14. The Effects of Bromocriptine on Speech and Language Function in a Man with Transcortical Motor Aphasia

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Over the years, a number of ingestible agents ranging from "cashews to caffeine" have been used to treat aphasia (Albert, 1988b). Albert, Bachman, Morgan, and Helm-Estabrooks (1988) and Bachman and Morgan (1988) have reported on the use of Bromocriptine as a treatment for aphasia. Albert et al. hypothesized that impaired initiation of speech production in transcortical motor aphasia may be due in part to reduced dopaminergic activity and might respond to treatment with a dopamine agonist such as Bromocriptine. Recent investigations have shown that midbrain dopaminergic systems project to medial frontal areas. Because lesions of the left medial frontal region can result in the syndrome of transcortical motor aphasia, they speculated that selected features of the syndrome might be caused by interruption of the mesocortical dopaminergic projection. In addition, Bachman and Morgan (1988) cite several reports of aphasic adults with psychiatric disorders, which suggest that limbic system activity partially mediates language function in aphasia. They suggested that use of Bromocriptine may potentially alter limbic system activity and improve language function in aphasia.

In the first study of the use of Bromocriptine in aphasia, Albert et al. (1988) evaluated the effect of this drug on the performance of one man who had transcortical motor aphasia 3½ years after onset of a left frontal intracerebral hemorrhage. After drug treatment, they observed a marked reduction in the number of pauses within and between utterances during free conversation but not in a picture description task. They also reported a decrease in paraphasias and a reduction in response latency on the Confrontation Naming and Responsive Naming subtests of the *Boston*

Diagnostic Aphasia Examination (*BDAE*) (Goodglass & Kaplan, 1983). These improvements diminished when the drug was withdrawn. At the highest dose (30 mg daily), the patient experienced an exacerbation of a chronic sensation of vertigo. He also experienced low-frequency facial tics. Albert et al. observed that low-dose treatment (15 mg) was as effective as high-dose treatment at reducing pauses and response latencies.

In their brief report, Bachman and Morgan (1988) compared the results of Bromocriptine treatment for the Albert et al. patient with treatment for two aphasic adults who did not have transcortical motor aphasia. One man exhibited severe Broca's aphasia 1½ years after a thromboembolic infarct. The other man exhibited a mixed aphasia and bilateral brain damage 3 and 4 years after multiple thrombotic cerebral infarcts. These two patients did not demonstrate obvious changes with Bromocriptine treatment, although the patients and their wives reported increased use of novel words, increased initiation of conversations at home, and modest improvement in mood. High-dose treatment (35 and 40 mg) did not appear to be any more effective than low-dose treatment (15 and 20 mg). Bachman and Morgan did not mention whether these subjects experienced side effects.

The Albert et al. and Bachman and Morgan reports contained cautionary statements about the preliminary nature of the findings as a result of the limited number of subjects and use of an open-label design. However, other articles discussing this study did not include such statements (Albert, 1988a, 1988b). In describing the effects of Bromocriptine on the patient with transcortical motor aphasia, Albert (1988a) concluded that Bromocriptine "was successful in treating the patient's aphasia" and further stated that this patient "exemplifies the conclusion that aphasia is a medical disorder now amenable to treatment."

Although the rationale for the Albert et al. and Bachman and Morgan studies was intriguing, these studies provided weak support for the effectiveness of Bromocriptine in the treatment of aphasia for several reasons:

1. Only three subjects were treated and only one of those demonstrated obvious changes with treatment.
2. The design of the studies did not include a placebo phase.
3. Baseline performance was not established for any of the measures used in the studies.
4. The reliability of scoring speech production measures was not reported.

The present study investigated the effects of Bromocriptine on the speech and language performance of a man with transcortical motor aphasia using a design that included baseline measures, a placebo phase, and connected speech measures with verified reliability.

