CHAPTER

9

The Right Hemisphere's Role in Recovery from Aphasia: Evidence from Intracarotid Sodium Amytal Testing

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It is frequently suggested in the literature that recovery from aphasia depends not only on the size and site of the lesion that produced it, but also on the relative patency of the other hemisphere, particularly in its temporoparietal and motor speech areas. Pure word deafness is much more likely to occur with bilateral temporal lobe lesions, for example, than when only the left hemisphere is involved. It is thought that individuals with multiple bihemispheric lesions typical of multi-infarct dementia have limited resources for recovery from aphasia-producing stroke. Neuropsychological profiles from patients who have recovered well from aphasia, according to Aaron Smith (1972), show superior performances in so-called right-hemisphere functions over less well recovered aphasic patients.

One of the provocative possibilities that explains the success of Melodic Intonation Therapy (MIT) is that it possibly capitalizes on the language potential of the right hemisphere, and data from Naeser and Helm-Estabrooks (1985) suggest that left-hemisphere-damaged individuals who have concomitant right lesions do poorly with the technique. West (1977) and Myers (1984) have both taught us well to involve the aphasic patient's right hemisphere if we expect to maximize recovery. But studying the role of the right hemisphere in recovery from aphasia is a difficult one. Animal models are inappropriate, and neuropsychological testing of assumed right-hemisphere functioning is often confounded by language deficits in recovering patients.

Intracarotid Amytal Testing (IAT) is an intriguing tool for the clinical aphasiologist, primarily because it provides an unusual opportunity to observe cognitive functioning in individuals as they undergo brief and reversible functional hemispherectomies, one to the left and the other to the right side of the brain. Injection of sodium Amytal into one internal carotid artery anesthetizes the cerebral hemisphere served by that artery for a short time, usually 8 to 10 minutes. The Amytal then passes from the hemisphere, leaving no long-term or even immediate effects. The same procedure is followed an hour later with the other hemisphere anesthetized. The goal of IAT is a practical one. It is used to determine when the patient's *unanesthetized* hemisphere is capable of sustaining the memory functions that might be compromised if a portion of one hemisphere, usually the anterior temporal lobe and involving hippocampus, is removed from the *anesthetized* hemisphere or if a callosotomy is performed. The test furnishes information to the neurosurgeon that can be useful in guiding decisions regarding the cognitive risks of particular types of tumor or epilepsy surgery.

We routinely conduct a standard IAT of our own design as part of the extensive evaluation protocol of our Epilepsy Center. Our IAT assesses serial speech, recall of stimuli presented before the test has begun, recall of personally relevant material, object and color recognition, reading, con-

frontation naming, sentence comprehension, memory for designs, limb apraxia, repetition, and finally visual imagery. It is administered while the patient is experiencing anesthesia resulting from a standard dose of 125 mg of sodium Amytal administered to the internal carotid artery through an angiographic catheter placed in the femoral artery. The patient is instructed to raise his or her arms and begin counting as Amytal is injected. Testing is begun when the patient's contralateral arm falls, indicating a functional hemiplegia and anesthetization of the hemisphere. When arm strength returns, it is presumed that the sodium Amytal has cleared the brain. At that time, our test enters its recall phase, and patients are asked to recollect, with specific guidance, the questions they were asked, the stimuli they were shown, and so forth. The test contains no difficult or surprise material. The day before the test is given, it is described in detail to the patient, and example items are provided. The test relies heavily, but not totally, on verbal stimuli and responses. This is primarily because it is faster to use such material, and it ensures that a substantial number of items can be presented for subsequent recall. However, we have specifically designed the IAT also to allow us to observe some putative special cognitive functions of the right and left hemisphere during the testing procedure itself and to compare right- and left-hemisphere functioning in the same individual. Our protocol's design has thus been made compatible with some of the potential uses of IAT that Code (1987) has succinctly outlined.

This chapter concerns verbal behavior only during *left*-hemisphere Amytal anesthesia. To date, 17 patients with intractible complex partial seizures have been tested with our measure. We are reporting here on 14 of them. These 14 are all right-handed and have unequivocal left-hemispheric dominance for language. We have not included the fifteenth, because he appeared to have bilateral language dominance. The final two patients are not included because they are part of study testing prospectively the hypothesis we present here using retrospective data.

