The Effect Of Alerting And Tranquilizing Drugs Upon The Performance of Aphasic Patients

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The few reports available for the use of drugs as adjuncts to aphasia rehabilitation generally fail to support the notion that medication facilitates the language performance of aphasic patients.

Several investigators have reported on the use of intravenous injections of sodium amytal (a sedative, hypnotic, and anti-convulsant). Linn and Stein (1946) reported a favorable result on a group of soldiers with post-traumatic aphasia, but Linn (1947) later reported only transitory benefits with a post-surgical (meningioma) aphasic patient and a patient with aphasia of vascular origin. Billow (1949) reported only temporary improvement in speech and mood in two aphasic patients. Bergman and Green (1951) used sodium amytal with 27 patients. They reported no significant improvement in any of them; in fact, larger amounts of the drug usually made the aphasia worse. In some cases there was an apparent increase in a patient's ability to speak or understand, but the increase was judged to be within the limits of the fluctuations which occurred spontaneously before administration of the drug. D'Asaro (1955) reported equivocal results with sodium amytal on 30 subjects; the only improvement in performance on various experimental tasks was on tests involving automatic language.

West and Stockel (1965) reported the use of a meprobamate (a tranquilizer, muscle relaxant, and anti-convulsant) and a placebo condition in a double-blind procedure with 29 aphasic patients. No significant differences were found which would indicate that language training was facilitated by use of the drug. Sarno, Sarno, and Diller (1972) administered hyperbaric oxygen to stroke patients; they reported a complete absence of effect on the course of aphasia.

We have been interested in the possible differential effects on aphasia performance of drugs which alter behavior in quite different ways. We were interested in studying the effects of an altering drug and a tranquilizing drug. For the alterting drug we selected Ritalin (Methylphenidate). This is described in the 1967 Physicians Desk Reference (1966) as "a mild stimulant and antidepressant, which brightens mood and improves performance, usually without producing hyperexcitability or depressive rebound" (p. 611). For the tranquilizing drug we selected Librium (Chlordiazepoxide), described in the 1976 Physicians Desk Reference (1976) as "a versatile therapeutic agent...for the relief of anxiety and tension...over a wide range of emotional disorders" (p. 1290). We wondered whether administration of these drugs might lead to observable differences in overall performance on the Porch Index of Communicative Ability (PICA) and on a word fluency measure. Secondarily we were interested in the effects of the two drugs on performance in different modalities (gestural, verbal, graphic) as well as on speed of response as measured by the length of time required for test administration.

Procedure

Fourteen aphasic patients participated in a study involving a double-blind procedure. These patients were eight men and six women who ranged in age from 19 to 68 years, with a mean age of 55 years. Their schooling ranged from 7 years to 16 years, with a mean of 11 years. Aphasia was of traumatic etiology in two cases, vascular in 12 cases. We wanted patients who could be considered to be physiologically stable and not overly agitated or depressed. Therefore we selected only patients who were at least 21 days beyond the onset of their aphasia and who were judged by their physicians to be physiologically stable and able to participate in the study. No patient presented any evidence of motor speech impairment, confusion, or dementia.

Each subject served as his own control. Intraoral administration of 20 mg each of Ritalin, Librium, and a placebo encased in identical capsules constituted three treatment conditions. Each treatment condition was given on three days for a total of nine administrations on consecutive days. The sequence of treatments was randomized among subjects and was known only to the pharmacist providing the drugs. Capsules were administered 2½ hours after breakfast or lunch; the language evaluation battery was given 45 min. after administration of the capsule.

The language evaluation battery consisted of 11 PICA subtests and the Word Fluency Test. We shortened the PICA by omitting seven subtests: three gestural (Tests II, III, XI); one verbal (XII); and three graphic (D,E,F). These seven subtests were omitted primarily in order to shorten the testing time. We also felt that the kinds of responses elicited by Tests II, III, XI and F were somewhat peripheral to the aspects of language ability we were most interested in; and it seemed to us that Tests XII, D and E were such that the test stimuli themselves constituted cues which would be conducive to a learning effect in patients in repeated test administrations. The Word Fluency Test (1967) required the patient to enumerate as many words as he could think of in one minute beginning with a given letter of the alphabet; the four letters s, p, c, and t were selected on the basis of high frequency (decreasing in this order) with which words beginning with each of these letters appear in Webster's Collegiate Dictionary.