METHOD

Subject

D. S. was a 63-year-old man who had sustained a left-hemisphere thromboembolic infarct approximately 4 years prior to this study. He had 12 years of education and was managing a fleet of trucks for a local company at the time of his infarct. He had received 14 months of speech and language treatment immediately following his stroke. His language profile was classified as transcortical motor aphasia on the *Western Aphasia Battery* (*WAB*) (Kertesz, 1982). Spontaneous speech was sparse, well articulated, and moderately agrammatic (*WAB* Information Content = 8/10, Fluency = 5/10). Auditory comprehension of single words was relatively intact (*WAB* Auditory Word Recognition = 55/60). Auditory comprehension was good for short simple sentences but was impaired for lengthy or grammatically complex sentences (*WAB* Sequential Commands = 36/80). Repetition was relatively intact (*WAB* Repetition = 96/100). Word fluency was moderately impaired (*WAB* Animal Naming = 5/20), as was confrontation naming (33/60) (*Boston Naming Test*, Kaplan, Goodglass, & Weintraub, 1983).

Design

This was a single-blind study in which the subject did not know when he was receiving Bromocriptine or when he was receiving the placebo but the investigators did. The baseline phase involved three administrations of a test battery over a 1-week period with no drug or placebo administered. A 4-week placebo phase followed the baseline phase. A 7-week drug treatment phase followed the placebo phase. The study concluded with a 4-week withdrawal phase. The test battery was administered at 2-week intervals during the placebo, drug treatment, and withdrawal phases of the study. At the end of each phase of the study, D. S. and his wife individually filled out a questionnaire measuring their subjective impressions of D. S.'s communication and mood.

D. S. was seen each week of the study by a neurologist. At these times, he was given the placebo or drug (as appropriate) for the following week. The placebo and Bromocriptine were dispensed in identical capsules and the number of capsules taken per day was constant throughout the study.

In order to minimize potential side effects, D. S. was started at a low dose of Bromocriptine (5 mg). This was to be increased to 20 mg over a 4-week period. However, during the first day of drug treatment he experienced dizziness. He was seen by the neurologist, who determined that this

was caused by hypotension related to his use of Bromocriptine. His dose was reduced to 2.5 mg per day and the dosage was gradually increased to 15 mg over a 4-week period. He was maintained at this dose (rather than the 20 mg originally intended) for the remaining 3 weeks of the drug treatment phase of the study. He experienced no further side effects during the study.

Test Battery

The test battery included the following tests:

Visual Reaction Time. A commercially available computer program was used to assess visual reaction time (Captain's Log–Stimulus Reaction Time) (Sandford & Browne, 1987). In this program, colored squares appeared at random intervals and locations on a computer screen. D. S. was instructed to respond to these squares as quickly as possible by pressing a button. Reaction time was measured in milliseconds.

Auditory Comprehension. Performance was assessed on Part F of the Spreen and Benton *Token Test* (1977).

Comprehension Naming. A 20-item naming test was created by selecting 15 error items and 5 correct items from a prior administration of the *Boston Naming Test*.

Word Fluency. Performance was measured on two letters ("S" and "T") and two semantic categories (animals and food). D. S. was instructed to produce as many examples of each category as he could in 1 minute.

Connected Speech. Four speech samples were obtained, including (a) description of the Cookie Theft picture from the *BDAE* (Goodglass & Kaplan, 1983), (b) description of a six-picture sequence, (c) a response to "Tell me where you live and describe it to me," and (d) a controlled interview in which D. S. responded to a specific series of questions about his family. Each sample was analyzed for (a) number of words; (b) number of correct information units (CIUs)—words that were accurate, relevant, and informative to a listener (Nicholas & Brookshire, 1989); (c) percentage of CIUs ([# of CIUs / # of words] × 100), which is a measure of how efficiently words are used to communicate information; (d) total time for each sample; and (e) speaking rate in words per minute.

Communication and Mood Questionnaire. This included seven questions related to the subject's mood and ability to communicate (see

Appendix 14.A). D. S. and his wife completed the questionnaire individually. D. S. responded to the questionnaire in the presence of the first author, who read aloud each question to D. S. as he read them to himself.

Testing was done by the first author. Connected speech samples were taped in random order by the first author and scored without knowledge of the test session by the second author. Scoring reliability between the two authors was calculated for 3 of the 11 sessions. Point-to-point interjudge reliability was 99% for number of words and 91% for number of CIUs. Agreement between the two authors on timing of speech samples was within 3 seconds for all samples.

