

### **13. Response to Amphetamine to Facilitate Recovery from Aphasia Subsequent to Stroke**

Delaina Walker-Batson, Michael D. Devous, Sr., Sandra S. Curtis, D. Hal Unwin, and Ralph G. Greenlee

A large number of animal studies (Boyeson & Feeney, 1984; Feeney, Gonzales, & Law, 1982; Feeney & Hovda, 1983, 1985; Feeney, Sutton, Boyeson, Hovda, & Dail, 1985; Goldstein, Miller, Cress, Tyson, & Davis, 1988; Hovda & Feeney, 1984; Krobert, Boyeson, & Scherer, 1987) have provided evidence about the role of certain neurotransmitters in central nervous system (CNS) recovery processes. Specifically, norepinephrine (NE) has been shown to be critical to recovery of various lost behavioral functions. D-amphetamine (an NE agonist) administered early after experimental lesions in animals has been reported to produce significant improvements in motor function on beam-walking tasks. This functional improvement occurs only when motor training is paired simultaneously with drug treatment, not with administration of the drug alone. NE mediation of CNS recovery is further supported by the fact that drugs which act as NE antagonists have been found to reinstate motor deficits in animals (Feeney et al., 1982) and impede speech and language recovery in humans (Porch & Feeney, 1986; Porch, Wyckes, & Feeney, 1985).

There has been recent evidence, in a small number of patients, supporting the use of amphetamines to facilitate recovery of motor function following stroke (Crisostomo, Duncan, Propst, Dawson, & Davis, 1988; Davis, Crisostomo, Duncan, Propst, & Feeney, 1987). Davis and his colleagues have reported that patients who received a single 10-mg dose of d-amphetamine (Dexatrine) paired with physical therapy demonstrated a

---

*The authors would like to thank Dr. Michael Boyeson for his advice in the development of the protocol, Dr. Deanie Vogel for training the research clinicians on the Porch Index of Communicative Ability, and the Speech Pathology Staff of Parkland Memorial Hospital, Dallas, Texas, for the administration of the Western Aphasia Battery.*

*This study was funded in part by the Texas Advanced Research Program, Grant #003646.*

40% greater rate of improvement in motor skills than patients who received physical therapy alone over a 3-day period.

We were interested in the long-term effects of d-amphetamine on recovery of speech and language disorders subsequent to stroke, and we present what we believe to be the first reported case of its use in aphasia. The amphetamine protocol that we employed was adapted from both animal and human reports (Crisostomo et al., 1988; Hovda & Feeney, 1984). The patient received d-amphetamine every 4 days for a 6-week period of drug and language therapy and was followed for 1 year.

## CASE DESCRIPTION

A 53-year-old strongly right-handed man (Oldfield, 1971) was admitted to the Cerebrovascular Disease Research Center of the University of Texas Southwestern Medical Center with right hemiparesis and aphasia. He had a high school education and was a truck driver prior to hospitalization. Risk factors included a long history of heavy smoking and hypertension. Magnetic resonance imaging obtained 9 days after admission revealed a large area of infarction in the territory of the left middle cerebral artery including involvement of subcortical white matter and portions of the basal ganglia with some cortical sparing of frontal and temporal association cortices. An arteriogram revealed complete occlusion of the left internal carotid artery at its origin. Physiological imaging of regional cerebral blood flow (rCBF) with single-photon emission tomography (SPECT) using HMPAO (Technetium 99m) as the tracer showed perfusion deficits extending beyond the boundaries of the structural lesion. Neurological evaluation during the acute period indicated a dense right paralysis of both arm and leg and right sensory loss, with no speech output but the ability to follow some simple commands. By day 9 postictus the patient could say "no," "okay," and "key" but could not perform any of the language production tasks on the standardized stroke assessment used in our Center (Adams, Meador, Sethi, Grotta, & Thompson, 1987). Speech and language evaluation performed 19 days postictus, based on hospital records, indicated a moderate-to-severe Broca-type aphasia. His *Western Aphasia Battery* (WAB) (Kertesz, 1982) Aphasia Quotient was 32.5. There was also a co-occurring apraxia of speech rated 2 on a 7-point scale. Speech output was limited to automatic-type utterances up to four words in length.

