INTRACAROTID INJECTION OF SODIUM AMYTAL FOR
THE LATERALIZATION OF CEREBRAL
SPEECH DOMINANCE

EXPERIMENTAL AND CLINICAL OBSERVATIONS

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I
n 1948, during the course of studies on seizure mechanisms, one of us
(J.W.) carried out intracarotid injection of Sodium Amytal and Metra-
zol to investigate the mechanism of the spread of epileptic discharge
between the cerebral hemispheres in man.9–11 The intracarotid injection of
Sodium Amytal was found to induce a temporary loss of function in the
ipsilateral cerebral hemisphere, including aphasia when the dominant hemi-
sphere was injected. The suggestion was made that this would be a useful
technique for the determination of the lateralization of cerebral speech
dominance. Approximately 80 patients were tested in this way in Japan
during the period 1948–1954, using doses of 50 to 300 mg. of 10 per cent
Sodium Amytal, and no complications were encountered.

In the surgical treatment of focal epilepsy, the presence of speech repre-
sentation has often been verified by electrical stimulation of the speech zones
in the frontal and parietal opercula with the cortex exposed under local anes-
thesia.4–7 Interruption of counting or naming produced by such stimulation
gives positive evidence in this regard. Lack of such response, however, is not
certain proof that speech is in the other hemisphere, since in some instances
the electrical stimulating current does not seem to be an adequate stimulus
and no effect is observed, even though speech is actually subserved by the
convolutions being stimulated. In view of the obvious importance of accurate
knowledge of the lateralization of speech dominance when operating near
the Sylvian regions in ambidextrous and left-handed individuals, further
studies regarding the technique of intracarotid injection of Sodium Amytal
seemed indicated, particularly with regard to the margin of safety in relation
to dose and to the effect of accidental injection into the vertebral artery.
This report concerns some experimental studies on the monkey bearing on
these points, and a brief clinical report on the use of this test in a consecutive
series of 20 patients.

EXPERIMENTAL STUDIES

I. METHODS

Eleven experiments (Table 1) were carried out in 8 macaque monkeys (2.4–5.5
kg.). In each experiment the animal was lightly anesthetized with Pentothal an-

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couver, B. C.
### LATERALIZATION OF CEREBRAL SPEECH DOMINANCE

#### TABLE 1

*Summary of monkey experiments (11 experiments in 8 monkeys)*

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Date of Experiment</th>
<th>Artery Injected</th>
<th>Dose of 10% Sodium Amytal (mg.)</th>
<th>Date of Sacrifice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Apr. 12, 1956</td>
<td>Right common carotid</td>
<td>7</td>
<td>Apr. 19, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Apr. 19, 1956</td>
<td>Right vertebral</td>
<td>7</td>
<td>Apr. 19, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10</td>
<td>(at end of experiment)</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Apr. 25, 1956</td>
<td>Right common carotid</td>
<td>140</td>
<td>May 4, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>210</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>May 2, 1956</td>
<td>Right vertebral</td>
<td>210</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Apr. 29, 1956</td>
<td>Right common carotid</td>
<td>350 (20%)</td>
<td>May 19, 1956</td>
</tr>
<tr>
<td></td>
<td>May 18, 1956</td>
<td>Right vertebral</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>May 16, 1956</td>
<td>Right common carotid</td>
<td>10</td>
<td>May 17, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>May 16, 1956</td>
<td>Right vertebral</td>
<td>10</td>
<td>May 18, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>May 22, 1956</td>
<td>Right common carotid</td>
<td>10</td>
<td>May 24, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>May 22, 1956</td>
<td>Right common carotid</td>
<td>10</td>
<td>May 24, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>May 23, 1956</td>
<td>Right vertebral</td>
<td>10</td>
<td>May 24, 1956</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Anesthesia, and either the right common carotid or right vertebral artery was exposed in the neck. One to 6 injections of varying doses of Sodium Amytal (10 per cent solution with 1 exception) were made in each monkey into the exposed common carotid or vertebral artery, using a tuberculin or 2 cc. syringe. The artery was cannulated with a polyethylene tube in the first few experiments, but thrombosis in the cannulated artery developed in 2 animals. In the remainder of the experiments, the in-
jection was made through a 27 gauge hypodermic needle inserted into the artery. The dosages ranged from 7 to 350 mg., approximately 1 to 35 times the proportional maximal human dose that was used in this series of patients (200 mg.), based on comparative average brain weights for monkey and man. When more than one injection was given in an experiment, the interval between injections ranged from 30 to 60 min., depending on the time required for the animal's vital signs and electroencephalogram to return to base-line levels. Respiration, pulse, movement of limbs in response to pin prick and pupillary response to light were recorded at frequent intervals in each experiment. Femoral arterial pressure was recorded on the side contralateral to the injection in 5 monkeys, using a Lilly capacitance transducer coupled to a D.C. Sanborn amplifier, and to a Sanborn industrial recorder. When respiratory arrest occurred after injection of the vertebral artery, the animal was placed in an artificial respirator until spontaneous breathing resumed.

The electroencephalogram was recorded in 7 experiments, 1 each in 7 of the 8 monkeys. Monopolar derivations were used with phonograph-needle electrodes placed in the frontal, central and occipital regions bilaterally, 1.5 cm. lateral to the mid-line. These electroencephalographic studies will be reported in detail in a later communication.