RESULTS AND DISCUSSION

Simple visual reaction time decreased throughout the study (Figure 14.1). However, inspection of Figure 14.1 indicates that reaction times in the drug treatment phase were not substantially different from those in the placebo and withdrawal phases of the study. The shortest reaction time in the drug treatment phase was only 10 ms faster than the shortest reaction time in the placebo phase. These results do not suggest that Bromocriptine affected D. S.'s reaction times.

Performance on the *Token Test* (Part F) and on a 20-item *Boston Naming Test* was relatively stable throughout the study (Figures 14.2 and 14.3). Performance on these tests during the drug treatment phase was not appreciably different from performance in the other phases of the study.

Performance on the word fluency measures showed a slight trend toward improvement over the course of the study (Figure 14.4). However, the largest change occurred during the placebo phase, suggesting that Bromocriptine was not responsible for the increase in word fluency.

There was an increase in the number of words (Figure 14.5) and, to a lesser extent, the number of CIUs (Figure 14.6) during the drug treatment phase. D. S. was clearly producing more words and more CIUs in the drug treatment phase than he did during the baseline and placebo phases. However, this trend began during the placebo phase and the rate of increase did not change during the drug treatment phase, suggesting that Bromocriptine was not responsible for the observed changes.

The relationship between number of words and number of CIUs was reflected in the percentage of CIUs in connected speech samples (Figure 14.7). D. S.'s production of words and CIUs increased throughout the study. However, the increase in number of CIUs was proportionate to the increase in number of words, suggesting that D. S.'s communication was no more informative to a listener despite increased verbal output. He was

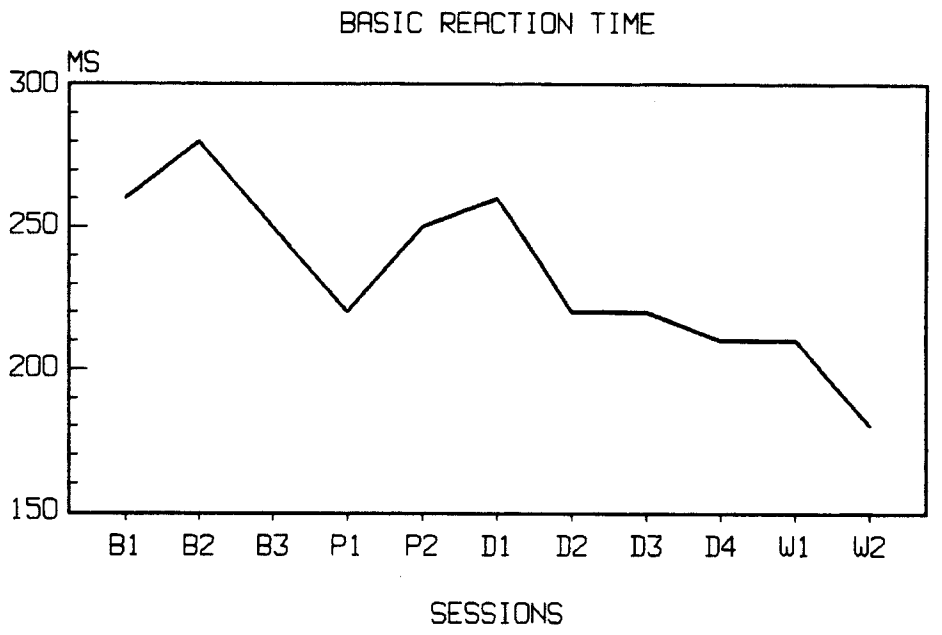

Figure 14.1. D. S.'s average basic reaction time on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

