

Prediction of Short-term Outcome of Neurotic-depressive Inpatients

Results of an Empirical Study of 134 Inpatients

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Summary. A study was carried out involving 134 neurotic-depressive inpatients (according to ICD-9) treated with cognitive behaviour therapy and in a subgroup additionally with antidepressants. Using standardized rating instruments, a large set of potential predictor variables was tested. After cross-validation according to the split-half technique, only very few of these proved to be suitable as predictors for the main outcome criteria. These predictors included certain aspects of social functioning before index admission, intensity of depressive symptoms at admission and the degree of self-evaluated mood disturbances three weeks after admission. Several predictors known from the literature could not be reproduced in this study, demonstrating the well-known instability of most predictor findings. On the other side, the predictor profile of the neurotic-depressive patients was quite similar to that found in endogenous depressives, a result which might – together with other findings, such as the response of neurotic depressives to antidepressants – question the traditional subclassification of functional depressive states into these subgroups.

Key words: Neurotic Depression – Short-term Outcome – Predictors – Cognitive Behaviour Therapy – Antidepressants

Introduction

Most predictor studies on short-term prognosis of patients suffering from a depressive syndrome were carried out without subtyping the patients into neurotic or endogenous depressives (compare the review of Bielski and Friedel 1976 and Woggon 1983). This holds especially true for studies on patients treated with antidepressants in which mixed groups of endogenous and neurotic depressive patients were included. The results concerning predictors of short-term outcome of depressives in gen-

eral under therapy with antidepressants are very inconsistent, but seem to concur somewhat in the following predictors for an unfavorable outcome: unmarried, poor premorbid adjustment, neurotic personality traits, high number of episodes, duration of episode more than one year, poor response to antidepressants during the last episode, weak depressive symptoms and presence of depressive delusional ideation, poor response to antidepressants in the first 2 or 3 weeks of treatment (Bielski and Friedel 1976; Möller et al. 1987; Woggon 1980, 1983).

In some of these studies the prognostical implications of the diagnostic subtype itself were tested. The results were inconclusive. While some studies found a better response to antidepressants in endogenous patients (Deykin and DiMascio 1972; Friedman et al. 1961; Kiloh et al. 1962; Paykel et al. 1973; Raskin and Crook 1976), others could not find such differences (Abraham et al. 1963; Kupfer and Spiker 1981; Rose and Westhead 1967) or even in one study a better response in neurotic depressives (Wittenborn and Kiremitci 1975).

Among others, the following characteristics were described as negative predictors of long-term outcome of neurotic depressive patients: problematic childhood, personality disturbances, high neuroticism and low extraversion, chronicity of depressive symptoms, comorbidity with anxiety or panic attacks (Greer and Cawley 1966; Kerr et al. 1972; Weissman et al. 1978; Clancy et al. 1978; Avery et al. 1983; Ernst and Ernst 1968).

Very few studies have investigated the predictors of response to antidepressants in neurotic-depressive patients. In a placebo-controlled study with amitriptyline, Downing and Rickels (1972) found the following characteristics as predictors of a favorable outcome: acute onset of depression, higher social class, good premorbid adjustment, intensity of depressive symptoms at admission.

In a study on neurotic depressives undergoing psychotherapy and/or treatment with amitriptyline, Weissman et al. (1978) found a high score of neuroticism as a predictor of chronicity. The following predictors were

described in the literature on psychotherapy of depressives, mostly neurotic depressives, as negative signs: chronicity of illness, higher depressive scores, greater degree of impairment, higher neuroticism score (De Jong 1986, 1987; Fennell and Teasdale 1982).

Variations in methodology may be responsible for the inconsistent findings, among others, the high selection of the patients and the small sample sizes (Bielski and Friedel 1976; Möller et al. 1987). The latter might be a very important factor especially in the studies on neurotic depressives.

The following study attempted to overcome some methodological problems of former predictor studies on neurotic-depressive patients. The study was based on the routine documentation system for the Psychiatric Department of the Max Planck Institute for Psychiatry (Barthelmes and v. Zerssen 1978; Möller et al. 1983). To a great extent, this approach may avoid some methodological pitfalls of predictor studies. For, along with a large sample, the extensive data banks and the standardized processing of the majority of the variables under consideration, it is important that the patients involved were not part of a special research project and thus selected, but were integrated into routine clinical procedures.

Materials and Methods

The sample consisted of 195 consecutively admitted patients having neurotic depression (according to ICD-9) as a primary diagnosis. The diagnosis was made by the doctor in charge of the patient and checked by the head of the department or his representative in a weekly case conference. The patients were treated as inpatients between 1971 and 1982 in the Max Planck Institute for Psychiatry (MPIP). According to further criteria for the inclusion in the study sample only 134 patients remained in the study. Most frequently the patients were excluded because of missing data, problems with respect to ratings by the doctor; other reasons were: hospital stay shorter than 3 weeks, diagnostic uncertainties after review of the patient's record, age not in the range of 18–65 years.

A brief presentation of the distributions of several important characteristics serves to describe the collective ($n = 134$). The average age of the patients was 37 years. The sex distribution showed an overrepresentation of women (50: 41%) which is typical for the illness. Forty-nine percent were unmarried, 15% divorced, separated or widowed. According to the social class scoring of Moore and Kleining (1960), 3% of the patients were from the upper class, 68% from the middle class, and 29% from the lower class. Twenty-five percent of the patients experienced the first episode of their depression, 75% suffered from a relapse of their depressive illness. The average duration of hospitalization was 77 days with a range extending from 21 to 263 days.