One animal was sacrificed at the completion of an experiment in which the vertebral was injected, which had been preceded 7 days earlier by an experiment in which the common carotid artery was injected. The remaining 7 animals were sacrificed either 34 or 48 hours after the experiment (or after the final experiment in the case of 2 animals who had both carotid and vertebral injections 1 and 3 weeks apart). During the interval between experiments and sacrifice, the neurologic status was recorded.

II. RESULTS

A. Carotid Injection. Fifteen injections of varying doses of Sodium Amytal were made in 6 monkeys (3 injections each, except for 2 monkeys receiving the largest doses, who were given 2 and 1 injections each). A contralateral hemiparesis developed promptly after each injection.

(1) 7-35 mg. (1 to 3× the proportional human dose—9 injections in 4 monkeys). There was no change in the pulse after any of the 9 injections. Seven of these injections caused no alteration in respiration. In 1 monkey, after injection of 20 mg., the respirations stopped for 10 sec., then returned at the pre-injection rate. When the injection was repeated in this animal a short time later, giving 30 mg., the respirations became irregular for a similar 10-sec. period but did not stop. The blood pressure was measured during 3 of these 9 injections, and in each instance there was a fall of the order of 25 mm. Hg in systolic and diastolic pressures with a return to the pre-injection level in 15 to 20 min. There was no alteration of the pupillary or corneal reflexes following any of these injections.

(2) 100-140 mg. (10 to 14× the proportional human dose—1 injection in each of 4 monkeys). There was no change in either the pulse or respiration after any of these 4 injections. The blood pressure was measured only during 1 injection of 140 mg., which produced a prompt fall from 145/100 to 110/70 mm. Hg. The pressure gradually rose during the next 7 min. to
135/105 mm. Hg, where it stabilized. With this injection the pupillary light reflex remained normal, but the corneal reflex disappeared 3 min. after injection, returning 25 min. later.

(3) 210 mg. (20× the proportional human dose—1 injection; this animal had received an injection of 140 mg. of Sodium Amytal into the same carotid artery 30 min. earlier, described in the preceding paragraph). Immediately after the injection the blood pressure fell from 140/115 mm. Hg to 40/20, remained at this level for 5 min., then gradually rose at the rate of 10 mm. Hg every 10 min. to a level of 100/75. The respirations were not immediately affected, but began to slow after 1 min. During the next 10 min. they slowed from 34/min. to 14/min. and became irregular. Forty min. after the injection, an injection of picrotoxin resulted in a regular respiratory rhythm and the rate increased to 20/min. The pulse rate slowed from 180 to 140/min., and remained stable for the ensuing 8 hours, at which time the animal began to rouse and the pulse rate increased to the pre-injection rate. The pupils dilated bilaterally, and both the light reflex and the corneal reflex disappeared 1 min. after the injection. The light reflex returned after 6 hrs., the corneal reflex after 10–12 hrs. It is felt that these changes in respiration, pulse and eye reflexes appearing only after 1 min. following the injection were caused by action of the Amytal on the brain as a whole after mixing with the general circulation, and were not caused by the initial impact on the ipsilateral hemisphere.

(4) 350 mg. (35× the proportional human dose—1 injection, given as 20 per cent solution to reduce the quantity injected). This animal was given only this 1 injection into the right carotid artery. There was no significant change in the pulse rate until 1 hr. later, when the rate slowed from 170 to 130. Following the injection the respirations slowed promptly from 40 to 28/min., then, after 1 hr. slowed further to 18/min. These late effects were attributed to the generalized effect of this large dose of Amytal. There was a moderate fall of blood pressure from 90/70 to 60/30 mm. Hg where it remained stable. The corneal and light reflexes disappeared 2 min. after the injection, the latter reappearing 8 hrs. later and the former 12 hrs. later. There was edema of the right side of the face, eyelids, conjunctiva, tongue and submandibular region, which persisted for 4 days. The animal was alert 14 hrs. after the injection, and during the 3-week survival period, exhibited an homonymous hemianopsia, a tendency to circle to the left, but no other obvious neurological deficit. This injection caused several microscopic areas of infarction (see Pathological Results below).

(5). Neurological Status. Each injection was followed by an immediate contralateral hemiplegia, detected in these lightly anesthetized animals by lack of movements of the contralateral extremities in response to painful stimuli. With doses of 100 mg. and more, the animals became deeply anesthesitized after 1–2 min. and movements could not then be elicited on either side. The animals awakened after varying intervals, 5 to 14 hrs., depending on the total dose of Amytal administered, and, except for the animal receiv-
ing the largest dose (350 mg.) described in the preceding section, exhibited no alteration in their neurological status. The electroencephalographic changes, which were unilateral and of short duration with the smaller doses, and more marked, prolonged and generalized with the higher doses, will be reported in a separate communication.

**Summary of Carotid Injections.** Injection of 10 per cent Sodium Amytal in doses up to 140 mg. (14× the proportional human dose) produced no significant alterations in respiration or pulse, and only minimal transient fall in blood pressure. With larger doses (210 and 350 mg.), more marked and prolonged fall in blood pressure occurred and the respiratory rate became slow and irregular, because of the effect of the Amytal on the whole brain after mixing with the general circulation. An immediate contralateral hemiplegia was produced in each animal, followed in 1–2 min. by deep anesthesia with doses of 100 mg. and more. On awakening no residual neurological abnormalities were found except in 1 animal, who was given the Sodium Amytal in 20 per cent concentration instead of the 10 per cent used in all the other injections.

