NEUROTICS WHO FAIL TO TAKE THEIR DRUGS

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Neurotics Who Fail to Take Their Drugs*

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Introduction

Patients who do not comply with therapeutic procedures have been of longstanding concern to the clinician and have presented knotty methodological problems to those involved in evaluating the effectiveness of different treatments and treatment modalities (1, 2, 4, 6, 10, 11, 12, 13).

The present paper is intended to further the very sketchy literature (2, 6) on factors related to non-adherence to protocol among neurotic out-patients receiving pharmacotherapy. Parallels will be drawn between the results of the present study and results from other relevant drug and psychotherapy studies.

Setting, Procedures and Clinical Sample

The Psychiatric Clinic of the University of Pennsylvania, the Henry Phipps Psychiatric Clinic at the Johns Hopkins University, and the Neuropsychiatric Clinic at the Philadelphia General Hospital, following identical protocols, participated in this six-week, double-blind, placebo-controlled evaluation of meprobamate (3).

Patients were screened for the study—anxious tense neurotics without sociopathy, organic impairment, or marked depression—by experienced intake psychiatrists. During a "semi-structured" interview, which typically lasted an hour, the intake psychiatrist filled out a pretested and precoded questionnaire which contained the following kinds of information: previous in-patient or out-patient treatments, chronicity of illness, previous medication experience, the type of treatment the patient was seeking, and the type of treatment the psychiatrist thought would be most suitable for the patient. Patients on a psychotropic drug at intake were instructed to discontinue medication until their first treatment appointment the following week. Patients accepted for the study were then seen by a technician who recorded demographic information (these data are recorded in Table III of the "Results" section). The patient then completed a 64-item Symptom Check List (SCL) of common psychoneurotic complaints (5) and was scheduled for the first of four bi-weekly appointments with one of 15 psychiatric residents.

Before seeing the psychiatric resident the following week the patient again completed the SCL. Residents were trained to conduct a short (up to 30 minutes) symptom-focused interview in which patients were urged to (a) keep their regularly scheduled appointments, (b) take their medicine faithfully, and (c) not to take any other "nerve" medicine. The psychiatrist prescribed (fixed dosage) two pills q.i.d. (1,600 mg. of meprobamate) and gave each patient three bottles of medication (50 caps. per bottle), asking the patients to return any unused medicine at their next visit. Immediately after the first patient visit the psychiatrist completed a pretested and precoded questionnaire which contained information regarding the patient's attitude toward being put on medication, the type of treatment the patient seemed to expect, how much the psychiatrist liked the patient, how comfortable he felt with the patient, etc. (these data are recorded in Table III of the "Results" section).

* These data were collected as part of an investigation supported by two NIMH-PSCPHS research grants from the National Institute of Mental Health to the University of Pennsylvania (MH-04731) and to the Johns Hopkins University (MH-04732).

Patient Classification and Sample Size

More than 75 per cent. of the patients returned their unused medication. Pill counts provided an objective index of medication intake. In addition, the psychiatrists independently inquired, at each patient visit, into dosage taken and into any other medicine the patient may have taken. These data (pill count was used in preference to verbal report) provided the bases for patient classification.

To be classified as "Adhered" a patient must have (a) kept his regularly scheduled post-medication appointments (a four-day make-up period was allowed), (b) averaged a minimum daily dosage of 6 caps. of meprobamate (1,200 mg.) or placebo, and (c) not taken other psychotropic medication.

"Deviated" patients were classified as follows:

The "Insufficient Medication Only" and the "Insufficient Medication and Other Medication" and/or "Other Medication Only" categories refer to patients who kept their treatment appointments but who deviated from protocol in so far as dosage (averaged less than 6 caps. of meprobamate or placebo daily) and/or other medication was concerned. The "No-Shows Early" category refers to patients who never returned after having been given medication at their initial visit. "No-Shows Subsequent" are patients who returned for the first post-medication visit and then dropped by the second or third post-medication visit. In a study by Rickels *et al.* (14) it was found useful to make this distinction between "No-Shows" patients.