The patients were treated in the framework of a routine care, in general by psychotherapy alone. According to the special training of the doctors and the individual needs of the patients, different approaches of psychotherapy were applied, among others behaviour therapy (De Jong 1986, De Jong et al. 1986), especially the cognitive oriented behaviour therapy, was most frequent. Thirty-eight patients (36%) were treated additionally with antidepressants. In most cases the reason for this psychopharmacological treatment was the severity of depression. The antidepressive medication of first choice was amitriptyline, administered orally in dosages up to 150 mg per day. In addition to the main medication, tranquilizing antidepressants or neuroleptics were administered in low dosages according to need (e.g., for sedation or for sleep induction).

A very comprehensive set of potentially prognostically relevant characteristics was included in this investigation. The routine documentation (Möller et al. 1983) supplied the following predictor variables for all patients, so that these did not have to be determined retrospectively:

a) Sociodemographic data.

b) Psychopathological symptoms at admission, as judged by the Inpatient Multidimensional Psychiatric Scale (IMPS; Lorr 1974). Only the three dimensions of depression: depressive syndrome, retardation and apathy, impaired functioning, were taken into consideration.

c) Self-evaluation of psychopathological symptoms at admission using the Paranoid-Depression Scale (PD-S) and the Adjective Mood Scale (AMS) and their parallel forms (v. Zerssen 1976, 1986).

d) Different dimensions of premorbid personality, including cyclothymic disposition, typus melancholicus, and schizoid, oral, anancastic, hysteric, or neurotic personality structure. Information regarding premorbid personality was obtained for all the personality dimensions under discussion by administering self-evaluation questionnaires, for some dimensions by having relatives complete corresponding questionnaires. The self-evaluation questionnaires instructed the patient to describe himself/herself as experienced before the onset of illness (v. Zerssen 1980, 1982). The questionnaires were normally completed during the first week after admission.

In order to ensure the comprehensiveness and validity of the personality test battery employed, the number of items in the self-evaluation scales presented above was subsequently reduced according to retest reliability criteria (v. Zerssen et al. 1988). The resulting item set was reformulated to produce the dimensions of the "Premorbid Personality Inventory" (PPI) which was then incorporated into the procedure of this study. The dimensions of the PPI are extraversion, frustration, tolerance, self-insecurity, schizoidism, and orderliness.

e) Intelligence, tested for orientation purposes at admission by the subtest "general knowledge" from the Hamburg-Wechsler Intelligence Test (Wechsler 1964).

Retrospectively, the following potential predictor characteristics were taken from the patient's records: a list of historically relevant variables, including broken home, psychosis in the family, number of prior depressive phases, total duration of inpatient psychiatric treatment in the 2 years prior to the index admission, total duration of occupational desintegration (disability, unemployment, premature retirement) in the 2 years prior to the index admission, restriction of occupational performance in the year prior to the index admission, duration of the last phase before admission, duration of the symptomless interval between the last phase and the previous one, response to antidepressants in the previous episode, psychosocial stressors prior to the initial manifestation, psychosocial stressors prior to the index admission (according to DSM-III), degree of social adaptation during the year previous to the index admission (according to DSM-III), acuity of the initial manifestation, acuity of the index manifestation, duration of the index manifestation prior to the start of inpatient treatment, psychopathological characteristics of the index manifestation (e.g., depressive delusional ideation, suicidality, inhibition, agitation, insomnia, weight loss, vitally depressed mood), disturbances in premorbid social adaptation, as determined by the scale of Gittelman-Klein and Klein (1969), and disturbances in premorbid social adjustment, as measured by the abridged Phillips Scale (Harris 1975).

Since both of these latter scales refer to definite chronological development stages independently of the initial manifestation of the illness, a modified form of the Phillips Scale was employed to determine premorbid disturbances in the strict sense, i.e., disturbances which already exist prior to the symptoms observed by the patient or his/her relatives (Premorbid Scale). Determination of

important variables relating to general prognosis by means of an adapted version of the Strauss-Carpenter Prognosis Scale (Strauss and Carpenter 1974) which was originally conceived for the prognosis of schizophrenic disorders.

Since the patients' records kept by the MPIP were relatively well-structured and for the most part very informative, the retrospective determination of the set of characteristics listed above could be carried out without great difficulty by the examining physician (M. Krokenberger) who was, of course, "blind" to the standardized discharge data. Noteworthy "gaps" in the data were present only in the scale for determining disturbances in premorbid social adjustment. In this respect, the abridged Phillips Scale according to Harris supplied the most data, a circumstance probably related to the fact that this scale was specifically developed for the retrospective evaluation of patients' records.

The data supplied by the IMPS, PD-S, AMS and the premorbid personality scales were not compared by statistical analysis on the item level, since the evaluation of individual symptoms often causes considerable problems regarding reliability. In addition to this, the large number of the ensuing correlations (the IMPS alone has 90 items) would have possibly generated pseudo-significances and thus led to difficulties in interpretation. Therefore, the values of selected item groups were subsumed under syndrome scores in keeping with the evaluation directions stated in the respective manuals (Lorr 1974, Hiller et al. 1986). Of five superfactors (v. Zerssen and Cording 1978), however, only the "depressive-apathetic syndrome", which combines the depressive syndrome, the apathetic syndrome and impaired functioning, was used in this study.