**B. Vertebral Injection.** Sixteen injections (Table 1) of varying doses of Sodium Amytal were made in 5 monkeys (3 injections each, except for monkeys #2 and #1, who received 1 and 6 injections respectively).

(1) 7–35 mg. (1 to 3× the proportional human dose—11 injections in 4 monkeys). Prolonged respiratory arrest occurred after 4 injections, transient arrest after 3, and transient decrease in respiratory amplitude only in 5 (Table 2). There was no change in pulse rate after any of these 11 injections. The blood pressure was measured in 5 instances. With injection of 7 and 10 mg., there was no effect on the blood pressure. With injection of 15 to 35 mg. there was a fall of ~10 to 70 mm. Hg, with gradual recovery starting after 4 to 8 min.

The corneal reflex disappeared promptly in each instance, returning after 5 to 25 min., depending on the dosage given. The pupillary light reflex remained normal in 7 injections and became sluggish for several minutes, but not absent, in the other 4. The pupils became transitorily dilated bilaterally, more marked and prolonged with the injections of 20–35 mg. than with injections of 7–15 mg.

(2) 70–100 mg. (7 to 10× the proportional human dose—1 injection in each of 4 monkeys, each injection made after previous injections of smaller doses). Prolonged respiratory arrest followed each injection, but in each instance spontaneous respirations resumed after an interval of artificial respiration (Table 2). The pulse rate showed either no change, or minimal and transitory slowing. The blood pressure was measured during 1 injection of 70 mg. which produced a fall from 135/105 mm. Hg to 60/25, with return to 135/80 after 20 min. The corneal reflex disappeared promptly in each instance, returning in 5 min. in the largest animal, and after 3 to 4 hrs. in the others. The pupillary light reflex became sluggish in the largest animal.
TABLE 2
Respiratory disturbances induced by injection of Sodium Amytal
into the vertebral artery of the monkey

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Body Weight (Kg.)</th>
<th>Dosage Injected (Mg.)</th>
<th>Respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>7</td>
<td>Temporarily shallow, slow, irregular</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>10</td>
<td>10-sec. arrest; shallow, irregular for 20 sec., then normal</td>
</tr>
<tr>
<td>5</td>
<td>2.6</td>
<td>10</td>
<td>Arrested; returned 25 min. later</td>
</tr>
<tr>
<td>3</td>
<td>2.4</td>
<td>10</td>
<td>Became slow</td>
</tr>
<tr>
<td>8</td>
<td>5.5</td>
<td>10</td>
<td>No change</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>15</td>
<td>10-sec. arrest; shallow for 20 sec., then normal</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>21</td>
<td>Arrested; returned 25 min. later</td>
</tr>
<tr>
<td>5</td>
<td>2.6</td>
<td>30</td>
<td>Arrested; returned 25 min. later</td>
</tr>
<tr>
<td>3</td>
<td>2.4</td>
<td>30</td>
<td>Temporarily shallow, irregular</td>
</tr>
<tr>
<td>8</td>
<td>5.5</td>
<td>30</td>
<td>Temporarily shallow, irregular</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>35</td>
<td>Arrested; no return within 30 min. when next injection was made</td>
</tr>
</tbody>
</table>

1. Injected under controlled respiration. Spontaneous respiration returned 20 min. later.
2. Arrested; returned 4 hrs. later.
3. Arrested; returned 3 hrs. later.
4. Arrested; returned 10 min. later.

Thrombosis of vertebral artery on side of injection and disappeared in the other 3, returning in 15 to 25 min. In each instance the pupils became dilated bilaterally.

(3) 210 mg. (20 × the proportional human dose—1 injection made into the right vertebral artery via a polyethylene catheter). Respirations stopped immediately, then reappeared after 40 min. of artificial respiration (Table 2). Respirations continued to be shallow and irregular, and after 1½ hrs. it was necessary to resume artificial respiration. The blood pressure fell promptly from 155/90 mm. Hg to 40/0, rose to 60/10 after 1 min., then after another 15 min. gradually rose to 110/70, where it stabilized. The corneal reflex disappeared immediately, and the pupillary light reflex after 10 sec. The latter reappeared after 80 sec., and the former after 7 hrs. The animal began to awaken 9 hrs. after the injection, and after another 3 hrs. was completely alert. There was, during the remainder of his 40-hour survival period, a complete tetraplegia and analgesia with paralysis and sensory loss of the right side of the face as well. After 40 hrs. in the respirator, the animal was sacrificed. Autopsy showed thrombosis of the right vertebral artery from the site of cannulation up to its junction with the basilar artery. This is attributed to trauma to the artery incident to the use of the polyethylene catheter, since no thrombosis was found in any of the other animals in which comparable or
larger total doses of 10 per cent Sodium Amytal had been injected by means of a hypodermic needle.

(4) Neurological Status. At the onset of each injection, these lightly anesthetized monkeys usually moved all extremities and vocalized, then became completely flaccid a second or two after the injection was completed. Except in the case of the smallest doses, within another minute or two, the animals became deeply anesthetized. With injections of 15 to 35 mg. the animals began to waken after 30 to 60 min. With the larger doses of 70 to 100 mg. they began to waken after 3 1/2 to 5 hrs. With the exception of the animal described in the preceding paragraph, no abnormal neurological findings were evident once the animals were well awake. The electroencephalographic changes, studied in 4 of the animals, were more generalized at the onset than in the case of the carotid injections, but were otherwise similar in their dependence on levels of dosage. These will be reported in a separate communication.

