacientes, el 54,74% de los casos fueron mujeres, con una mediana de edad de inicio de las convulsiones de 11 años. El 92,66% de los casos presentó epilepsia lesional; de éstos, el 68,56% fue secundario a esclerosis hipocampal. El hemisferio izquierdo fue el más frecuentemente afectado (65,68%), y éste fue dominante para la memoria y el lenguaje en la mayoría de los pacientes, con una proporción del 42,82 y el 81,3%, respectivamente. La mediana de adecuación funcional fue de 43,75 (rango intercuartílico: 0-75) y la reserva funcional de 75 (rango intercuartílico: 25-93,75). En 104 pacientes, el test de Wada determinó un riesgo de resección. En pacientes con lesiones izquierdas se encontró que la reserva funcional (razón de prevalencia ajustada: 0,99; intervalo de confianza al 95%: 0,9997-0,9998) y tener dominancia del hemisferio derecho para la memoria (razón de prevalencia ajustada: 0,92; intervalo de confianza al 95%: 0,547-0,999) fueron factores asociados para determinar el riesgo de resección posquirúrgico en el test de Wada.

**Conclusión.** El test de Wada es una herramienta útil para la toma de decisiones quirúrgicas en pacientes con epilepsia del lóbulo temporal farmacorresistente. Componentes como la dominancia de la memoria y la reserva funcional en el test de Wada deben considerarse como factores que se deben tener en cuenta en la predicción de la preservación de la función cognitiva posquirúrgica en pacientes con lesiones izquierdas.

Palabras clave. Cognición. Epilepsia. Lenguaje. Memoria. Test de amobarbital intracarotídeo. Test de Wada.