Beyond these data gained from the histories and the findings at admission, intervention-related variables, as experienced by the mood-assessment scores after 3 weeks and the mood-improvement quotient after 3 weeks, were also considered in the analysis of potential predictors.

The formulation of efficacy criteria proceeded according to the principle of multiple outcome measurement (Baumann and Seidenstücker 1977), i.e., the fact was taken into account that different, incompletely correlating criteria are necessary in the evaluation of therapy efficacy. Since in the various previous studies more or less different efficacy criteria were employed, for this investigation it seemed expedient to implement a number of efficacy criteria to compare all results adequately. As was the case with the set of predictors, among the efficacy criteria the distinction was made between those criteria derived retrospectively from the records (and which therefore could be expected to be of inferior quality) and those which could be established within the context of routine documentation at the time when the data arose. Criteria of the latter type are not only those derived from the data of the IMPS, the PD-S and the AMS – all concerning psychopathology at discharge – but also a global evaluation based on the scale of the Clinical Global Impressions (CGI; Guy 1976) which records the extent of improvement at discharge; and the AMS data at fixed intervals 3 and 6 weeks after admission. Information relating to length of hospitalization was also used in formulating efficacy criteria. Finally, on the basis of data from patient's records, the extent of improvement after 3 weeks was evaluated using the CGI, and the time needed to reach a definitive improvement was determined.

Following the selection of the relevant dimensions of the IMPS and the self-evaluation scales, the following efficacy criteria were formulated:

1. IMPS factor "depressive syndrome" at discharge
2. IMPS superfactor "depressive-apathetic syndrome" at discharge
3. Improvement quotient for the IMPS factor "depressive syndrome"¹
4. Improvement quotient for the IMPS superfactor "depressive-apathetic syndrome"¹

¹ The improvement quotients were calculated as follows: score upon admission minus score at specific times (3 weeks, 6 weeks, discharge, etc.), divided by the score upon admission.

5. Depression factor (PD-S) at discharge (self-rating)
6. Improvement quotient for the depression factor (PD-S) at discharge¹ (self-rating)
7. Mood score after three weeks (self-rating)
8. Mood score after six weeks (self-rating)
9. Improvement quotient for mood score after three weeks¹ (self-rating)
10. Improvement quotient for mood score after six weeks¹ (self-rating)
11. Mood score at discharge (self-rating)
12. Improvement quotient for mood score at discharge¹ (self-rating)
13. Length of hospitalization
14. CGI of the psychopathological state after 3 weeks
15. CGI of the psychopathological state at discharge.

Thus 15 efficacy criteria were included in the statistical analysis. However, it was possible to reduce this rather broad-based measurement of efficacy to a few primary efficacy criteria; most appropriate in this regard were the IMPS superfactor "depressive-apathetic syndrome" and the corresponding improvement quotient, a presumption which was confirmed by the product-moment correlation of all outcome criteria. The efficacy criteria which reflect the conditions of the patient at discharge showed the fairly close correlation with the depressive-apathetic syndrome; less close were the relationships between the latter and the self-rating mood data of the patient after 3 or 6 weeks. Although the other efficacy criteria did not correlate with the length of hospitalization, this "hard" criterion was nevertheless chosen as a primary criterion, since among the patients discharged in a sufficiently improved condition there were those who only improved after a relatively lengthy treatment. If merely the psychopathological condition at discharge were to be chosen as an efficacy criterion, then these "poor responders" would be left unconsidered.

In the sense of an orientating analysis, the product-moment correlations between the potential predictor variables and the above efficacy criteria were calculated. Only correlations significant at the level of $P < 0.01$ or better were judged as being relevant for practical prognosis and will be presented here. In order to test the stability of the results, a cross-validation employing the "split-half" technique was carried out. Those predictors were viewed as consistent whose correlation coefficients relative to the respective efficacy criteria in both subcollectives were at the $P < 0.05$ or better significance level.

In a second part of the statistical analysis, the patients treated with antidepressants were compared with the others treated only with psychotherapy ($n = 86$) with respect to different predictor variables as well as to the efficacy criteria. By this, the question of homogeneity/inhomogeneity of predictor characteristics and efficacy criteria was tested.

For a more sophisticated comparison of treatment response to antidepressants a matched subgroup of patients treated with psychotherapy alone or with psychotherapy and antidepressants was compared with respect to the primary efficacy criteria. The matching criteria were: age, sex, duration of former inpatient treatment and IMPS superfactor at admission. The same comparison was calculated for a subgroup of patients who were treated with antidepressants in addition to psychotherapy for more than 3 weeks ($n = 26$). The differences were tested by a non-parametrical U-test.