Summary of Vertebral Injections. The injection of 10 per cent Sodium Amytal into one vertebral artery altered respirations in all except 1 instance. With injections of 7-35 mg., the respirations were rendered temporarily shallow and irregular in 4 instances, were temporarily arrested after 6 injections, and in 1 there was no change. With larger doses, more prolonged respiratory arrest was produced (10 min. to 41/2 hrs.), with resumption of spontaneous respirations in each instance, except in the animal receiving 210 mg. described in the preceding section. The pulse rate was not altered by any of the injections, and the blood pressure was lowered only with doses of 15 mg. and above. The corneal reflex disappeared promptly after each injection, returning after 5 min. to 7 hrs., depending on the dose. The pupils usually dilated bilaterally and the pupillary light reflex disappeared for 15 to 30 min. with doses of 70 mg. and above.

In each instance the injection was followed almost immediately by a flaccid paralysis of all extremities. After another 1–2 min. deep anesthesia was established from which the animals began to awaken in 30 min. to 5 hrs., depending on the dosage employed. With the use of adequate artificial respiration the animals appeared normal neurologically after awakening, except in 1 animal in which thrombosis of the vertebral artery was found at autopsy, presumably caused by cannulation of the artery with a polyethylene catheter.

C. Pathological Results. The right cerebral hemispheres (the side injected) and the brain stems of each of these 8 monkeys were normal to gross examination. Each animal had been utilized in various earlier experiments, and showed lesions elsewhere which, however, did not interfere with the evaluation of the pathological effects of the carotid Amytal injections.

Histologically the brains were also completely normal, with 3 exceptions. Animal #1, who received 3 injections of 10 per cent Sodium Amytal (7, 20 and 35 mg.) into the right common carotid on April 12, and 1 week later 6 injections (7, 10, 15, 21, 35 and 70 mg.) into the right vertebral artery, was sacrificed at the end of the latter experiment 1 1/2 hrs. after the last injection.
The cerebral hemispheres showed no histological abnormalities attributable to the carotid injection 1 week before sacrifice, but the medial portion of the ventral half of the pons showed marked swelling of myelin tubes with balloon- ing, fragmentation and eosinophilic staining of axis cylinders. The nerve cells and glial cells in and around these altered fibers were quite normal. In this animal the vertebral artery had been cannulated with a polyethylene tube and at autopsy a thrombus was found in the vertebral artery extending up from the end of the tube.

Similar but less marked microscopic changes were seen in animal #2, who received a single injection of 210 mg. of 10 per cent Sodium Amytal (20 times the maximal proportional human dose) into the right vertebral artery also through a polyethylene catheter, and was sacrificed 40 hrs. later (see above). In this animal also thrombosis was present in the cannulated vertebral artery extending up into the basilar artery. We believe the histological changes in the brain stems of these 2 animals were related to thrombosis induced by the polyethylene tube, since none of the animals receiving comparable doses of 10 per cent concentration injected via hypodermic needles showed any such microscopic alterations.

Animal #3 received 350 mg. of 20 per cent Sodium Amytal (35 times the maximal proportional human dose) into the right common carotid, and was sacrificed 3 weeks later. Microscopic sections of the brain showed small areas of infarction in the right insula and in two adjacent gyri. This we believe to be the only instance of histological damage attributable to the Sodium Amytal injections in this series of experiments, and this was the only injection in which 20 per cent concentration was used instead of 10 per cent.

In summary, from the pathological standpoint, the monkey brain seems to tolerate without evidence of damage injection into the carotid or vertebral artery of 10 per cent Sodium Amytal in single or divided doses at least as great as 210 mg., which, according to brain weight, is equivalent to 20 times the maximal human dose we have employed. A large dose of 20 per cent concentration produced microscopic patches of infarction, indicating that this concentration of Sodium Amytal should not be injected into the cerebral circulation.

CLINICAL STUDIES

During the past 2 years we have used this test in 20 patients, and our experiences in this consecutive series of patients are summarized in the following section (Table 5).

I. TECHNIQUE

An 18 or 19 gauge needle was inserted into the common carotid artery as for a carotid angiogram. The right and left sides were usually injected on different days. In order to have maximum alertness and co-operation from the patient, no premedication was given ordinarily. Using a 2 or 5 cc. syringe, 10 per cent Sodium Amytal in doses of 150–200 mg. was injected moderately quickly (in 1–2 sec.). The injection was made with the patient counting, with the forearms up in the air and the fingers
either moving constantly or gripping an examiner's hands. The knees were drawn up so the feet were resting on the bed close to the buttocks. As the injection was completed, the contralateral arm and leg would slump to the bed and become flaccid. The ipsilateral arm and leg would remain up in the air and voluntary movements could be carried out on this side on command as soon as the initial few seconds of confusion were over. The patient would usually hesitate or stop counting near the end of the injection, but if the nondominant hemisphere had been injected, would resume on request within 5 to 20 sec., and then would name objects accurately while the contralateral hemiplegia was still complete.