As stated, we conducted the study of the three treatment conditions on nine consecutive days. In addition, we administered the language battery under the placebo condition on the day preceding and the day following the nine treatment days. We wanted to use scores from these two administrations to estimate the effect of administering the same language battery so many times in succession. The test battery was administered by the same examiner (R.L.K.) throughout the entire experiment.

Results

An analysis of variance was performed using a treatment by subjects design. Analysis revealed no difference between treatment conditions. There was no suggestion of any difference between the effects of the two drugs or between the placebo and either of the other drugs. Table 1 presents data concerning the three treatment conditions. We can see that in the case of all 14 subjects, the overall mean scores for the three administrations of the PICA in each of the three conditions are close together. For Subject 1

the value 12.90 in column A represents the mean overall score for the three administrations of the PICA battery on the days when Librium was administered; the value of 13.01 is the mean of the three administrations of the battery on the days when placebo was administered; the value of 13.00 represents the mean of the administrations on the three days when Ritalin was administered. This pattern of similarity between the three mean scores is observed in all 14 cases. There was no evidence of an order effect with regard to treatment conditions.

Data concerning the time required for test administration are shown on the left in Table 1. There are no significant time differences among the three treatment conditions. Although we might have expected test times to be shorter in Condition C, with Ritalin, administration under this condition did not take a shorter time than under the other conditions. (Mean times for the three conditions are 26.2 minutes, 27.0 minutes, and 27.4 minutes.)

To show further how the data went, we have selected a single subject, Subject 3, and present his scores in Table 2. His pattern of scores is typical of the pattern found in all 14 subjects. We can see the daily overall scores and also the breakdown of the gestural, verbal, and graphic subtests. The lack of a significant difference on the overall score between the treatment conditions is repeated when we consider the subtest scores. There was no differential effect on performance in the different modalities (gestural, verbal, graphic) any more than there was overall.

Returning to Table 1, it is easy to understand the second finding: the analysis of variance revealed a significant difference between patients. This was expected in view of the wide range of abilities represented. It can be seen, for example, that subjects 3, 5, and 14 are much more severely aphasic than subjects 4 and 10.

The data revealed a learning effect arising from serial administrations of the test battery. This learning effect from Day 1 to Day 11 is evident on all PICA scores (overall, verbal, gestural, and graphic) and in the reduction of PICA administration time. If you will look at Table 1 and consider the data under PICA overall for Day 1 and Day 11, you can see that all subjects earned a higher overall score on the 11th day than they did on the first day. The magnitude of the gain ranged from .12 of a scale point to 2.26 points. On the left hand side of Table 1 it can be seen that the time required for administration of the PICA was less on Day 11 than on Day 1 for all except Subject 11, for whom the two administration times were equal. The significance of the differences in overall scores between Day 1 and Day 11 and of the differences in test administration time was not tested statistically.

We had expected that there might be such a learning effect. Porch reported, after analyzing the PICA scores for 40 patients with test-retest intervals of two weeks or less, that the mean differences in test scores between the two tests were small but in a positive direction, suggesting "a slight practice effect, or in this case, possibly a recovery effect, as may be expected with a sample of aphasic patients" (1967, p. 45).

The Word Fluency Test yielded no useful information. Our patients found this a difficult task and were able to produce few words. On the first day they produced a mean of 3½ words (range = 0 to 12) and on the eleventh day a mean of 5 words (range = 0 to 14). Over the 11 days nine patients showed an increase in words produced, two showed a decrease, and three remained the same. There were no evident treatment effects on this measure.

Table 1. Results Of Treatment Conditions.

Subj.	Time (Min) Day 1	Day 11	Conditions*(X) A	B	C	PICA Overall Day 1	Day 11	Conditions*(X) A	B	C
1	38	26	29	28	27	12.68	13.23	12.90	13.01	13.00
2	29	28	31	28	27	9.90	10.32	10.30	10.20	10.16
3	55	39	44	55	49	7.10	8.39	8.07	7.90	8.21
4	28	14	16	14	15	14.21	14.45	14.28	14.16	14.30
5	38	33	35	40	35	6.48	6.60	7.01	7.19	6.89
6	28	20	19	21	20	13.34	14.82	14.05	13.99	14.01
7	22	17	19	19	20	12.82	13.48	13.70	13.70	13.66
8	46	17	24	23	23	10.98	13.24	12.88	12.71	12.80
9	31	23	27	26	27	12.93	13.80	13.78	13.61	13.65
10	20	16	17	17	19	13.86	14.11	14.06	14.12	13.90
11	23	23	26	25	26	12.67	13.65	13.08	12.93	13.01
12	24	20	21	22	20	11.87	12.78	12.59	12.21	12.56
13	30	16	19	20	19	12.27	13.13	12.49	12.45	13.09
14	38	35	40	40	47	6.27	7.16	7.23	7.12	7.17

*Conditions: A = Librium; B = Placebo; C = Ritalin

Table 2. Data on Subject No. 3 (Male, 55, infarct).