Results

The following presentation of the predictors is restricted to a significant correlation ($P < 0.01$) between predictor variables and the three primary efficacy criteria. The other results will be mentioned only if they proved to be of particular interest. In the tables only those relationships between predictor variables and efficacy criteria

Table 1. Significant anamnestic predictors ($P < 0.01$); * by cross-validation significant correlation confirmed ($P < 0.05$)

	Poor outcome after 3 weeks (retrospective)	AMS after 3 weeks (self-rating)	IQ – AMS after 3 weeks	AMS after 6 weeks (self-rating)	IQ – AMS after 6 weeks	Duration of hospital stay (days)	AMS at discharge (self-rating)	IQ – AMS at discharge	Depressivity (PD-S) at discharge (self-rating)	IQ – Depressivity (PD-S) at discharge	Poor outcome at discharge	ANX (IMPS) at discharge	IQ – ANX (IMPS) at discharge	Superfactor “depressive-apathetic syndrome” (IMPS) at discharge	IQ – Superfactor “depr.-apathetic syndrome” (IMPS) at discharge
Frequent leadership in adolescence (Goldstein Scale)						–29* (134)									
Poor heterosexual relationship (Phillips Scale)						0.22 (133)									
Age at index admission (years)						–0.25 (134)									
Frequent change of jobs prior to index admission											0.24 (134)				
Number of previous depressive episodes	0.24 (133)														
Poor social adaptation in the year prior to index admission														0.23 (134)	
Duration of depressive episodes prior to index admission												0.24 (134)			

AMS = Adjective Mood Scale; IQ = Improvement Quotient; PD-S = Paranoid-Depression Scale; IMPS = Inpatient Multidimensional Psychiatric Scale; ANX = Depressive syndrome

Table 2. Self-rated premorbid personality: significant predictors ($P < 0.01$); * by cross-validation significant correlation confirmed ($P < 0.05$)

	Poor outcome after 3 weeks (retrospective)	AMS after 3 weeks (self-rating)	IQ – AMS after 3 weeks	AMS after 6 weeks (self-rating)	IQ – AMS after 6 weeks	Duration of hospital stay (days)	AMS at discharge (self-rating)	IQ – AMS at discharge	Depressivity (PD-S) at discharge (self-rating)	IQ – Depressivity (PD-S) at discharge	Poor outcome at discharge	ANX (IMPS) at discharge	IQ – ANX (IMPS) at discharge	Superfactor “depressive-apathetic syndrome” (IMPS) at discharge	IQ – Superfactor “depr.-apathetic syndrome” (IMPS) at discharge
Anancasm (AHOS)		0.24 (125)		0.27 (97)			0.24 (123)								
Orality (AHOS)				0.31 (102)					0.32* (115)						
Orality (AHOSS)		0.27 (125)		0.38* (97)			0.24 (123)		0.39* (110)						
Neuroticism (ENR)				0.30 (102)											
Neuroticism (AHOS)		0.29* (131)		0.37 (102)					0.31* (115)						
Neuroticism (AHOSS)		0.29 (125)		0.38* (97)					0.30 (110)						
Schizoidism (Sc)		0.29* (130)		0.28 (101)											
“Typus melancholicus” (Sc)				–0.28 (101)											
Unassertiveness (PPI)						0.26 (127)	0.28 (125)	–0.23 (124)	0.35 (113)						
Schizoidism (PPI)									0.26 (113)						

AMS = Adjective Mood Scale; IQ = Improvement Quotient; PD-S = Paranoid-Depression Scale; IMPS = Inpatient Multidimensional Psychiatric Scale; ANX = Depressive syndrome; AHOS = Anancasm-Hysteria-Orality-Scale; AHOSS = Parallel form of AHOS; ENR = Extraversion-Neuroticism-Rigidity-Scale; Sc = Schizoidism-Scale; PPI = Premorbid-Personality Inventory

Table 3. Psychopathological syndromes and self-rating data at admission: significant predictors ($P < 0.01$); * by cross-validation significant correlation confirmed ($P < 0.05$)

	Poor outcome after 3 weeks (retrospective)	AMS after 3 weeks (self-rating)	IQ – AMS after 3 weeks	AMS after 6 weeks (self-rating)	IQ – AMS after 6 weeks	Duration of hospital stay (days)	AMS at discharge (self-rating)	IQ – AMS at discharge	Depressivity (PD-S) at discharge (self-rating)	IQ – Depressivity (PD-S) at discharge	Poor outcome at discharge	ANX (IMPS) at discharge	IQ – ANX (IMPS) at discharge	Superfactor “depressive-apathetic syndrome” (IMPS) at discharge	IQ – Superfactor “depressive-apathetic syndrome” (IMPS) at discharge
Superfactor “depr.-apathetic syndrome” (IMPS) at admission													0.47* (134)	0.23* (134)	0.50* (134)
ANX at admission (IMPS)													0.53* (133)		0.51* (134)
RET at admission (IMPS)													0.23 (133)	0.29 (134)	0.28* (134)
IMF at admission (IMPS)															0.27 (134)
AMS at admission		0.35* (132)	0.56* (131)	0.36 (102)	0.50* (102)		0.34* (131)	0.33 (131)	0.28 (116)						
Depressivity (PD-S)		0.30 (127)		0.41* (99)					0.28 (111)	0.43* (118)					
Paranoid (PD-S)									0.30 (113)						
AMS after 3 weeks				0.79* (103)		0.27* (134)	0.62* (113)		0.42* (116)		0.25* (133)	0.33* (133)	0.24* (133)	0.29* (133)	-0.24* (133)
IQ – AMS after 3 weeks				-0.33* (103)	0.85* (103)										

AMS = Adjective Mood Scale; IQ = Improvement Quotient; PD-S = Paranoid-Depression Scale; IMPS = Inpatient Multidimensional Psychiatric Scale; ANX = Depressive syndrome; RET = Retardation syndrome; IMF = Impaired functioning

are shown for which at least one significant correlation was found.