SUBJECTS

All 14 subjects had normal or near normal language, as measured by the Western Aphasia Battery (WAB), although compromised reading and writing skills were noted in the majority, possibly due to disturbed educational experiences typical of individuals with histories of intractible epilepsy. They ranged in age from 16 to 38 years; five were female, nine were male. These patients demonstrated two distinctive patterns of language behavior when Amytal was injected into the left cerebral hemisphere. Patients are grouped according to the patterns (Table 9-1).

TABLE 9-1. PATIENT SUMMARY

ID	*1st vocalization*	*1st word*	*Arm strength return*	*Hemisphere Okay*	*Focus of seizure*
M 1	2:21	4:00 ("farming")	4:55	LH	?
M 2	3:43 ("red")	3:43 ("red")	3:25	RH, LH	?
M 3	7:09 ("Ozzie")	7:09 ("Ozzie")	4:12	LH	?
M 4	2:08 ("Yes")	2:08 ("Yes")	4:03	RH, LH	L temporal
M 5	3:24	5:43 ("Hi")	9:13	LH	Multi
M 6	3:20 ("Stop it!")	3:20 ("Stop it!")	4:10	RH, LH	Multi
M 7	8:20 ("Monday")	8:30 ("Monday")	8:20	LH	R temporal
	$\bar{X}$ = 4:21	$\bar{X}$ = 4:55	$\bar{X}$ = 5:46	3 RH/7 LH	
A 1	:35	1:23 ("April")	3:15	RH	Bifrontal
A 2	:10	1:30 ("yeah")	3:00	RH	L temporal
A 3	1:18	2:15 ("Yeah")	8:29	?	R temporal
A 4	:31	2:50 ("Monday")	8:28	RH, LH	R temporal
A 5	1:53	2:26 ("1 outa 4")	1:28	RH, LH	L temporal
A 6	:25	3:18 ("Red")	7:07	RH, LH	Bitemporal
A 6	:29	3:20 ("You should")	12:00	RH, LH	R occipital
	$\bar{X}$ = :46	$\bar{X}$ = 2:26	$\bar{X}$ = 6:15	6 RN/4 LH/1?	

L = left; R = right; H = hemisphere; M = mute; A = aphasic.

The first pattern was characterized by vocal unresponsiveness, or "mute." Seven patients manifested this pattern. They did not vocalize until close to the time that total arm strength returned, signaling the clearance of Amytal from the brain. For five of the seven, the first vocalization occurred less than a minute before arm strength, and for six of the seven, this first vocalization was a substantive word, used correctly and in context of the stimulus question. In effect, these patients appeared to be obtunded until most of the anesthetic had cleared the hemisphere and then came out of the experience talking almost normally.

The second pattern is aphasic-like, with vocalizing preceding return of arm strength by almost 4 minutes and undergoing a progressive approximation to normal speech in a manner resembling recovery from global aphasia via a fluent evolutionary course. Typically, the seven patients who demonstrated this pattern spoke enough with their left hemispheres anesthetized for us to recognize the perseverations, paraphasias, repetition difficulties, and so on that characterize aphasia. Therefore, we will refer to them as "aphasic."

PROCEDURE

The purpose of this chapter is to describe what contributes to these markedly different performances under Amytal. The first step was to analyze all available neuropsychological test performances to see if explanatory differences could be found there. Mute and aphasic groups were compared on the Weschler Adult Intelligence Scale (WAIS) Verbal and Performance IQs, California Verbal Learning Test, Raven's Progressive Matrices, Trailmaking, and Cognitive Laterality Battery using chi-square analysis. No statistically significant differences were found between groups on these measures. Similarly, no statistically significant differences were found concerning group composition for age, gender, patient size, or the order in which the hemispheres were anesthetized. We then turned our attention to any structural differences that may have existed between the groups.