When it was the dominant hemisphere that had been injected, the patient was unable to continue counting while the contralateral hemiplegia was complete. On command the patient would carry out voluntary movements with the ipsilateral extremities, as soon as the initial brief period of confusion had passed, demonstrating that the patient was co-operating and that the lack of speech was not caused by disturbances of consciousness or co-operation. As tone and power began to return in the contralateral arm and leg, the patient began to respond with "yes" and "no," and then was able to count. There was usually a period of 1–3 min. during which typical dysphasic responses such as perseveration and inability to name objects would occur, then normal speech returned. We have used a form (Tables 3 and 4) to permit easy notation of the patient's responses and motor performance at short intervals after the injection.

All except one of these patients were being studied from the standpoint of possible surgical therapy of intractable focal seizures. The exception was a left-handed 10-year-old girl with a deep-lying glioma of the left hemisphere, moderate hemiparesis but no speech disturbance, in whom the advisability of operation was being considered. Twelve of the patients considered themselves to be primarily left-handed, 6 were right-handed and 2 had marked infantile type of right hemiplegia. In the latter 2 groups some aspect of the seizure pattern raised a question as to the lateralization of speech dominance. The youngest patients were a boy (B.S.) and a girl (J.M.), each 10 years of age, 5 were in the early or middle teens and the remaining 13 were young adults, the oldest patient being 47 years of age (W.T.).

II. RESULTS

A. Duration of Contralateral Hemiplegia. Results after dosages of 10 per cent Sodium Amytal were as follows:

(a) 100 mg. (1 injection). No hemiparesis and no speech disturbance resulted.

(b) 150 mg. (5 injections in 3 patients). Two injections were followed by only a minimal hemiparesis, but the other 3 injections resulted in satisfactory hemiplegias which were complete for 1 to 4 min., with return to normal strength in an additional 1½ to 3 min.

(c) 175 mg. (20 injections in 11 patients). Nineteen injections were followed by a complete hemiplegia lasting as a rule 1½ to 2 min., with the longest duration 4 min., and requiring an additional 1½ to 4 min. to return to normal. The other injection produced only a partial paresis of the arm lasting 4 min. with no weakness of the leg.

(d) 200 mg. (15 injections in 9 patients). A complete hemiplegia was pro-
### TABLE 3

*Right carotid Amytal test in Patient R.C.*

<table>
<thead>
<tr>
<th>Handedness Drug</th>
<th>Left 10% Sodium Amytal</th>
<th>Dose Pt.'s weight</th>
<th>175 mg. 145 lb.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min. after Inj.</td>
<td>0</td>
<td>½</td>
<td>1</td>
</tr>
<tr>
<td>Speech</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Counting</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Naming</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>right</td>
<td>left</td>
<td></td>
</tr>
<tr>
<td>Arm</td>
<td>right</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>left</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Leg</td>
<td>right</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>left</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sensation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face</td>
<td>right</td>
<td>left</td>
<td></td>
</tr>
<tr>
<td>Arm</td>
<td>right</td>
<td>left</td>
<td></td>
</tr>
<tr>
<td>Leg</td>
<td>right</td>
<td>left</td>
<td></td>
</tr>
<tr>
<td>Visual fields</td>
<td>Complete left hemianopsia at 2½ min.—no field defect evident at 6 min.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective</td>
<td>Felt dizzy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interpretation</td>
<td>Speech represented in right hemisphere</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key: 0 = Absent 2 = Markedly reduced 1 = Perceptible 3 = Slightly reduced 4 = Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Note complete aphasia (0) while left hemiplegia is complete (0). 
† Perseveration.

...duced in each instance, lasting as a rule 3 to 4 min., with the longest duration 5 min., and requiring an additional 2 to 6 min. to return to normal.

B. *Speech Interference.* (1) *Nondominant hemisphere.* Half the patients continued counting throughout the injection and immediately afterward, although often a few numbers at the end of the injection were poorly enunciated. The remaining patients stopped counting at the end of the injection, but resumed counting on command either immediately or after an interval of up to 20 sec., during which they seemed confused and didn't obey commands. Normal ability to name objects and normal spontaneous speech were invariably demonstrated within 30–60 sec., when the hemiplegia was still complete, or nearly so.
TABLE 4

Left carotid Amytal test in Patient R.C.*

<table>
<thead>
<tr>
<th>Handedness Drug</th>
<th>Left 10% Sodium Amytal</th>
<th>Dose</th>
<th>Pt.’s Weight</th>
<th>175 mg. 145 lb.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>½</td>
<td>1</td>
<td>1½</td>
</tr>
</tbody>
</table>

Speech
- Counting: 0
- Naming: 4 4

Motor
- Face
  - right 0 0 0 0 2 4
  - left 4 4 4 4 4 4
- Arm
  - right 0 0 0 0 3 4
  - left 4 4 4 4 4 4
- Leg
  - right 0 0 0 0 3 4
  - left 4 4 4 4 4 4

Sensation
- Face
  - right 0 2 4
  - left 4 4 4
- Arm
  - right 0 2 4
  - left 4 4 4
- Leg
  - right 0 2 4
  - left 4 4 4

Visual fields

Subjective: Felt dizzy—no visual sensation

Interpretation: Speech not in left cerebral hemisphere

Key: 0 = Absent  2 = Markedly reduced
      1 = Perceptible  3 = Slightly reduced
      4 = Normal

* Note normal speech (4) while right hemiplegia is complete (0).