Only one variable of the sociodemographic characteristics demonstrated a prognostic relationship to the outcome criteria: age at admission was negatively correlated with the duration of hospital stay ($r = -0.25$). Also the scales of premorbid social adjustment were disappointing under prognostical aspects. Only one item of the Goldstein Scale – frequent leadership in adolescence – was negatively correlated with the hospital stay ($r = -0.29$) and one item – poor heterosexual relationship – of the Phillips Scale was correlated with the hospital stay ($r = 0.22$) (Table 1).

Of the numerous premorbid personality dimensions tested in the study, only one – the unassertiveness of the PPI – demonstrated a prognostical relevance with the duration of hospital stay ($r = 0.26$). It was also significantly related to the self-rated mood score and depression score at discharge. All other self-evaluation personality dimensions were only correlated to self-rated mood or depression scores, but not to the outcome criteria rated by the doctor (Table 2).

The depression-related IMPS factor scores at admission demonstrated almost a close relationship to the

amelioration score of the IMPS superfactor “depressive-apathetic syndrome” ($r = 0.27-0.51$), in case of the superfactor “depressive-apathetic syndrome” and the syndrome “retardation” also with the superfactor syndrome itself at discharge ($r = 0.29$), not with the duration of hospital stay. The best correlations concerning a main outcome criterion were found between the superfactor “depressive-apathetic syndrome” or the depressive syndrome, respectively, at admission and the improvement quotient for the IMPS superfactor “depressive-apathetic syndrome” at discharge ($r = 0.51!$) (Table 3). It is interesting that none of these three characteristics correlated with the self-evaluated efficacy criteria. Conversely, also self-evaluated depressivity (PD-S) and mood disturbance (AMS) at admission showed almost no correlation with depressive scores evaluated by experts at discharge. There were a number of correlations among the self-evaluated depressivity and mood parameters, to the effect that a high admission score for particular characteristics was related to a higher score for the same characteristics after 3 and/or 6 weeks and at the time of discharge as well as to greater improvement at the respective time.

There were many correlations between the mood score after 3 weeks and various outcome criteria. The AMS

Table 4. Significant predictors of the Strauss-Carpenter-Scale ($P < 0.01$); * by cross-validation significant correlation confirmed ($P < 0.05$)

	Poor outcome after 3 weeks (retrospective)	AMS after 3 weeks (self-rating)	IQ - AMS after 3 weeks	AMS after 6 weeks (self-rating)	IQ - AMS after 6 weeks	Duration of hospital stay (days)	AMS at discharge (self-rating)	IQ - AMS at discharge	Depressivity (PD-S) at discharge (self-rating)	IQ - Depressivity (PD-S) at discharge	Poor outcome at discharge	ANX (IMPS) at discharge	IQ - ANX (IMPS) at discharge	Superfactor "depressive-apathetic syndrome" (IMPS) at discharge	IQ - Superfactor "depressive-apathetic syndrome" (IMPS) at discharge
No useful occupation in the year prior to index admission															-0.25* (134)
Occupational incompetence in the year prior to index admission	0.26 (134)														
Low social class	0.24 (134)														
Family history of psychiatric hospitalization											0.26 (132)				
Duration of psychiatric hospitalization									0.25 (117)						
Duration of longest period with mild depressive symptoms (days)												0.25 (134)			
Empty life in the year prior to index admission														0.23 (134)	
Score sum of the Strauss-Carpenter-Scale														0.23 (131)	

AMS = Adjective Mood Scale; IQ = Improvement Quotient; PD-S = Paranoid-Depression Scale; IMPS = Inpatient Multidimensional Psychiatric Scale; ANX = Depressive Syndrome

value after 3 weeks correlated significantly with the depressive-apathetic syndrome at the time of discharge ($r = 0.29$), with the depressive syndrome at discharge ($r = 0.33$), with the duration of stay ($r = 0.27$) and with different self-rated mood or depression scores, among other with the mood score (AMS) at discharge ($r = 0.62!$) and the self-rated depression score at discharge ($r = 0.42$). The improvement quotient for mood after three weeks achieved less prognostic significance, being only correlated with self-rated mood variables after 6 weeks (see Table 3).

The characteristics based on the history of illness were also disappointing with respect to prognosis. Among these items only a poor social adaptation (according to the DSM-III rating) before the beginning of the depressive episode was correlated with the principal outcome criterion, the superfactor "depressive-apathetic syndrome" of the IMPS ($r = 0.23$). A few others correlated not to a principal outcome criterion but to others: frequent change of jobs with the global judgement of a poor outcome at discharge ($r = 0.24$), number of depressive episodes with the global judgement of a poor outcome after 3 weeks ($r = 0.24$), duration of the depressive syndrome before admission to the hospital with the depressive syndrome at discharge ($r = 0.24$) (see Table 1).

The total score of the Strauss-Carpenter Scale as well as the item "no useful occupation" correlated significant-

ly with the superfactor "depressive-apathetic syndrome" ($r = 0.23$) or its improvement quotient ($r = -0.25$) at discharge. Some other items of the Strauss-Carpenter Scale demonstrated correlations with other outcome criteria but not to the principal ones (Table 4).

