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# The utility of the intracarotid Amytal procedure in determining hemispheric speech lateralization in pediatric epilepsy patients undergoing surgery

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**Abstract** The usefulness of the intracarotid Amytal (amobarbital) procedure (also called the Wada procedure) in identifying hemispheric language dominance in pediatric patients has not been independently confirmed with intraoperative language mapping techniques. Currently, data are extrapolated from adult studies. To better establish the usefulness of the intracarotid Amytal procedure in identifying hemispheric language dominance in pediatric patients, we reviewed the records of 77 consecutive pediatric patients who underwent sodium amobarbital testing. Among these 77 subjects, 34 underwent intraoperative language mapping, the results of which all completely confirmed the Amytal results. It was also shown that among these pediatric epileptic patients who underwent Amytal testing, there existed not only a strong correlation between left-handedness and atypical speech lateralization (right, bilateral hemisphere), but also between right-sided hemiparesis (i.e., early left-hemisphere injury) and atypical speech.

**Key words** Wada procedure · Sodium amobarbital testing · Hemispheric speech dominance · Language mapping · Atypical speech

## Introduction

In recent years there has been an increased interest in the surgical treatment of children with intractable epilepsy. Utilization of electroencephalography (EEG) video monitoring, readily available quantification of serum levels for antiepileptic drugs, and the recognition that uncontrolled seizures are not only psychosocially disabling, but also biologically damaging [17, 18, 45], have broadened the indications for surgical intervention [25, 32].

Brain tumors are the second most common neoplasm within the pediatric population, and many children with supratentorial brain tumors may present with intractable seizures [3, 16, 35, 39]. Recent investigations have also influenced the indications for surgical intervention by demonstrating a prolongation in the time to tumor progression and, ultimately an increase in survival, following an aggressive surgical resection of the tumor prior to instituting adjuvant therapy [3, 7, 9, 10, 14, 19, 20, 22, 23, 34, 40, 42]. The quality of life is also improved with more aggressive resections, especially when separate seizure foci are searched for and resected along with the tumor [2, 4].

When planning for the removal of a tumor or epileptic focus that involves the hemisphere associated with speech, it is helpful to identify the cortical regions associated with speech and language functions, in order to facilitate the extent of resection and minimize the operative morbidity. This is achieved in adults with an awake craniotomy and stimulation mapping, or by using extraoperative techniques in children. The majority of these patients also undergo preoperative intracarotid Amytal (amobarbital) perfusion testing, as originally described by Wada [43, 44], to lateralize speech and memory function.

Since the initial investigations performed by Wada, there have been a multitude of studies investigating and documenting both the ease of administration and the utility of the Wada procedure in determining hemispheric language localization in adults [11, 13, 21, 33, 47, 48]. However, the utility of the Wada procedure has not been well-defined for pediatric patients with respect to the type of information that is gained in this particular patient population.

A recently published study suggested that the Wada procedure appears to be an effective tool in determining hemispheric language dominance in a pediatric population [46]. However, this investigation did not provide independent confirmation of language dominance using intraoperative stimulation mapping techniques.

The purpose of this study is to analyze how useful the intracarotid amobarbital (Wada) procedure is in children and adolescents for reliable identification of hemispheric language lateralization preoperatively with comparison to the intraoperative findings.

## Patients and methods

### Subjects

The clinical history, radiographic and surgical reports, and neuropsychological testing results of 77 pediatric patients who underwent intracarotid Amytal testing (Wada procedure) at the Regional Epilepsy Center in Seattle, Washington, were retrospectively reviewed. All but one of these patients had intractable seizures and had undergone testing for evaluation prior to the scheduled surgery. There were 43 male and 34 female patients. Ages ranged from 7 to 18 years, with a mean age of 14.2 years. Seventeen patients had tumors, i.e., oligodendrogliomas ($n=4$), astrocytomas ($n=6$), gangliogliomas ($n=6$), and a recurrent choroid plexus carcinoma ($n=1$). Seven patients had a pre-existing hemiparesis: two left-sided (one mild, one severe), five right-sided (two mild, one moderate, and two severe).

### Intracarotid Amytal procedure

The intracarotid Amytal (Wada) test involves insertion of a catheter under local anesthesia into the femoral artery at the groin. From there it is threaded up into the internal carotid artery just beyond the bifurcation. Cerebral angiography is performed to eliminate the possibility of any unusual vasculature. Fluoroscopy is used to confirm catheter placement.

On the day before catheterization, baseline testing is performed for 5 min and an explanation of the procedure is given; any object or reading card that the patient does not get consistently correct is withdrawn from the test in an attempt to have the baseline error rate as low as possible. A 1-min baseline examination which includes object naming, distraction reading, and recall of the object is done to refamiliarize the patient with the technique and to further establish the baseline error rate [12].