Using a composite of computed tomography (CT), magnetic resonance imaging (MRI), and regional cerebral blood flow (rCBF) findings, we sought to determine whether structural abnormalities differentiated the groups. Chi-square analysis was statistically significant for fewer of the mute group having left-hemisphere abnormalities ($\chi^2 = 4.67$, df = 3) that were visualized on these measures. It approached statistical significance for fewer patients in the aphasic group having similarly visualizable right-hemisphere abnormalities. Thus, mute patients appeared to have substantially intact *left* hemispheres; aphasic patients tended to have substantially

intact *right* hemispheres. Focus of seizure is defined in the Epilepsy Center as a composite of information including continuous 3- to 5-week recordings from depth electrodes inserted into the brain at four temporal and frontal sites, seizure activity measured by standard electroencephalogram (EEG), and thiopentathol-induced seizure activity. Five of the seven patients in the aphasic group had a single focus of seizure activity (two left temporal, two right temporal, and one occipital). In the mute group, six of seven had multiple seizure foci or no apparent focus, with seizures appearing in both hemispheres and quickly generalizing to the whole brain. The resulting chi-square was 7.14, $p \leq .001$ ($df = 3$).

DISCUSSION

These data support the following interpretations of why the "mute" patients were mute and the "aphasic" patients were aphasic under conditions that required them to respond only with their right hemispheres:

1. Mute patients could not communicate because their right hemispheres were compromised, due either to long-term effects of the patterns of their seizure activity or to their right-hemisphere abnormalities. These mute patients had increased reliance on their left hemisphres, and when that hemisphere underwent a functional hemispherectomy, no compensation or substitution from the right was possible.
2. Conversely, those individuals who behaved in an aphasic manner had generally more intact right hemispheres, which makes compensation or substitution possible. It is also possible that because their left hemispheres were more likely to have abnormalities, the right hemispheres of these individuals may have already been assuming some language functioning, however aphasic-like it might have been.

We relate these data to *real* aphasia by hypothesizing a similar role to the right hemisphere for recovery from that disorder. The mute group, whose right hemispheres had higher likelihood of abnormality, demonstrated no right-hemisphere language during Amytal anesthetization of their left hemispheres. Our hypothesis is that this group is analogous to aphasic individuals whose right hemispheres cannot be adequately stimulated to participate in language behavior. In this regard, our hypothesis is compatible with the observations of Kinsbourne (1971), who noted that post-stroke aphasic individuals maintained their aphasic behavior under anesthesis of the left hemisphere, but became mute when their right

hemispheres were anesthetized with sodium Amytal. Kinsbourne interpreted his results to suggest that aphasic language was a function of right-hemisphere participation in language.

Our "aphasic" group did not generate much normal language when the left hemisphere was anesthetized, and they were relying on the right hemisphere. But they did vocalize early in the procedure, they responded aphasically throughout it, and the severity of their "aphasic-like" difficulties appeared to lessen over time. Our hypothesis is that this group is analogous to aphasic individuals whose right hemispheres are in good shape and that can be stimulated to participate in more normal language behavior over time.

Figure 9-1 compares the left-hemisphere-anesthetized recall performances with the right-hemisphere-recall performances for the mute and aphasic subjects. It can be seen that both groups do relatively well when they are relying on their *left* hemispheres alone, a topic not discussed here. Further, both groups do much less well under the conditions described in this chapter. But do note that the recall performance of the "aphasic" group is almost twice that of the mute group for right-hemisphere responding. We believe that this further supports our hypothesis.

These are preliminary data, retrospective in nature. The next step is to do a prospective study, which we are currently doing. One of us is predicting the mute-aphasic distinction on the basis of focus of seizure and structural abnormality. The other is predicting focus of seizure and structural abnormality immediately following the Amytal test, on the basis of test performance. In both of our last two patients, our predictions have been correct.

We really do not yet understand the mechanisms by which recovery from aphasia occurs. Mostly, ways in which recovery of function following lesioning in experimental animals have been invoked to explain it. Rubens (1977) has suggested that some recovery derives from reversals of physiological changes that accompanied the aphasia-producing event itself. These include the lessening of edema, the reestablishment of pretraumatic neurotransmitter activity, the absorption of the hemorrhagic mass in the case of intracerebral hemorrhage, and recovery from the remote effects, or diaschisis. Johnson and Almli (1978) summarize other mechanisms invoked to account for recovery. These mechanisms probably play a role later than the changes outlined by Rubens. They include

1. Substitution — a secondary neural system takes over the functions of the primary one, implying either redundancy or multiple representation in the central nervous system.
2. Vicariation or equipotentiality — previously nonspecified areas assume the function. (There are two mechanisms that are im-