The orientating product-moment correlation analysis revealed but few prognostically relevant relationships between the various predictor variables and primary efficacy criteria. In the face of the large number of correlations calculated, those few significant correlations which did result must be regarded critically with respect to their possibly being chance phenomena. The results of the cross-validation were even more disappointing, even though the necessary significance level was reduced to $P < 0.05$. With respect to the principal outcome criteria only the following characteristics proved as being prognostically relevant: frequent leadership during adolescence, no useful occupation in the year before index admission, IMPS factor "depressive-apathetic syndrome", IMPS factor "depressive syndrome", IMPS factor "retardation", IMPS factor "impaired functioning", self-rated mood score (AMS) after 3 weeks. If the restriction regarding only significant correlations with the primary efficacy criteria was removed, and all prognostic correlations between potential predictor variables and efficacy criteria which have been confirmed by cross-validation were accepted, as expected, a larger number of prognos-

Table 5. Predictors which were confirmed by cross-validation

Predictor variables (all efficacy criteria considered)	Predictor variables (only primary efficacy criteria considered)
– Frequent leadership in adolescence	– Frequent leadership in adolescence
– No useful occupation in the year prior to index admission	– No useful occupation in the year prior to index admission
– Self-rated mood score (AMS) at admission	– Self-rated mood score (AMS) after three weeks
– Self-rated depression score (PD-S) at admission	– Superfactor “depressive- apathetic syndrome” at admission
– Self-rated mood score (AMS) after three weeks	– IMPS factor “depressive syndrome”
– Orality	– IMPS factor “retardation”
– Neuroticism	– IMPS factor “impaired functioning”
– Schizoid personality traits	
– Superfactor “depressive- apathetic syndrome” at admission	
– IMPS factor “depressive syndrome”	
– IMPS factor “retardation”	
– IMPS factor “impaired functioning”	

tically relevant characteristics resulted (Table 5). The best predictors with respect to outcome were the superfactor “depressive-apathetic syndrome” and the “depressive syndrome” at admission.

Comparing patients with ($n = 48$) and without antidepressant treatment ($n = 86$) few differences were found: the syndrome “retardation” and the self-rated depression score (79 vs 61) at admission were higher in the group treated with antidepressants ($P < 0.01$ and $P < 0.05$, respectively). At discharge no difference could be found between the two groups.

After matching the patients with respect to age, sex, duration of former inpatient treatment and depressive-apathetic syndrome at admission, again the syndrome “retardation” (54 vs 41) and the self-rated depression score (51 vs 37) were statistically significantly different ($P < 0.05$). All outcome criteria were without significant differences between the two groups. Taking into account only the patients who have been treated at least 3 weeks with antidepressants and a matched control-group ($n = 26$) again the same differences regarding the syndrome “retardation” (32 vs 21) and the self-rated depression factor (27 vs 20) were found ($P < 0.01$ or $P < 0.05$, respectively). With respect to outcome the group treated with antidepressants had a longer duration of hospital stay (31 vs 22 days; $P < 0.05$).

Discussion

Although a large number of potential predictors have been tested, only a few proved to have prognostical im-

portance. The findings of the study were thus disappointing, especially if only the results of the cross-validation are considered. Several predictors described in the literature could not be reproduced with respect to the primary efficacy criteria. The discrepancy between the number of significant correlations in the primary analysis and the number of significant results in the cross-validation analysis underlines the well-known fact that results of predictor analyses are very unstable and therefore have to be confirmed in several cross-validation studies before they can be accepted as realistic. A similar statement holds true with respect to the outcome criteria. If we do not restrict our findings on significant correlations between potential predictor variables and the three principal outcome criteria but taking also into consideration the other outcome criteria, many more predictors can be described. A certain specificity between predictors and corresponding outcome criteria can be observed and one should differentiate between almost global predictors and corresponding global outcome criteria and more specific predictors which tend to have a closer relationship to corresponding outcome criteria, but not to outcome criteria in another field: e.g., psychopathological data seem to have a closer connection with themselves than with data on social functioning. A similar conclusion can be drawn concerning the relationship of observer-rating data and self-rating data.

In general, these experiences are in agreement with findings or other predictor studies in different fields (Angst 1965; Ananth 1978; Bielski and Friedel 1976; Woggon 1983; Strauss and Carpenter 1974).

If we consider only the findings of the cross-validation analysis with respect to the primary outcome criteria only the following characteristics were described as predictors: frequent leadership in adolescence, no useful occupation in the year before index admission, intensity of depressive symptoms at admission and self-rated mood disturbances after 3 weeks of treatment. The tendency of the prognosis was in general plausible and in accordance with the findings in the literature: leadership in adolescence as sign of a good premorbid functioning and greater intensity of depressive symptoms at admission as indicator of a clear depressive psychopathology proved to be predictors for a favorable outcome; the lack of useful occupation in the year before index admission as indicator of a bad premorbid adjustment or as a sign of a disturbance of social functioning secondary to a more chronic depressive disorder, and the degree of self-rated mood disturbance after 3 weeks of treatment as sign of a poor treatment result in the first part of the treatment period, came out as predictors for an unfavorable outcome.

In general, the correlation coefficients were quite low, only explaining 10% of the outcome variance. The best predictor were the superfactor “depressive-apathetic syndrome” and the “depressive syndrome” at admission which correlated with the improvement quotient of the IMPS superfactor “depressive-apathetic syndrome” at a level of about 0.50.