## PROCEDURE

Inclusion criteria required that the patient have a single thromboembolic infarct; exhibit aphasia, defined as a score between 10 and 70 on the *Porch*

*Index of Communicative Ability (PICA)* (Porch, 1981); be neurologically stable; have a premorbid ability to read and write; and enter the protocol between day 10 and day 30 postictus. Exclusion criteria included a history of head injury or extensive alcohol or drug abuse, unstable cardiac dysrhythmia or uncontrolled hypertension (160/100), and medication with major or minor tranquilizers or alpha-adrenergic antagonists or agonists.

On day 19 postictus, our patient was evaluated with baseline speech and language assessments and physiological brain imaging of rCBF with SPECT. The *PICA* was chosen as the dependent language measure because of its good test-retest reliability and quantifiable prediction method of recovery (Porch, 1981; Porch & Callaghan, 1981).

On the 21st day post-CVA the patient entered the protocol. He received an oral dose of 10 mg of d-amphetamine 45 minutes prior to a 75-minute speech and language therapy session. Drug and language therapy sessions continued every 4th day for 6 weeks. Total language therapy during the drug phase was 12½ hours. This was in addition to ongoing rehabilitation for both motor and language deficits not carried on during drug intoxication.

Our treatment tasks focused on verbal performance. Contrastive stress drills and "laddering"-type activities were coupled with traditional tasks designed to improve speaking, reading, and auditory comprehension. Little time was spent on writing. The total amount of language treatment, combining both ongoing rehabilitation and the 10 drug intoxication sessions the first 11 months poststroke, was 37 hours. Within-session speech and language behaviors (immediately before drug administration and during the intoxication phase) were monitored with four subtests and the Picture Description Task from the *Boston Diagnostic Aphasia Examination* (Goodglass & Kaplan, 1983). Post-treatment language assessment was made 3 days after the conclusion of the drug study and again at 3, 6, 10, and 11 months from the date of treatment initiation. A follow-up neurological examination was performed at the 6- and 10-month evaluations. Physiological rCBF imaging was done before drug administration and again at 6 weeks and 3 months after initiation of treatment. All *PICA* tests were videotaped and triple-scored by *PICA*-trained clinicians. Agreement was reached on all responses.

## RESULTS

Porch's prediction method (Porch, 1981) was computed for the patient, using the Overall Score at 1 month post-onset (MPO) to predict 6-month scores. At 1 MPO the patient's Overall Score was at the 19th percentile, resulting in a 6-MPO predicted Overall Score in the 42nd percentile. At 6

MPO the patient's *PICA* Overall Score was at the 58th percentile. We also compared this patient to 15 similar middle cerebral artery patients reported by Porch in terms of Target Difference Scores. The Target Difference Score indicates how positively or negatively a patient's performance at 6 MPO approaches the target predicted at 1 MPO. These comparisons are shown in Table 13.1. Our subject's 6-MPO Target Difference Score was 16. This compares to the mean Target Difference Score of Porch's 15 patients of 3.8.

At 11 MPO or 10 months after initiation of the study, our patient's Overall Score was at the 61st percentile. At 11 MPO our patient received 19 additional therapy sessions and his Overall Score climbed to the 76th percentile. Changes across time from 1 MPO to 12 MPO are shown in Table 13.2. Of particular interest are the Verbal Subtest Scores that range from 1 MPO to 11 MPO. Recall that in addition to the drug and language stimulation condition, this patient received only 25 hours of direct language therapy during this 10-month period. The initial *PICA* Verbal Score of 17 increased to 73 at the 10-month poststudy follow-up.

We were also able to obtain our patient's *WAB* scores from hospital records. Table 13.3 shows *WAB* Aphasia Quotient (AQ) scores before drug and therapy treatment and across the 6 weeks of the study. The patient's AQ scores changed from 32.6 predrug to 80.0 after the 10 drug and therapy sessions.