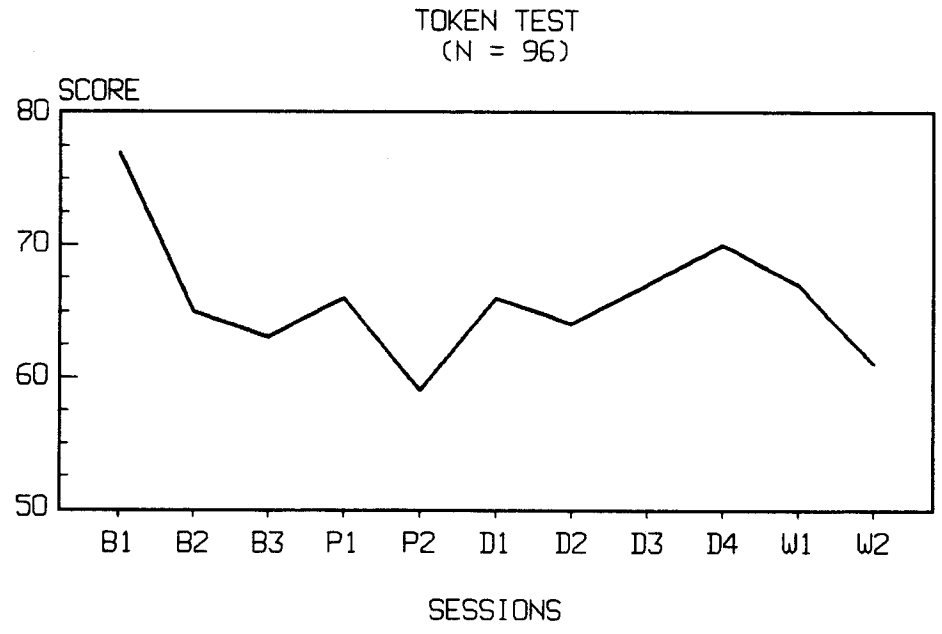

Figure 14.2. D. S.'s *Token Test* performance on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

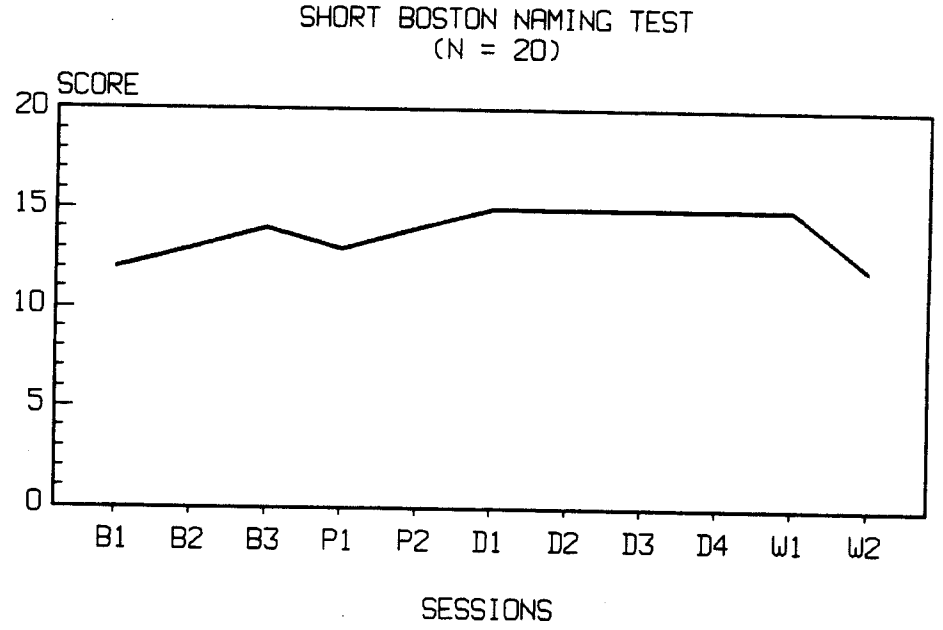

Figure 14.3. D. S.'s 20-item *Boston Naming Test* performance on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