The study sample comprises 254 patients who entered the treatment phase of the drug trial. Of this sample, 72 meprobamate patients and 66 placebo patients adhered to the prescribed drug programme, whereas 53 meprobamate and 63 placebo patients deviated from protocol. Although these figures indicate some tendency for a higher proportion of meprobamate than placebo patients to adhere to protocol, this difference is not reliable ($\chi^2<1$). Further, since no systematic differences between meprobamate "Adhered" vs. "Deviated" as compared with placebo "Adhered" vs. "Deviated" obtained on the background dimensions examined, data have been pooled across medication categories.

Patient classification data are presented in Table I.

Table I indicates that the percentage of patients falling into the different classifications is roughly equivalent within each clinic. It seemed reasonable, therefore, to pool our data additionally over clinics in comparing patient categories.

Results

Since more than 25 separate analyses were made in comparing "Adhered" and "Deviated"

Table I

Patient Classification by Clinic

Patient Classification	Clinics						Total	
	U. Penn.		Hopkins		P.G.H.			
	N	%	*N*	%	*N*	%	*N*	%
I. Adhered to drug procedures	44	(59·4)	48	(53·4)	46	(51·2)	138	(54·3)
II. Deviated from drug procedures:								
(1) No-shows early	9	(12·2)	12	(13·3)	13	(14·4)	34	(13·4)
(2) No-shows subsequent	8	(10·8)	11	(12·2)	13	(14·4)	32	(12·6)
(3) Insufficient medication only	9	(12·2)	12	(13·3)	13	(14·4)	34	(13·4)
(4) Other medication only or Other medication plus Insufficient medication	4	(5·4)	7	(7·8)	5	(5·6)	16	(6·3)
Totals	74	(100)	90	(100)	90	(100)	254	(100)

patient categories, in an hypothesis seeking spirit, the p values which are reported here should be interpreted as suggestive rather than definite (16). Future replication is called for and planned.

SCL:

Data from intake and the first treatment visit yielded equivalent results so that only Visit 1 data have been tabled.

A comparison of patients who adhered or who deviated from drug protocol revealed that the "Deviated" group had a significantly higher mean pretreatment distress level (2·01 vs. 1·84; $t=2\cdot55$, $p < 0\cdot05$). The theoretical range of mean distress levels can vary from 1·00 (no distress) to 4·00 (extreme distress). As shown in Table II, the "No-Shows Early" were the "sickest" of the patients. "No-Shows Subsequent" were by comparison less distressed (1·88 vs. 2·15; $t = 2\cdot02$, $p < 0\cdot05$).*

Intake and Visit 1 data are shown in Table III. These data are arranged by the two main patient categories, "Adhered to Drug Procedure" and "Deviated from Drug Procedure". Percentages have been shown to take care of cases of missing data. Where a particular subcategory of "Deviated" patients is responsible for the obtained difference between main categories,† this is commented on in the text.

* These results are opposed to an earlier finding by Rickels *et al.* (10). In their study "No-Shows Subsequent" had the reliably higher pretreatment distress levels as compared with completed patients and "No-Shows Early". However, the fact that the Rickels study employed (*a*) a cross-over design, (*b*) medical clinic rather than psychiatric clinic patients, and (*c*) two additional tranquillizers may account for the discrepancy of findings.

Discussion

To organize these data it seemed logical to conceptualize our findings in four main categories. These are: (a) degree of psychopathology, (b) prior experiences with psychotropic medication, (c) social class, and (d) doctor attitude toward patient.