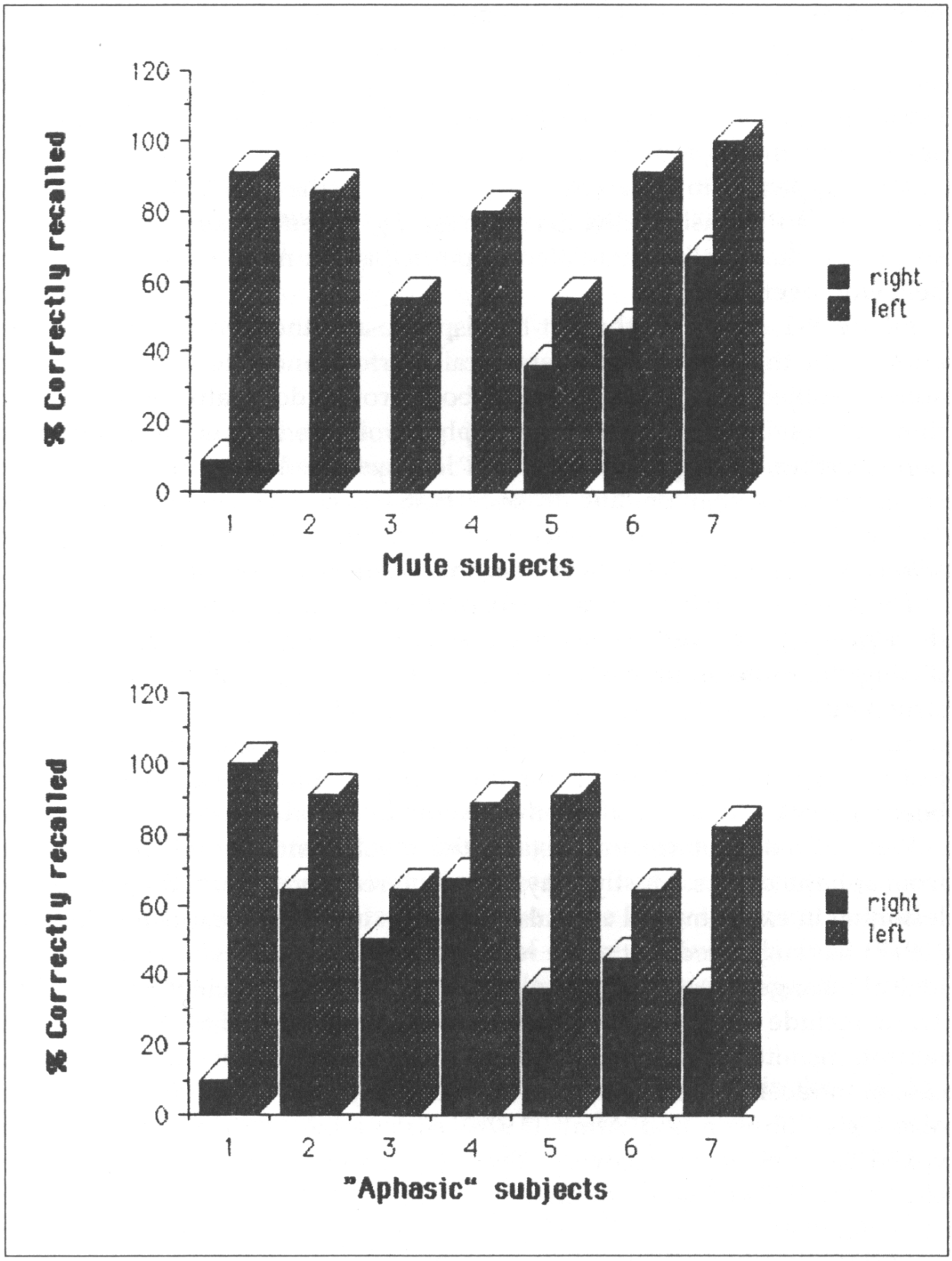

Figure 9-1. Recall performances with left and with right hemispheres anesthetized.

plied to be operative as far as the present working hypothesis is concerned.)

3. Regeneration — new growth in damaged neurons.
4. Collateral sprouting — new growth in areas adjacent to damaged tissue.
5. Denervation sensitivity — increased sensitivity to neurotransmitters by neurons that have lost innervation.
6. Behavioral strategy change — new patterns of internal and external environmental cues are used to maintain functions.