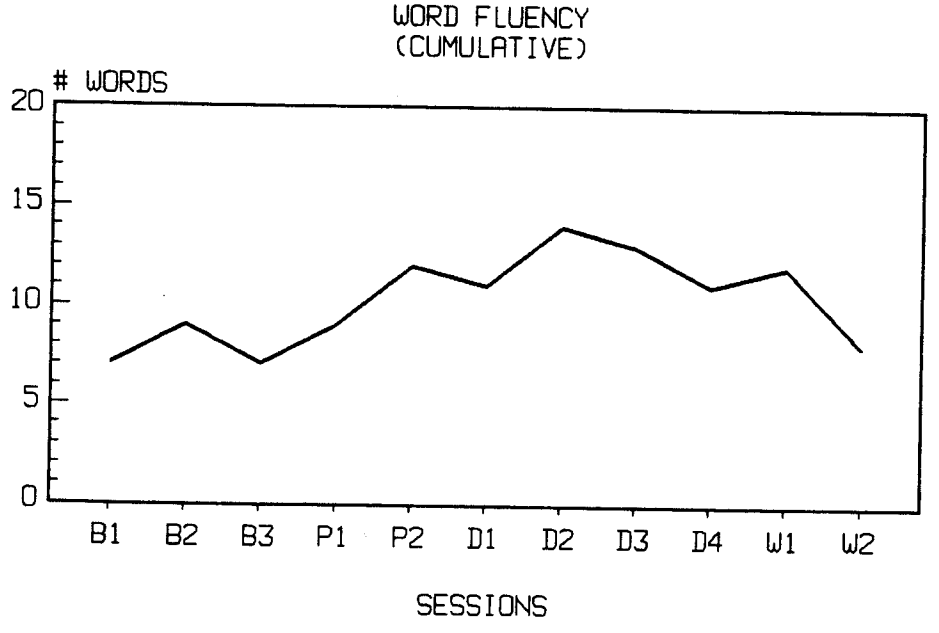

Figure 14.4. D. S.'s cumulative word fluency performance on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

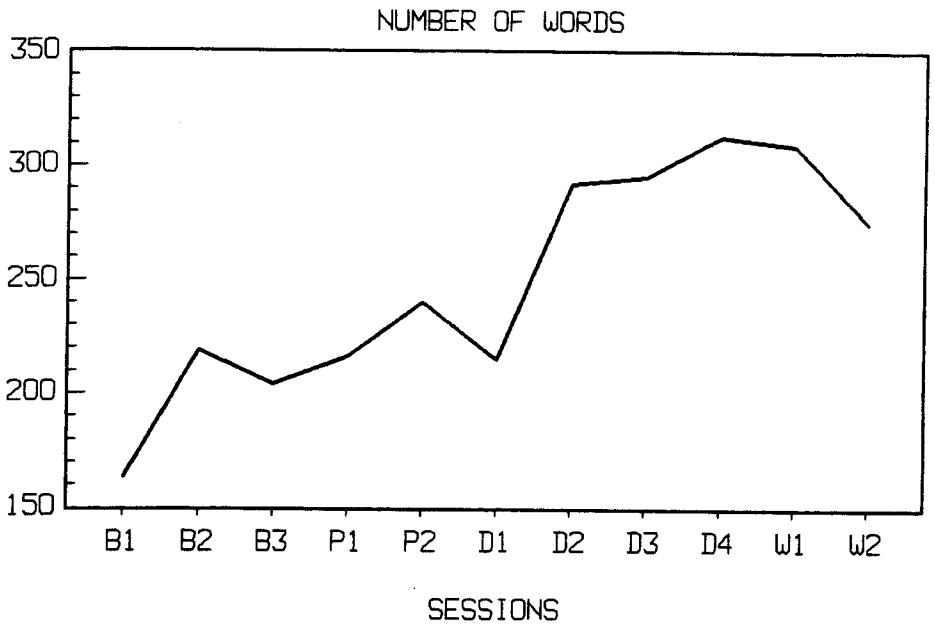

Figure 14.5. Number of words in D. S.'s connected speech samples on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