Subsequently, the internal carotid artery ipsilateral to where the planned surgery is usually catheterized first. Sodium Amytal (50–125 mg) is injected by hand into one and subsequently the other carotid artery over approximately 4 s. Upon injection, the patient, with both hands held in the air, commences the object naming, distraction reading, and recall tasks. Usually the contralateral hand will become flaccid in the first 10 s following injection. The task is continued for at least 6 min or until the patient has returned to baseline, whichever is longer. Errors in naming, reading, and recall are recorded. Once the patient is back to baseline (usually 30 min after the first injection), the other hemisphere (nonsurgical side) is then injected and the same procedure is carried out.

Typical speech is defined as language lateralization to the left hemisphere. Patients who have speech lateralized to the right or to both hemispheres are considered to have atypical speech.

### Intraoperative language mapping

Stimulation mapping to identify language cortex has been previously reported by our group [5, 30]. Briefly, electrocorticography is used to identify any epileptiform activity and to determine the afterdischarge threshold following cortical stimulation. The largest current that does not result in afterdischarges is used for language mapping. The rolandic cortex is first identified using a bipolar electrode (5-mm spacing) that delivers a current between 2 and 16 mA (60 HZ, 2.5 ms duration; biphasic square wave pulses). The patient first counts numbers and speech arrest is identified contiguous to the face motor cortex, i.e., Broca's area. Following this, language function is assessed using naming errors as the paradigm for testing as slides of common objects are presented to the patient during stimulation mapping. Cortical areas where repetitive errors in naming are localized indicate sites essential for language. All intraoperative testing was recorded on audiotapes for future analysis and sterile tickets were placed on the cortical surface and a photograph taken to permanently record each patient's language map. Thirty-four children and adolescents in this study underwent intraoperative speech localization using these methods.

### Radiographic studies

Patients underwent a variety of diagnostic imaging studies. Because intracarotid Amytal testing and radiographic studies are often performed at separate institutions, there were eight children for whom no radiology report was available. One child had a pneumoencephalogram, 2 patients had angiographic studies, 44 individuals had computed tomography (CT) scans, 13 patients had magnetic resonance imaging (MRI) scans, and 9 children had both CT and MRI studies.

### Handedness

Handedness was established for seven different activities: writing, throwing a ball, hammering a nail, using an eraser, turning a doorknob, cutting with a knife, and using scissors. The patient was considered right-handed if writing was done with the right hand, and left-handed if writing was done with the left hand. Nine patients had no testing to determine handedness, or documentation in the medical records.

### Statistical analysis

All significance values were calculated using Fisher's exact method [15].

## Results

### Wada testing and intraoperative mapping

One patient in the study group had indeterminate Amytal testing results, while the other 76 children had clear findings with respect to speech lateralization. As shown in Table 1, there was a perfect correlation of Wada test results (typical speech versus atypical speech) with intraoperative stimulation mapping (typical versus atypical: $P=0.00002$). In other words, children with left-sided speech lateralization based on Wada testing had this confirmed in every instance with intraoperative stimulation mapping where that mapping was performed. The group that received intraoperative mapping ($n=34$) had a mean age of 14.35 years, while the group that did not receive any intraoperative testing ($n=35$) had a mean age of 14.6 years. A separate variance estimate had a two-tail probability of 0.746, making it highly likely that these two groups did not differ in age constituency, and, most likely, did not differ as sample groups.

### Amytal testing and handedness

As shown in Table 1, if a subject was left-handed (unless he or she had a right hemiparesis), there was a significant likelihood that that subject would have atypical Amytal results ($P=0.005$); similarly, there was a highly significant correlation between right-handed children and typical speech.

### Amytal testing and hemiparesis

As shown in Table 2, there were seven subjects who had hemipareses: two left-sided and five right-sided. In 100% of the patients in whom there existed a right-sided hemiparesis, atypical speech was found during Wada testing. In both of the patients with left-sided hemiparesis, typical speech was found. The average age of onset for right-sided hemiparesis was 2.38 years (28.6 months). In both children with left-sided hemiparesis, the onset of their deficit was at birth.