(2) Dominant hemisphere. In each instance counting was arrested within a second or two after completion of the injection, and the patients were unable to resume counting on command. They wiggled the fingers and toes of the extremities ipsilateral to the injection on command, demonstrating that they were in contact with the examiners and were co-operating. Thirty sec. to 1½ min. after power began to return in the paralyzed arm the patients regained the ability to say simple words like “yes” and “no” and to count. This was followed by a period of typical dysphasic responses on attempting to name objects. With injections of 175 mg. this dysphasic period ranged from 30 sec. to 2 min. With injections of 200 mg., this period varied from 1 to 5½ min., except in 1 patient who showed some dysphasic responses for 10 min.
C. Lateralization of Speech Dominance (Table 5). (1) “Left-handed” patients. Twelve patients considered themselves left-handed. In 6 of these left-handed patients the carotid Amytal test indicated that speech was represented in the right cerebral hemisphere. Left craniotomies were carried out in 5 of these patients, and large removals were made in the Sylvian region without producing any disturbance of speech. A right temporal lobectomy was carried out in the sixth patient, and this was followed by a temporary partial aphasia. Thus, in each of these 6 patients, operation produced either direct or indirect evidence of the correctness of the lateralization of speech representation by the carotid Amytal test.

In the remaining 6 left-handed patients, the carotid Amytal test indicated that speech was represented in the left cerebral hemisphere. In 3 of these patients, right craniotomies and removals bordering on the speech zones were followed by temporary partial aphasia, giving direct proof of the correctness of the carotid Amytal lateralization of speech. In 2 patients right-sided craniotomy and removal of the temporal, frontal and parietal opercula produced a transient hemiparesis, but no speech disturbance, thus giving indirect proof that speech was in the left hemisphere. The remaining 2 patients have not been operated upon.

(2) “Right-handed” patients. Six patients considered themselves to be right-handed, but some aspect of the seizure pattern in each patient raised some question as to the lateralization of speech dominance. In each instance the carotid Amytal test indicated the speech functions were in the left cerebral hemisphere. In 2 patients left-sided craniotomies and removals bordering on the speech zones were followed by temporary partial aphasia, giving direct proof of the correctness of the carotid Amytal lateralization of speech. In 2 patients right-sided craniotomy and removal of the temporal, frontal and parietal opercula produced a transient hemiparesis, but no speech disturbance, thus giving indirect proof that speech was in the left hemisphere. The remaining 2 patients have not been operated upon.

(3) Patients with right-sided infantile type of hemiparesis. Two patients had smallness and spastic hemiplegia of the right extremities dating from early life. We presumed on clinical grounds that speech had developed in the right hemisphere in each of these patients, and this was indicated also by the carotid Amytal test. Left hemicorticectomy was carried out in each without interference with speech.

D. Other Neurological Changes. The subjective response of the patients during the injection has varied. None has complained of any discomfort and none has objected to the second side being done. When asked afterward, about half the patients have noted a flash of light before both eyes during the injection, and this has often been described as yellow, green, blue or purple in color. Others have described a brief “dizzy” feeling or a flushed feeling in the ipsilateral side of the face. Transient inability to turn the eyes to the contralateral side was noted in 2 patients. Brief disturbances of eyeball
### Table 5