(a) *Degree of Psychopathology:* Congruent with the finding that "Deviated" patients were characterized by a higher initial SCL distress level ($p<0\cdot05$), Table III also indicates a higher proportion of previous hospitalizations for this group ($p<0\cdot02$) and a tendency toward having a poorer study prognosis as judged by both the intake and treating psychiatrist ($0\cdot20 > p > 0\cdot10$ for both). A closer inspection of these data by deviation category strongly suggests that these differences were mainly attributable to the "No-Shows Early" patients. The treatment offered was probably not sufficiently potent for these patients. This finding agrees

† The chi-square, with the Yates correction for continuity, was statistically employed for these tests unless otherwise specified. Probability values are for two-tailed tests.

Table II

Initial Symptom Distress Level

Patient Classification	Mean	S.D.	*N*
I. Adhered to drug procedures	1·84	0·53	138
II. Deviated from drug procedures	2·01	0·52	110
(1) No-shows early	2·15	0·58	31
(2) No-shows subsequent	1·88	0·45	31
(3) Insufficient medication only	2·02	0·51	34
(4) Other Medication only or Other medication plus Insufficient medication	1·95	0·48	14
III. Missing Data			6
Total = 254			

TABLE III

Information Obtained at Intake and Visit 1

	Patient Category	
	Adhered to Prescribed Drug Procedures	Deviated from Prescribed Drug Procedures
	$N = 138$	$N = 110$
Intake		
1. Age (mean and range, years)	33·9 (19–68)	33·4 (20–65)
	%	%
2. Female	65	70
3. Negro	56	65*
4. Marital status:		
(*a*) Single	28	23
(*b*) Married	52	55
(*c*) Divorced, separated, widowed	20	22
5. Education:		
(*a*) Eight grades or less	20	31†
(*b*) Some high school	43	44
(*c*) High school and beyond	37	25
6. Income: $2,999 or less	62	72
7. Current employment status:		
(*a*) Employed	39	36
(*b*) Unemployed	39	41
(*c*) Housewife	22	23
8. Previous out-patient treatments:		
One or more	31	31
9. Previous in-patient treatments:		
One or more	3	10‡
10. Duration of present complaint:		
More than 1 year	31	34
11. Previous psychotropics ever taken:		
One or more	78	65‡
12. Presently taking a psychotropic drug	50	42
13. Number of different psychotropic drugs taken during past year:		
Three or more	19·5	31*
14. Type of psychotropic drug taken during past year:		
(*a*) Tranquillizer only	61	42‡
(*b*) Non-tranquillizer only	28	34
(*c*) Combination of above	11	24

	Patient Category	
	Adhered to Prescribed Drug Procedures	Deviated from Prescribed Drug Procedures
	$N = 138$	$N = 110$
15. Primary purpose in seeking treatment:		
(*a*) Psychological readjustment through resolution of inner conflicts, social and inter-personal difficulties	25	17*
(*b*) Symptomatic relief of psychological or physical symptoms	75	83
16. Treatment patient most expects from clinic:		
(*a*) Psychotherapy	23	18
(*b*) Drug therapy	42	51
(*c*) Advice and guidance	35	31
17. Treatment psychiatrist feels most suitable:		
(*a*) Psychotherapy	38	24‡
(*b*) Drug therapy	19	26
(*c*) Combination	43	50
18. Prognosis (end of 6-week treatment period):		
(*a*) Excellent and Fair	72	65*
(*b*) Poor and Uncertain	28	35
Visit 1		
1. Patient's attitude toward being given medication:		
(*a*) Very eager, somewhat eager for medicine	39	46
(*b*) Neither eager nor reluctant	46	42
(*c*) Somewhat or very reluctant to take medicine	15	12
2. Patients who definitely did not take medicine, as instructed, between Intake and Visit 1	72	72
3. Treatment patient most expects from clinic:		
(*a*) Psychotherapy	21	17
(*b*) Drug therapy	41	47
(*c*) Advice and guidance	38	36
4. Doctor comfort with patient:		
(*a*) Extremely comfortable	37	30
(*b*) Moderately comfortable	54	62
(*c*) Uncomfortable	9	8
5. Doctor liking of patient compared to others seen in treatment:		
(*a*) Much less, a little less	28	28
(*b*) About same	40	39
(*c*) Much more, a little more	32	33
6. Prognosis (end of 6-week treatment period):		
(*a*) Excellent and Fair	79	71*
(*b*) Poor and Uncertain	21	29

* $p < 0{\cdot}20$.
† $p < 0{\cdot}10$.
‡ $p < 0{\cdot}05$.

with Brill *et al.* (2) who found that neurotic patients who dropped out of pharmacotherapy were more anxious initially than patients who completed treatment. The relevant psychotherapy literature regarding the relationship between degree of subjective distress and drop-out is very contradictory.