In contrast to our former findings with respect to intervention-related predictor variables like the self-rated mood disturbances after 3 weeks in endogenous depres-

sives (Möller et al. 1987), in this study on neurotic-depressive patients the self-rated mood disturbances after 3 weeks were not of such an important predictive relevance. This might be explained by the fact that the self-rating of neurotic-depressive patients is quite insensitive to treatment changes as compared to the observer-rating (Möller 1990).

It was astonishing that the dimensions of premorbid personality, mostly considered as very important for the characteristics of neurotic patients and their treatment outcome, which were very carefully investigated in this study, could not demonstrate prognostical implications. This might be explained by the hypothesis that such a sample of neurotic-depressive inpatients is much more homogeneous with respect to neurotic traits of premorbid personality than a mixed sample of major depressive disorders, which is composed by subgroups of patients with more neurotic traits in their personality and others without such traits. The prognostic relevance of personality traits might be greater in such a composite sample.

A subgroup of patients ($n = 48$) was treated in addition to the cognitive behaviour therapy with antidepressants according to the indication by the doctor in charge of the patient. These patients are characterized by a higher intensity of apathetic symptoms and of self-rated depression at admission. At discharge this difference was not more evident. It is difficult to answer from such findings of a naturalistic study the question whether the combined therapy leads to better results than cognitive behaviour therapy alone. Apparently, patients treated additionally with antidepressants reached a better degree of improvement between admission and discharge, but on the other hand not a better psychopathological state at discharge. Unfortunately, the results of empirical studies reviewed by Conte et al. (1986) also do not give a clear answer to the question whether the combination of psychotherapy and antidepressants is superior to each treatment strategy alone. A critical point, especially concerning neurotic depressives, might be that only patients suffering from a certain intensity of depression respond to antidepressants (Paykel et al. 1988). Apart from this discussion, the fact that in general not only endogenous depressives, but also neurotic depressives respond to antidepressants seem well established now (Covi et al. 1974, Klerman et al. 1974, Prusoff et al. 1980).

From a general viewpoint, the similarity between the prediction of treatment response in endogenous depression (Möller et al. 1987) and neurotic depression is remarkable. This could lead to the interpretation that traditional categorical subdivision of functional depressive states into an endogenous and a neurotic type seems not meaningful when seeking predictors.

An inherent problem of the study was that the primary efficacy criteria could not be established for a fixed time interval relative to the start of therapy; rather, the time interval varied according to the time of individual patient's discharge, which besides being variable in itself is also influenced by many other factors, not the least of which is improvement in or the reduction of the number of symptoms. On the other hand, the procedure in this form does full justice to the demand for predictors of in-

adequate therapy results under routine treatment conditions, thus opening up the possibility of adjusting the duration of treatment to the individual circumstances.

Additionally, it can be regarded as a methodological failing of the study that a portion of the predictor variables were established retrospectively from patients' records. However, the definite advantages offered by the present method in comparison with other investigations dealing with predictors should not be overlooked: the relatively high number of cases in the series examined, the multitude of predictor characteristics analysed, the largely standardized evaluation of characteristics, the multiple evaluation of efficacy by means of various criteria, and the cross-validation of the results.

References

- Abraham HC, Kanter VB, Rosen I, Standen JL (1963) A controlled clinical trial of imipramine (Tofranil) with outpatients. *Br J Psychiatry* 109:286-293
- Ananth J (1978) Clinical prediction of antidepressant response. *Int Pharmacopsychiatr* 13:69-93
- Angst J (1965) Zur Prognose antidepressiver Behandlungen. *Anglo-Germ Med Rev* 2:733-751
- Avery DH, Wilson LG, Dunner DL (1983) Diagnostic subtypes of depression as predictors of therapeutic response. In: Clayton PJ, Barret JE (eds) *Treatment of depression: old controversies and new approaches*. Raven Press, New York, pp 193-205
- Barthelmes H, Zerssen D v (1978) Das Münchner Psychiatrische Informationssystem (PSYCHIS München). In: Reichertz P, Schwarz E (eds) *Informationssysteme in der medizinischen Versorgung, Ökologie der Systeme*. Schattauer, Stuttgart, pp 138-145
- Baumann U, Seidenstücker G (1977) Zur Taxonomie und Bewertung psychologischer Untersuchungsverfahren bei Psychopharmakapfahrungen. *Pharmakopsychiatr* 10:291-331
- Bielski RJ, Friedel O (1976) Prediction of tricyclic antidepressant response. A critical review. *Arch Gen Psychiatry* 33:1479-1489
- Clancy J, Noyes R, Hoenk PR, Slymen DJ (1978) Secondary depression in anxiety neurosis. *J Nerv Ment Dis* 166:846-850
- Conte HR, Plutchik R, Wild KV, Karasu TB (1986) Combined psychotherapy and pharmacotherapy for depression. A systematic analysis of the evidence. *Arch Gen Psychiatry* 43:471-479
- Covi L, Lipman RS, Derogatis LR, Smith III JE, Pattison JH (1974) Drugs and group psychotherapy in neurotic depression. *Am J Psychiatry* 131:191-198
- De Jong R (1986) Das Ansprechen auf verhaltenstherapeutisch-kognitive Behandlung bei Untergruppen depressiver Patienten mit einer ungünstigen Prognose. *Verhaltensmodif* 7:152-168
- De Jong R (1987) Neurotische Depression und psychologische Therapie. Lang, Frankfurt
- De Jong R, Treiber R, Henrich G (1986) Effectiveness of two psychological treatments for inpatients with severe and chronic depression. *Cogn Ther Res* 10:645-663
- Deykin EY, DiMascio A (1972) Relationship of patient background characteristics to efficacy of pharmacotherapy in depression. *J Nerv Ment Dis* 155:209-215
- Downing RW, Rickels K (1972) Predictors of amitriptyline response in outpatient depressives. *J Nerv Ment Dis* 154:248-263
- Ernst K, Ernst C (1968) *Ergebnisse der Verlaufsforschung bei Neurosen. Eine vergleichende Literaturübersicht*. Springer, Berlin Heidelberg New York
- Fennell MJV, Teasdale JD (1982) Cognitive therapy with chronic, drug refractory depressed outpatients: A note of caution. *Cogn Ther Res* 6:455-460