**List of carotid Amytal tests in 20 consecutive patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Handedness</th>
<th>Cerebral Hemisphere Dominant for Speech Based on Clinical Evidence</th>
<th>Cerebral Hemisphere Dominant for Speech Based on Carotid Amytal Test</th>
<th>Surgical Verification of Lateralization of Speech Dominance</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.C.</td>
<td>Left</td>
<td>Right?</td>
<td>Right</td>
<td>Right temporal lobectomy—temporary hemiparesis &amp; aphasia</td>
</tr>
<tr>
<td>B.S.</td>
<td>Left</td>
<td>Right? (Rt. hemiparesis since head injury at 5 yrs.)</td>
<td>Right</td>
<td>Left frontal lobectomy—temporary increase in hemiparesis, no aphasia</td>
</tr>
<tr>
<td>N.O.</td>
<td>Left</td>
<td>Right?</td>
<td>Right</td>
<td>2-stage removal of left temporal, occipital &amp; frontal regions—temporary hemiparesis after 1st stage, no aphasia after either operation</td>
</tr>
<tr>
<td>G.R.</td>
<td>Left</td>
<td>Right?</td>
<td>Right</td>
<td>Left temporoparietal removal—no aphasia</td>
</tr>
<tr>
<td>J.J.</td>
<td>Left</td>
<td>Right? (Minimal rt. hemiparesis; febrile convulsions &amp; hemiplegia at 11 mos.)</td>
<td>Right</td>
<td>Left temporoparietal removal—no aphasia</td>
</tr>
<tr>
<td>A.Mc.</td>
<td>Left—trained to use right</td>
<td>Right?</td>
<td>Right</td>
<td>Radical removal of glioma from left temporal &amp; frontal lobes—no aphasia</td>
</tr>
<tr>
<td>R.W.</td>
<td>Left</td>
<td>Left?</td>
<td>Left</td>
<td>S-stage removal of left temporal lobe, face area &amp; orbital surface of frontal lobe—transient aphasia after 1st &amp; 3rd operations</td>
</tr>
<tr>
<td>N.H.</td>
<td>Left</td>
<td>Left?</td>
<td>Left</td>
<td>Left temporal lobectomy—temporary aphasia</td>
</tr>
<tr>
<td>C.B.</td>
<td>Left</td>
<td>Right?</td>
<td>Right</td>
<td>Left temporoparietal removal—no aphasia</td>
</tr>
<tr>
<td>G.M.</td>
<td>Left</td>
<td>?</td>
<td>Right</td>
<td>Right temporal lobectomy—no aphasia</td>
</tr>
<tr>
<td>J.L.</td>
<td>Left since meningitis at age 2½ yrs.</td>
<td>?</td>
<td>Left</td>
<td>Right temporoparietal removal—transient left hemiparesis, no aphasia</td>
</tr>
<tr>
<td>J.M.</td>
<td>Left</td>
<td>Right?</td>
<td>Left</td>
<td>No operation</td>
</tr>
<tr>
<td>E.L.</td>
<td>Right</td>
<td>Right?</td>
<td>Left</td>
<td>Left temporal lobectomy—transient minimal dysphasia</td>
</tr>
<tr>
<td>P.A.</td>
<td>Right</td>
<td>Left?</td>
<td>Left</td>
<td>Removal adjacent to left parietal operculum—transient aphasia</td>
</tr>
<tr>
<td>G.B.</td>
<td>Right</td>
<td>Left?</td>
<td>Left</td>
<td>Removal of right temporal lobe, frontal &amp; parietal opercula—transient hemiparesis, no aphasia</td>
</tr>
<tr>
<td>W.T.</td>
<td>Right</td>
<td>Left?</td>
<td>Left</td>
<td>No operation</td>
</tr>
<tr>
<td>J.W.</td>
<td>Right</td>
<td>Left?</td>
<td>Left</td>
<td>No operation</td>
</tr>
<tr>
<td>L.L.</td>
<td>Right since seizure at age 14 mo.</td>
<td>?</td>
<td>Left</td>
<td>Large right temporoparietal removal—no aphasia</td>
</tr>
<tr>
<td>F.S.</td>
<td>Left</td>
<td>Right? (Infantile rt. hemiplegia)</td>
<td>Right</td>
<td>Left hemicorticectomy—no aphasia</td>
</tr>
<tr>
<td>M.A.</td>
<td>Left</td>
<td>Right? (Infantile rt. hemiplegia)</td>
<td>Right</td>
<td>Left hemicorticectomy—no aphasia</td>
</tr>
</tbody>
</table>

Movement may actually have occurred more frequently, but escaped detection because of concentration of our observations on speech and motor functions of the extremities.

In order to avoid distractions that might interfere with the testing of speech, other neurological functions were not tested for routinely. Occasionally, however, time permitted such testing, with the demonstration of a contralateral homonymous hemianopsia and/or a contralateral hemihypalgesia for pin prick (Tables 3 and 4), and presence of a positive Babinski response during the period of paralysis or marked paresis of the leg.

Excepting the few patients with the most prolonged hemiplegia, most
patients believed that they had obeyed the various commands satisfactorily, and were unaware of either the hemiplegia or inability to speak. We have no good explanation for this curious amnesia during this period of from 1 to 3–4 min. when the patients seemed to be quite clear and co-operative.

**DISCUSSION**

Accurate knowledge of the lateralization of speech function is of urgent practical importance to the neurological surgeon in the course of a considerable proportion of surgical procedures for lesions above the tentorium. In the case of right-handed people, the left cerebral hemisphere can be considered to contain the representation of speech with a high degree of accuracy. On rare occasions, however, unpleasant surprises have occurred, and aphasia has followed operations on the right cerebral hemisphere in right-handed individuals. In some ambidextrous and left-handed patients, clinical data, such as the presence of aphasia caused by a tumor or other destructive lesion, or aphasia as part of the seizure pattern, give positive proof that speech is located in the hemisphere under consideration. In the absence of positive information of this type, it is necessary for the neurosurgeon operating in the vicinity of the Sylvian region in an ambidextrous or left-handed individual to assume that speech is represented in the hemisphere being operated upon, if his surgical manipulations are to be carried out with the least possible risk of aphasia.

When operation is carried out under local anesthesia, interruption of counting or naming produced by electrical stimulation of the frontal or parietal opercular regions gives positive evidence that speech is represented in the exposed cerebral hemisphere. Inability to arrest speech by stimulation in these regions is not reliable proof that speech is in the other cerebral hemisphere, however, since occasionally the electrical stimulating current does not seem to be an adequate stimulus, and no interference with speech occurs, even though speech is actually represented in the convolution being stimulated. In operations carried out under general anesthesia, there is, of course, no possibility of determining at the operating table whether speech is represented in the exposed hemisphere.

The pre-operative proof of the lateralization of speech functions afforded by the carotid Amytal test has increased our surgical efficiency in the case of left-handed or ambidextrous patients by permitting radical excisions in the Sylvian region when speech has been proven to be represented in the contralateral hemisphere. On the other hand, when the involved hemisphere has been proven to be dominant for speech, this knowledge has insured that the surgical manipulations were planned to produce the least possible risk of aphasia.

To date, it has been our custom to carry out the test on each side, to secure positive identification of both the dominant cerebral hemisphere (hemiplegia plus aphasia), and the nondominant hemisphere (hemiplegia with preservation of speech). With greater experience, injection of just one side might
prove to be equally accurate in most instances. When the period of confusion
is longer than usual, comparison of the two sides would seem wise, however,
even though the results are nearly always clear-cut and the interpretation is
easy.