Fazzini, Bachman, and Albert (1986) have recently organized the available facts regarding recovery and have developed a falsifiable theory of recovery. However, it is clear that at the present time we have only an incomplete picture. We do not even understand recovery of simple behaviors in organisms less complex than humans. And given the adaptive capacities of the central nervous system, we cannot even rule out the possibility that after the earliest trauma-related reversals, there is no further recovery of higher cortical functions at all. It is possible that what one observes as aphasia, then, might be the adaptive workings of a now imperfect nervous system. Therefore much work remains to be done if we are to understand recovery from aphasia. It is our hope that observations of performance under hemispheric anesthesia might be helpful in this regard.

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DISCUSSION

Q = question; A = Answer, C = comments.

Q. What kind of imaging techniques were you using to look for structural abnormalities, and what kind of abnormalities did you see?

A. We're pretty lucky in terms of the imaging that's available. The University of Pittsburgh Epilepsy Center uses a very extensive protocol including CT, MRI, measurement of cerebral blood flow, EEG, and continuous implanted depth electrode recording. There is also the angiography that precedes the Amytal test. So we have as extensive a set of imaging as there are tools available in Pittsburgh. As for the types of abnormalities that are found, they run the gamut. Two patients in the present study had right hemisphere tumors. We also have patients with enlarged ventricles, encephalomalacias, calcifications, and so forth. In some instances, some of these are seizure-focus related, in others they are probably consequences of having fallen during a seizure, and in still others, the abnormalities are possibly not related to the seizures at all.

C. At Madison, we thought we had discovered the wheel. We find out that we've only found one of your leftover wheels. It's also been our experience that it is a good hypothesis that the patient who has profound problems following left-hemisphere injection has in addition some right-hemisphere deficit. Thanks for that.

Q. I always worry about psychometric properties of tests. With a two-item test such as the one you describe, I wonder if you are sampling anything stable. For the most part, you can't test aphasia with two items. And also there is the question of test-retest reliability. I don't know how you might gather that. You certainly can't get the patients back again. You're not going to get volunteers. But I wonder if you can group your data and conclude anything until you have established the psychometric properties of your test?

A. I have a little trouble with your question. The procedure I have described is clearly not one with sound psychometric properties. It isn't really a test at all in that sense, but a protocol that is useful for finding out some important information that would be unavailable if it were necessary to use standardized tests. The protocol is used only to see if the patient remembers what has happened to him while it went on. For that reason we sample a lot of behaviors rapidly. But I think part of the story must be that most patients perform almost flawlessly

when they are working out of their left hemispheres alone. Recall is in the range of 85 to 100 percent.

By the way, it would be nice if Amytal procedures were a little more systematic across the country in terms of everything from behaviors sampled to dosage of Amytal used. I am much more concerned about this sort of systematization of a protocol than I am about its psychometric properties. Finally, I am not sure it helps you with your question, but I am very sure that I score the protocol reliably. I do it from the videotapes, corroborated with the written record and also an audiotape, and I do it over and over until my inter-rater reliability is 100 percent.

Q. Several years ago I had an experience that was fortunate for me but unfortunate for a patient. I observed him having a transient ischemic attack (TIA) while he was waiting for a therapy session. A code was called, but it was 4 to 5 minutes before people got there. So I had the fortunate experience of watching him have this TIA and recovering over about a 30-minute period. This man was about 3 years out of a single left-hemisphere stroke, and at about the 85-percent level on the PICA. So he had recovery to a functional level for basic ADLs. The evolution of his symptoms during that TIA was not unlike those of the patient on your videotape. Do you have any thoughts on whether sodium Amytal testing could be construed as a similar experience or a similar occurrence either clinically or neurophysiologically to a TIA?

A. That's an interesting hypothesis, but I don't know the answer. It does remind me of Kinsbourne's study that I mentioned earlier. The study observed language under Amytal in three aphasic patients. Kinsbourne found that when the right hemispheres of his aphasic patients were anesthetized, his patients were mute, but that when the left hemispheres were anesthetized, they wobbled along in their aphasic manner. This suggested that the aphasic speech itself was a right-hemisphere phenomenon, rather than a damaged left-hemisphere phenomenon.