At the 6-MPO follow-up, the neurologist reported that the patient had a moderately severe right hemiparesis with inability to ambulate independently, sensory function that was normal except for graphesthesia in the right upper extremity, speech comprehension that appeared intact, and word-finding difficulties in expressive speech. Physiological brain imaging with Xenon-133 SPECT showed continued rCBF hypoperfusion in a large territory of the left hemisphere.

Conversational speech at the 6-MPO follow-up was fluent, with utterances 8 to 10 words in length; three naive listeners could not determine that the subject's speech output was abnormal. To the trained observer, however, the subject's speech was typical of an anomic aphasic.

## DISCUSSION

Our patient's initial aphasia profile pattern was similar to that of other middle cerebral artery patients described by Porch. However, his 16-point Target Difference Score at 6 MPO was considerably more than the average Target Difference of 3.8 reported in 15 similar patients. AT 12 MPO, our patient had a 57-point change on the *PICA* Overall Score, again considerably more than the 20 to 30 points reported to be the range of change during recovery of Broca-type patients on the *PICA* (Wertz, Kitselman,

**TABLE 13.1. PICA<sup>a</sup> DATA COMPARING OUR PATIENT TO TYPICAL MIDDLE CEREBRAL ARTERY PATIENTS**

	<i>Overall: 1 MPO<sup>b</sup> (%)</i>	<i>Overall: 6 MPO (%)</i>	<i>Target Difference (%)</i>
Typical MCA <sup>c</sup> Patient	19.9	46.3	3.8
Our Patient	19.0	58.0	16.0

*Note:* Patient comparisons are from "Making Predictions About Recovery: Is There HOAP?" by B. Porch and S. Callaghan, 1981, *Clinical Aphasiology*, 11, pp. 187-200.

<sup>a</sup>PICA = Porch Index of Communicative Ability. <sup>b</sup>MPO = months post-onset.

<sup>c</sup>MCA = myocardial infarction.

**TABLE 13.2. PICA<sup>a</sup> MODALITY AND OVERALL SCORES ACROSS THE SIX ASSESSMENT PERIODS**

	<i>3/24/89 (Predrug)</i>	<i>5/4/89</i>	<i>6/29/89</i>	<i>9/11/89</i>	<i>1/23/90</i>	<i>2/26/90</i>
Overall	19	28	40	58	61	76
Gestural	26	37	44	65	57	67
Verbal	17	39	47	62	73	75
Graphic	10	14	20	48	58	50

<sup>a</sup>PICA = Porch Index of Communicative Ability.

**TABLE 13.3. WESTERN APHASIA BATTERY APHASIA QUOTIENT SCORES ACROSS 10 SESSIONS**

	<i>3/24/89 (Predrug)</i>	<i>4/18/89</i>	<i>5/6/89 (Postdrug)</i>
Aphasia Quotient	32.6	62.8	80.0

and Deal, 1981). Additionally, in various treatment studies that have used the PICA as the dependent measure, treatment time has ranged from 100 to 362 hours, which contrasts with 56 hours for our patient. If, as has been suggested (Basso, Capitani, & Vignolo, 1979), language therapy enhances the normal recovery course, perhaps pharmacological intervention accelerates the rate of recovery. This obviously cannot be determined from a single case study. Davis et al. (1987) acknowledged in their pharmacological study that only rate and not extent of motor recovery could be determined without long-term follow-up studies. Because we followed our patient over a 12-month period we believe that, in addition to rate, the extent of recovery in our patient is important. Although we acknowledge

the variability in aphasic recovery and the fragility of the PICA prediction method, if we consider the initial severity of our patient's aphasia, the degree of cerebral insult as demonstrated by the radiological procedures, and the amount of treatment that our patient received, we are intrigued about the potential of pharmacological therapy for aphasia. Although we are cautious regarding overinterpretation of a single case, we feel that this protocol merits further exploration in a larger number of patients under placebo/drug double-blind conditions; we are currently undertaking such a study.