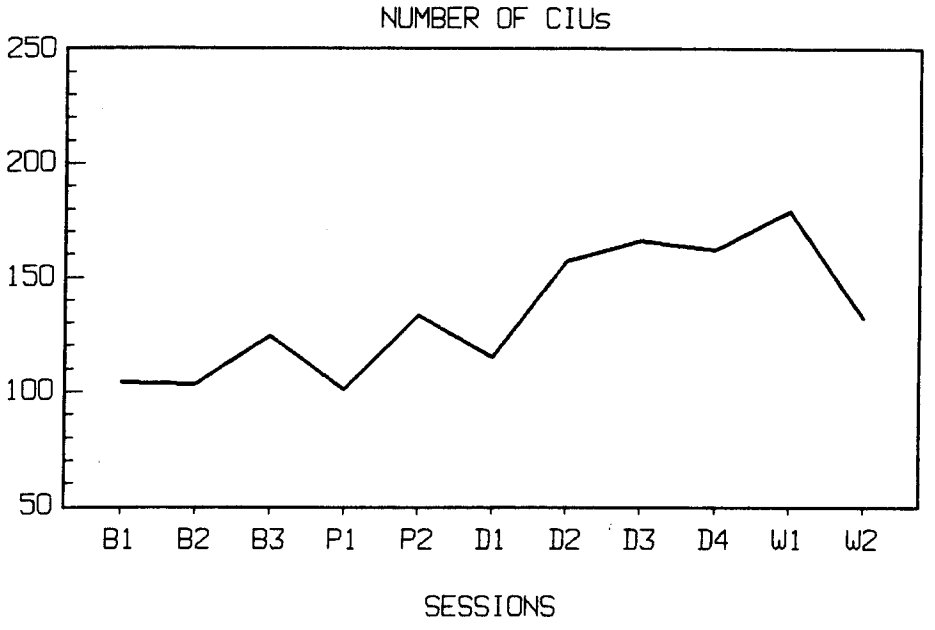

Figure 14.6. Number of correct information units (CIUs) in D. S.'s connected speech samples on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

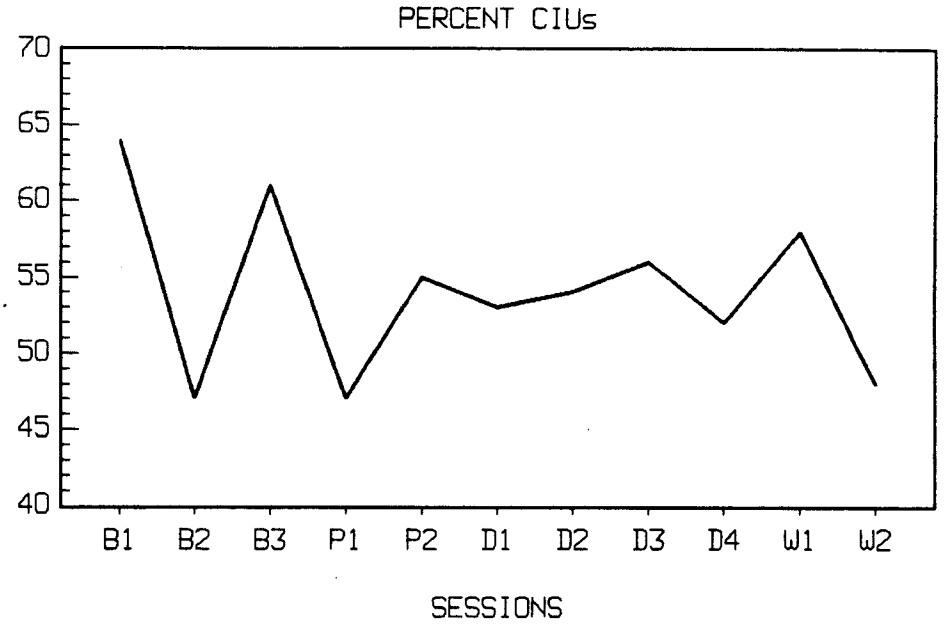

Figure 14.7. Percentage of correct information units (CIUs) in D. S.'s connected speech samples on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

saying more words, but the number of uninformative words increased as well as the number of informative words.

Changes in speaking rate during the drug treatment phase do not suggest a treatment effect when compared to performance during the baseline and placebo phases of the study (Figure 14.8). Since any substantial reduction in pauses within or between utterances would be reflected in an increased speaking rate, these data suggest that Bromocriptine had no effect on pauses within connected speech.

There were interesting differences between the responses of D.S. and his wife to the questionnaire. His wife's responses did not suggest that she perceived any change in her husband's mood or communication, except that she felt he was more interested in socializing with others during the drug and withdrawal phases of the study (a difference of 1 point in the rating for that item). However, D.S. reported substantial (2- or 3-point) positive changes on four of the questions, including question 2, how easily he communicated with others; question 3, how often he initiated conversations; question 4, how often he volunteered information; and question 6, how often he was interested in socializing with others. However, all but one of these positive changes began in the placebo phase.