Condition	Day	Word Fluency	PICA Overall	Gestural	Verbal	Graphic	Time (Min)
P	1	0	7.10	10.88	5.23	2.66	55
	11	0	8.39	11.50	6.60	5.00	39
A	3	0	7.76	11.26	6.03	3.66	42
(Librium)	5	0	8.21	11.32	6.46	4.80	50
	9	0	8.24	11.28	6.37	5.06	41
			$\bar{X}$ 8.07	11.29	6.29	4.51	44
B	2	0	6.84	10.22	6.06	2.00	52
(Placebo)	6	0	8.21	11.08	6.60	5.06	65
	10	1	8,64	11.30	7.80	5.06	48
			$\bar{X}$ 7.90	10.87	6.82	4.04	55
C	4	0	8.05	11.30	5.96	4.73	54
(Ritalin)	7	0	8.35	11.80	5.76	5.20	44
	8	0	8.22	10.88	6.76	5.26	50
			$\bar{X}$ 8.21	11.33	6.16	5.06	49

Discussion

Where does the outcome of this study leave us? Obviously we are not reporting that we are now regularly using these or any other medications as adjuncts to our aphasia therapy. These two drugs failed to yield even a flicker of evidence that the patients' language behavior was being influenced. They join the ranks of three other medications which have been shown to yield no consistent effect.

Did we use an appropriate dosage of each drug? We are not sure, but we followed what appeared to be the best procedure. It would have been desirable to determine what an optimum dosage of each drug might be for a given patient. It was impossible in this study to make such a determination. The usual dosage of Ritalin ranges from 5 to 20 mg. three times a day. The usual dosage of Librium is from 5 to 10 mg. three times a day. It was determined that a standard single dosage of 20 mg. would be used for both drugs in what our Neurology consultants considered a reasonable expectation that it would accomplish the desired pharmacologic effects. The drugs may have produced those effects—increasing alertness and reducing anxiety—but there was no demonstrable secondary effect on language function. Might we get language effects on given patients on long-term dosage of either drug? We don't know, but we suppose that we might with the right type of patient under appropriate circumstances.

We should make it clear that it would not have been reasonable to expect any direct effect of either drug upon the function of cerebral language circuitry in these patients with cortical infarctions and trauma. Ritalin is assumed to act at brain stem level on reticular formation, accelerating synaptic transmission. It could increase the alertness and the attentiveness of an aphasic patient. Librium presumably acts upon the limbic system to reduce anxiety and tension. It might reduce an aphasic patient's emotional upsetness. At best, then, the looked-for effects on language function would have been indirect. To the degree that an aphasic patient's language impairment is a function of lack of alertness, inattention, anxiety, or tension, we may find one or the other of these drugs to be helpful. It appears that the language function of none of our 14 subjects was importantly determined by these psychological factors and therefore the language performance was unaltered by either drug.

It seems to us that investigation of drug effects—indirect or direct—on language function in aphasic patients should not cease. There are no doubt other drugs to be studied. There are special kinds of patients whose management might well include a trial of some drug. It would be worthwhile to know whether drug effects depend upon the patient's stage of recovery. Such investigations require careful design and subject selection and a lot of time. Our experience here reported does not prompt us to undertake another such study soon.

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Discussion

Q. Was there any kind of lag time effect of the drug?

A. No, I don't think so. We think we got the effect and we think it cleared daily. I don't know how you ever know for sure, but that is the best prediction. We saw no evidence of unusual lag time.

Q. How long post-onset were the patients?

A. They were no less than 21 days beyond onset. Several subjects were new aphasic patients. Two had been aphasic for about 2½ years. Others fell between these extremes.

Q. I am interested in the changes over time and learning effect. Would that amount of time (11 days) effect those changes anyway?

A. We cannot be sure what part of the change is attributable to repeated exposure to the test, what part to spontaneous improvement or improvement due to treatment.

Q. What was the rationale for choosing those two drugs?

A. Because they are known to have quite different effects. They are popular drugs which seem to be effective with many people. For instance, if you give me Ritalin, I will become eloquent and verbose. We wondered if it might have a comparable effect on aphasic subjects. It did not.