(b) *Prior Experience with Psychotropic Medication:* "Adhered" patients were more likely than "Deviated" patients to have taken at least one psychotropic drug prior to entering this study ($p<0\cdot05$). Moreover, of drug treated patients, the "Adhered" group was somewhat less likely to have taken three or more different psychotropic drugs during the prior year ($0\cdot20>p>0\cdot10$) and, correspondingly, they were more likely to have only taken a drug in the tranquillizer class as contrasted with the non-tranquillizer class, alone, or in combination with a tranquillizer ($p<0\cdot05$).

(c) *Social Class:* It has been extensively documented that middle-class patients are much more likely to remain in psychotherapy than lower-class patients (1, 4, 10, 11). This same tendency, although far less marked, also appeared in the present study and in another drug study reported by Rickels *et al.* (15). Thus, having more education ($0\cdot10>p>0\cdot05$) and being white ($0\cdot20>p>0\cdot10$) is marginally related to adherence to protocol.

There may be a real culturally determined basis for more middle-class patients to "abide by the rules of the game" regardless of the specific nature of the treatment modality. Some possible explanation for the attenuation of the "deviated from drug procedure"-social class relationship in the present data as compared with psychotherapy-termination data are: (a) a closer correspondence between pharmacotherapy and lower social class treatment expectations—see Hollingshead and Redlich (9) (pp. 340, 345), as contrasted with psychotherapy and lower social class treatment expectations, and (b) a strong skew toward the lower end of the social class continuum in the present patient sample. (In a subsequent study using similar patients at these clinics, the use of the Hollingshead Two-Factor Index of Social Position [8] revealed that 48·1 per cent. of the sample [$N = 233$] fell in class V and 36·5 per cent. fell in class IV.)

Given the relationship between adhering to procedure and education (a rough index of social class), it seems likely that the judgment by our experienced intake psychiatrists that adhering patients were more suited for psychotherapy and less suited for drug therapy ($p<0\cdot05$) and that they were somewhat more apt to be seeking psychological readjustment rather than symptomatic relief ($0\cdot20>p<0\cdot10$) was reflecting, in part, differences in verbal ability, goal directedness and intelligence; variables which are clearly socio-economic class related (12).

(d) *Doctor Attitude Toward the Patient:* The lack of a reliable relationship between the doctor's liking of the patient and the patient's subsequent adherence or deviation to the doctor's instructions is somewhat disturbing in view of the importance attached to the initial doctor-patient relationship in the psychotherapy literature (7). Freedman *et al.* (6), however, also failed to detect a relationship (until they also examined the patient's attitude toward the doctor). It should be stressed that the importance of the doctor's personal feeling about the patient is probably not as critical in drug therapy as it is in psychotherapy, and, further, a semi-structured interview was employed in the present study which, presumably, further depreciated the importance of doctor "comfort with" or doctor "liking of" the patient.

Summary

The characteristics of patients who adhered to the prescribed procedures in a six-week meprobamate trial were compared with those of patients who did not comply with the doctor's instructions. Results suggest that patients who deviated from the prescribed drug programme were sicker initially, of lower socio-economic backgrounds, and were less apt to have had previous treatment with a psychotropic medication. However, of those patients who had prior exposure to psychotropic medication, the deviating group tended to have the greater density of exposure; i.e. to have taken more and a

greater variety of psychotropic medications within the last year.

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