We plan to insert the needle into the common carotid artery instead
of the internal carotid in order to insure as quick an arterial puncture as pos-
sible. This was felt to be important in maintaining good co-operation from
the patient. If the majority of the drug should happen to go into the external
carotid artery and hemiplegia fail to develop, there would seem to be no con-
traindication to repositioning the needle and repeating the injection after an
interval of 15–20 min.

We have not carried out angiography on the same day or through the
same needle insertion, fearing possible complications from cumulative effects
of the contrast medium and Sodium Amytal on the endothelium of the cere-
bral vessels.

Judging from these studies on the monkey, accidental injection into the
vertebral artery might be expected to produce a transient respiratory em-
barrassment, but no other serious ill effects. In a recent patient the injection
has apparently been inadvertently made into the vertebral artery. There was
immediate posturing type of stiffening of all extremities with unresponsive-
ness and turning of the head and eyes away from the side of the injection.
There were semipurposeful struggling movements for 1–2 min., then the pa-
tient quieted down and became clear mentally, but had complete amnesia for
the injection and succeeding events. No striking change occurred in the
respirations, but minor changes may have escaped detection. Subsequent
satisfactory carotid injections were made in this patient with clear-cut identi-
fication of the dominant and nondominant cerebral hemispheres.

Theoretically, one might expect an unusual response like this in case the
carotid being injected supplied both halves of the upper brain stem as a re-
sult of an occlusion or congenital absence of the opposite carotid artery.

Another lesion that might interfere with the satisfactory performance of
this test is an arteriovenous angiomatous malformation of one cerebral
hemisphere. The diversion of a considerable proportion of the carotid blood
flow through the vascular malformation instead of through the brain might
prevent the development of a hemiplegia unless a larger dose of Sodium
Amytal were used. In a recent patient this seemed to have occurred, since
two injections on the side of the malformation were without effect. Injection
of the opposite carotid artery produced a satisfactory hemiplegia without
aphasia. We considered this adequate evidence that the hemisphere contain-
ing the vascular malformation was dominant for speech.

The carotid Amytal test, of course, carries with it the small but definite
risks inherent in puncture of the wall of the carotid artery. The experimental
data on the monkeys presented here, however, support our clinical impres-
sion that the injection of 10 per cent Sodium Amytal in the doses used add
little to these risks. It seems clear also from the pathological data of animal
that more concentrated solutions of Sodium Amytal, at least in large doses, may produce brain damage. If a concentration of 10 per cent is not exceeded, however, this test provides a reasonably safe method of determining the lateralization of speech dominance and, in our opinion, is indicated whenever such knowledge seems likely to increase either the safety or efficacy of craniotomy for supratentorial lesions. Because carotid puncture and injection of a foreign substance, even normal saline, carry some risk, even though small, use of this test in patients not being considered for operation should not be undertaken lightly.

Intra-arterial injection of Sodium Pentothal is clearly contraindicated. The necrotizing effect of accidental injection of Sodium Pentothal into the great vessels of the extremities in the course of Pentothal anesthesia is now well known, and the devastating effect on the brain of intracarotid injection of 0.5 per cent Sodium Pentothal has been demonstrated in the cat by Ghersi et al. The use of other local anesthetic agents might well have some advantages over the use of 10 per cent Sodium Amytal, but use in man of other agents should obviously be preceded by demonstration of the safety of the agent in question in the experimental animal.

Use of this carotid Amytal test should result in gradual accumulation of more accurate data than we now possess on certain aspects of speech functions, such as the age at which speech transfer from one hemisphere to another becomes impossible (or rudimentary), the completeness with which such transfer occurs at various ages, the question of partial bilaterality of speech representation in left-handed patients without history of brain injury, etc.

SUMMARY

1. A technique is described for the intracarotid injection of 10 per cent Sodium Amytal to produce temporary inactivation of function of one hemisphere with the aim of providing proof of the lateralization of speech function when this is in doubt.

2. Experimental studies in the monkey have demonstrated the relative safety of intracarotid injections of 10 per cent Sodium Amytal in doses up to 15 times the proportional maximal human dose, as determined by relative brain weights.

3. Injections into the vertebral artery in the monkey produced temporary respiratory arrest with doses larger than the proportional human dose, but with adequate artificial respiration no permanent untoward effects were encountered with doses up to 10 times the proportional human dose.

4. Intracarotid injection of 20 per cent Sodium Amytal in large doses produced microscopic areas of necrosis in the area of distribution of the middle cerebral artery in one monkey.

5. A series of 20 consecutive patients were tested for lateralization of speech dominance by means of this carotid Amytal test, as a preliminary to operation for relief of focal cerebral seizures. Subsequent craniotomy and
cortical excision were carried out in 17 of these patients, and in each gave
direct or indirect evidence as to the correctness of the lateralization of speech
representation as determined by the Amytal test.

6. The intracarotid injection of 10 per cent Sodium Amytal has proven
to be a valuable and reasonably safe method for the determination of lateral-
ization of speech function. Its use is advocated as a preliminary to operations
in the vicinity of the Sylvian area in left-handed and ambidextrous patients,
and in right-handed patients in whom any doubt exists as to which cerebral
hemisphere is dominant for speech.

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