## REFERENCES

- Adams, R. J., Meador, K. J., Sethi, K. D., Grotta, J. C., & Thompson, D. S. (1987). Graded neurologic scale for use in acute hemispheric stroke treatment protocols. *Stroke*, *18*, 665-669.
- Basso, A., Capitani, E., & Vignolo, L. A. (1979). Influence of rehabilitation on language skills in aphasic patients. *Archives of Neurology*, *36*, 190-196.
- Boyeson, M. G., & Feeney, D. (1984). The role of norepinephrine in recovery from brain injury. *Society for Neuroscience Abstracts*, *10*, 68.
- Crisostomo, E. A., Duncan, P. W., Propst, M. A., Dawson, D. V., & Davis, J. N. (1988). Evidence that amphetamine with physical therapy promotes recovery of motor function in stroke patients. *Annals of Neurology*, *23*, 94-97.
- Davis, J. N., Crisostomo, E. A., Duncan, P., Propst, M., & Feeney, D. (1987). Amphetamine and physical therapy facilitate recovery of function from stroke: Correlative animal and human studies. In M. E. Raichle and W. J. Powers (Eds.), *Cerebrovascular Diseases 15th Conference* (pp. 297-305). New York: Raven Press.
- Feeney, D., Gonzales, L., & Law, W. (1982). Amphetamine, haloperidol, and experience interact to affect rate of recovery after motor cortex injury. *Science*, *217*, 855-857.
- Feeney, D., & Hovda, D. A. (1983). Amphetamine and apomorphine restore tactile placing after motor cortex injury in the cat. *Psychopharmacology*, *79*, 67-71.
- Feeney, D., & Hovda, D. A. (1985). Reinstatement of binocular depth perception by amphetamine and visual experience after visual cortex ablation. *Brain Research*, *342*, 352-356.
- Feeney, D., Sutton, R. L., Boyeson, M. G., Hovda, D. A., and Dail, W. G. (1985). The locus ceruleus and cerebral metabolism: Recovery of function after cortical injury. *Physiological Psychology*, *13*, 197-203.
- Goldstein, L. B., Miller, G. D., Cress, N. N., Tyson, A. G., & Davis, J. N. (1988). Studies of an animal model for the recovery of function after stroke. *Annals of Neurology*, *22*, 159-160.
- Goodglass, H., & Kaplan, E. (1983). *The Boston Diagnostic Aphasia Examination*. Philadelphia: Lea & Febiger.
- Hovda, D. A., & Feeney, D. (1984). Amphetamine and experience promotes recovery of locomotor function after unilateral frontal cortex injury in the cat. *Brain Research*, *298*, 358-361.
- Kertesz, A. (1982). *The Western Aphasia Battery*. New York: Grune & Stratton.

- Krobert, K. A., Boyeson, M. G., & Scherer, P. J. (1987). The role of the locus ceruleus in recovery of function from sensorimotor cortex injury. *Society for Neuroscience Abstracts*, 13.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, 9, 97-113.
- Porch, B. (1981). *Porch Index of Communicative Ability*. Palo Alto, CA: Consulting Psychologists Press.
- Porch, B., & Callaghan, S. (1981). Making predictions about recovery: Is there HOAP? In R. H. Brookshire (Ed.), *Clinical aphasiology* (Vol. 11, pp. 187-200). Minneapolis, MN: BRK Publishers.
- Porch, B., & Feeney, D. (1986). Effects of antihypertensive drugs on recovery from aphasia. In R. H. Brookshire (Ed.), *Clinical aphasiology* (Vol. 16, pp. 309-314). Minneapolis, MN: BRK Publishers.
- Porch, B., Wyckes, J., & Feeney, D. (1985). Haloperidol, thiazides and some antihypertensives slow recovery from aphasia. *Society for Neuroscience Abstracts*, 11, 52.
- Wertz, R. T., Kitselman, K. P., & Deal, L. A. (1981, October). *Classifying the aphasias: Contributions to patient management*. Paper presented to the Academy of Aphasia, London, Ontario, Canada.