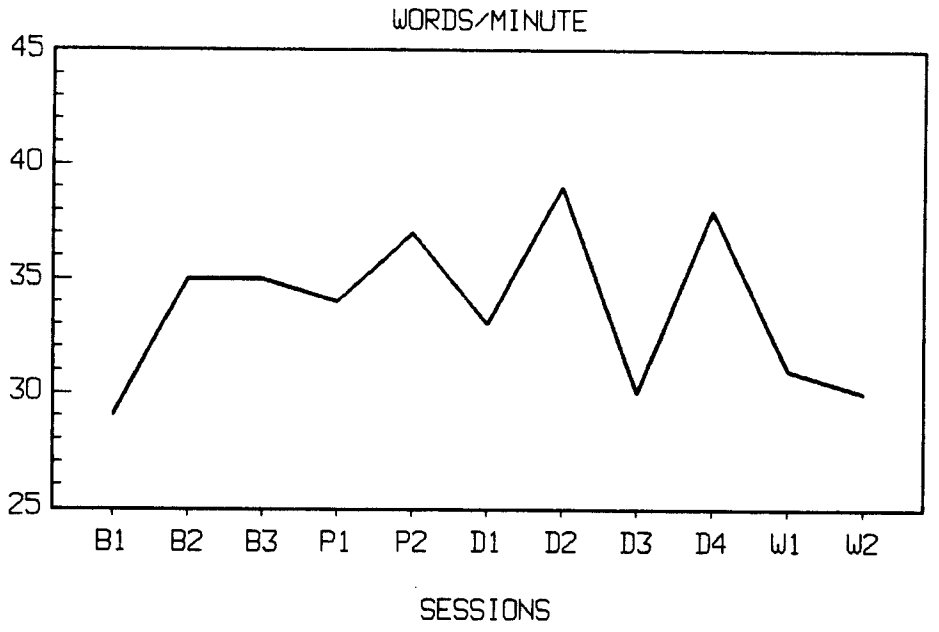

Figure 14.8. Number of words per minute in D. S.'s connected speech samples on each test occasion. B = baseline, P = placebo, D = drug treatment, W = withdrawal. Numerals denote test sessions within phases.

Results of the questionnaire suggest that changes in performance on language measures (nearly all of which started during the placebo phase) may have resulted from the patient's hope and expectation that the drug treatment would improve his communication. A decline in performance on all measures except visual reaction time at the final withdrawal-phase testing may reflect his feelings of sadness and disappointment that the treatment was over and that the results had not lived up to his expectations. This interpretation is also consistent with his lower ratings for mood and communication in the withdrawal phase.

Advocating the use of Bromocriptine for improving the communication of aphasic adults appears to be premature. Thus far, data to support the effectiveness of Bromocriptine are weak and inconclusive. Moreover, side effects are likely to occur even with low dosages of Bromocriptine. Further research concerning the effects of Bromocriptine on the speech and language performance of aphasic adults appears warranted. The following questions should be considered:

1. If Bromocriptine treatment is shown to be effective, which speech and language deficits are most likely to improve?
2. Is Bromocriptine treatment effective for both chronic aphasia and acute aphasia?

3. What dosage of Bromocriptine is necessary to generate speech and language improvements?
4. Must Bromocriptine be taken continuously to maintain improvements?
5. How prevalent and serious are the side effects of Bromocriptine?
6. Are speech and language changes obtained with Bromocriptine meaningful enough to justify the potential risks involved?

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APPENDIX 14.A

Respondent: _____ Date: _____

In the following questionnaire, you will be asked to make several judgments about your husband's speech and his general mood. Please circle the number that best describes your husband's present speech and mood.

1. How easily do you understand what he tries to communicate?

1	2	3	4	5
great difficulty	moderate difficulty	occasional difficulty	very little difficulty	no difficulty

2. How easily does he communicate with others?

1	2	3	4	5
great difficulty	moderate difficulty	occasional difficulty	very little difficulty	no difficulty

3. How often does he initiate conversations?

1	2	3	4	5
never	rarely	occasionally	frequently	very frequently

4. How often does he volunteer information?

1	2	3	4	5
never	rarely	occasionally	frequently	very frequently

5. How often is he interested in things in his environment (television, newspapers, neighborhood activities, etc.)?

1	2	3	4	5
never	rarely	occasionally	frequently	almost always

6. How often is he interested in socializing with others?

1	2	3	4	5
never	rarely	occasionally	frequently	almost always

7. How much of the time does he appear to be content and happy?

1	2	3	4	5
never	rarely	occasionally	frequently	almost always