**Table 1** Intracarotid Amytal test results as a function of intraoperative mapping data and handedness (excluding individuals with right hemiparesis)

| Wada results | Intraoperative mapping results ($n = 34$) | | Handedness ($n = 68$)[a] | |
|---|---|---|---|---|
| | Typical | Atypical | Right | Left |
| Typical[b] | 30 | 0 | 55 | 7 |
| Atypical[c] | 0 | 4 | 2 | 4* |

$P = 0.00002$; * $P = 0.005$

[a] In only 68 of the 77 patients was handedness tested or documented in the chart

[b] Typical = left hemisphere speech lateralization

[c] Atypical = right or bilateral hemisphere speech lateralization

**Table 2** Intracarotid Amytal test results as a function of hemiparesis

| Wada results | Hemiparesis | |
|---|---|---|
| | Left-sided | Right-sided |
| Typical | 2 | 0 |
| Atypical | 0 | 5 |

## Discussion

The usefulness of the intracarotid Amytal procedure in determining hemispheric lateralization for speech prior to epilepsy surgery has been documented in adults [11, 13, 21, 33, 47, 48], and the results correlate well with the surgical findings and outcome [11]. However, there has been some question as to how accurate Wada results are when right-hemisphere dominance is suspected [48]. A thorough review of the literature revealed no studies which attempted to examine the usefulness of the Wada procedure in pediatric patients or to correlate the findings with intraoperative stimulation mapping for language lateralization.

This study is the first to address the utility of the Amytal procedure in predicting hemispheric language dominance as compared with the intraoperative findings in a group of children and adolescents with intractable seizures. There was one patient in whom the Amytal procedure did not provide acceptable information regarding hemispheric language lateralization. This child had multiple injections followed by mild hemiparesis and the equivocal results may have been related to an ineffective drug injection. Thirty-four of the patients underwent intraoperative speech mapping, all of whom had complete correlation of the data with the results of their preoperative amobarbital test. These results confirm that the intracarotid Amytal procedure provides valuable and reliable information regarding hemispheric language dominance in pediatric patients.

Is the Amytal procedure safe and tolerable for pediatric patients to undergo? In our series, all of the Amytal testing was performed and interpreted by the same individual (C.D.), providing both consistency and uniformity of technique and interpretation of results. The test was performed in the same basic way as with adults, but with less Amytal and sometimes simpler test items. Rarely was the procedure stopped or altered due to the uncooperative nature of the patient, except in some of the very youngest children. The use of propofol (Diprivan) as an ultrashort-acting sedative-hypnotic agent for femoral arterial catheterization during pediatric Amytal tests may also be used to allay some of the problems with patient anxiety and fear [8], and we have used it successfully.

In regard to hemispheric language lateralization, 11 of 76 children (14%) demonstrated atypical language representation, of whom 9 (82%) were left-handed. Five of these 11 patients (45%) with atypical language representation also had various degrees of a pre-existing right-sided hemiparesis with an early age of onset. These results corroborate previous studies in adults suggesting that not only is there a relationship between left-handedness (independent of hemiparesis) and atypical speech representation among epileptic patients undergoing Amytal testing [1, 36, 37, 38, 41, 47], but there also exists a relationship between atypical speech and right hemiparesis from left-hemisphere injury [6, 35, 41]. Early left-hemisphere damage, e.g., within the first few years of life, supports plasticity with regard to language lateralization to the right hemisphere. This study emphasizes that very young children may transfer language to contralateral hemispheric regions even after they have started to talk and form sentences – a finding that has not been critically assessed before.

An important concept in this paper is based on the assumption that intraoperative stimulation mapping for language localization is accurate and effective in determining cortical areas responsible for speech. While it appears that there exists a great deal of variability in cortical areas associated with language representation [24], this technique has been proven to be very accurate and safe, thus preventing significant postoperative speech and language-related deficits in both adults and children [25–31]. For patients who are unable or too uncooperative to undergo awake intraoperative language stimulation mapping, a subdural electrode may be inserted 1 week prior to the definitive surgery to obtain the necessary information [5]. Language mapping is achieved via the electrode array by applying small currents between electrode contacts, resulting in bipolar stimulation. The parameters used for this are the same as described above.

This study does not document memory testing, due to the complex and variable nature of analyzing this function in children. While memory testing is a part of the Amytal procedure, a recent study has shown that various testing methods vary significantly in presaging memory loss after surgery [12]. Thus, the area of memory needs to be approached carefully.

There are two major limitations to this study. First, intraoperative language mapping was performed only on one side in any given patient. Thus, we were not able to provide positive confirmation of speech sites in about half the patients because they had speech on the other side. However, it is of interest to note that we never found speech in those patients on the side opposite that indicated by the Amytal test, although we did not always look for it systematically.

The second limitation is the small sample size and relatively large number of older adolescents within the study group. Statistics were performed utilizing Fisher's exact method in an attempt to take into account the small sample number. The older adolescents were included in the study not only to increase sample size, but also because a large majority of these individuals had had their seizure disorder since early childhood or infancy, i.e., average duration of seizure disorder was 101.3 months, as determined from the patient history.

In summary, the data presented in this retrospective analysis suggests that the intracarotid Amytal procedure provides valuable and accurate preoperative information pertaining to language lateralization in pediatric epilepsy patients. This data also further corroborates previous studies suggesting a relationship between left-handedness and atypical speech as well as a relationship between right-sided hemiparesis (early left-brain injury) and the development of atypical speech.

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