- Friedman C, DeMowbray MS, Hamilton V (1961) Imipramine (Tofranil) in depressive states. *J Ment Sci* 107:948–953
- Gittelman-Klein R, Klein D (1969) Premorbid asocial adjustment and prognosis in schizophrenia. *J Psychiatr Res* 7:35–53
- Greer HS, Cawley RH (1966) Some observations on the natural history of neurotic illness. *Archdall Medical Monograph*, No 3. Australasian Medical Publishing, Sidney
- Guy W (1976) Clinical Global Impressions (CGI). In: Guy W (ed) ECDEU assessment manual for psychopharmacology. Rockville, Maryland, pp 217–222
- Harris JG (1975) An abbreviated form of the Phillips rating scale of premorbid adjustment in schizophrenia. *J Abnorm Psychol* 84:129–137
- Hiller W, v Zerssen D, Mombour W, Wittchen HU (1986) Die IMPS. Beltz, Weinheim
- Kerr TA, Roth M, Schapira K, Gurney C (1972) The assessment and prediction of outcome in affective disorders. *Br J Psychiatry* 121:167–174
- Klerman GL, DiMascio A, Weissman M, Prusoff B, Paykel ES (1974) Treatment of depression by drugs and psychotherapy. *Am J Psychiatry* 131:186–191
- Kiloh LG, Ball JR, Garside RF (1962) Prognostic factors in treatment of depressive states with imipramine. *BMJ* II:1225–1227
- Kupfer DJ, Spiker DG (1981) Refractory depression: prediction of non-response by clinical indicators. *J Clin Psychiatry* 42:307–311
- Lorr M (1974) Assessing psychotic behaviour by the IMPS. In: Pichot P, Olivier R (eds) Psychological measurement in psychopharmacology (Modern problems in pharmacopsychiatry, vol 7). Karger, Basel, pp 50–63
- Möller HJ (1990) Möglichkeiten und Grenzen von Selbstbeurteilungsskalen zur Verlaufsbeurteilung depressiver Symptomatik im Rahmen der Therapie-Evaluation. In: Baumann U, Fährdrich E, Stieglitz R-D, Woggon B (eds) Veränderungenmessung in Psychiatrie und Psychologie. Theoretische, methodische und empirische Beiträge. Profil, München, pp 307–328
- Möller HJ, Barthelmes H, Zerssen D v (1983) Forschungsmöglichkeiten auf der Grundlage einer routinemäßig durchgeführten psychiatrischen Basis- und Befunddokumentation. *Psychiatr Clin* 16:45–61
- Möller HJ, Fischer G, v Zerssen D (1987) Prediction of therapeutic response in acute treatment with antidepressants. Results of an empirical study involving 159 endogenous depressive inpatients. *Eur Arch Psychiatr Neurol Sci* 236:349–357
- Moore H, Kleining G (1960) Das soziale Selbstbild der Gesellschaftsschichten in Deutschland. *Kölner Z Soziol Sozialpsychol* 12:86–119
- Paykel ES, Prusoff BA, Klerman GI, Haskell D, DiMascio A (1973) Clinical responses to amitriptyline among depressed women. *J Nerv Ment Dis* 156:149–165
- Paykel ES, Freeling P, Hollyman JA (1988) Are tricyclic antidepressants useful for mild depression? A placebo controlled trial. *Pharmacopsychiatry* 21:15–18
- Prusoff BA, Weissman MM, Klerman GL, Rounsaville BJ (1980) Research diagnostic criteria. Subtypes of depression. *Arch Gen Psychiatry* 37:796–801
- Raskin A, Crook TH (1976) The endogenous-neurotic distinction as a predictor of response to antidepressant drugs. *Psychol Med* 6:59–70
- Rose JT, Westhead TT (1967) Treatment of depression. A comparative trial of imipramine and desimipramine. *Br J Psychiatry* 113:659–665
- Strauss JS, Carpenter WT (1974) Prediction of outcome in schizophrenia. II. Relationship between predictor and outcome variables. *Arch Gen Psychiatry* 31:37–42
- Wechsler D (1964) Die Messung der Intelligenz Erwachsener. Hamburg-Wechsler-Intelligenz-Test für Erwachsene (HAWIE). 3. Aufl., Huber, Bern
- Weissman MM, Prusoff MA, Klerman GL (1978) Personality and the prediction of long-term outcome of depression. *Am J Psychiatry* 135:797–800
- Wittenborn JR, Kiremitci N (1975) A comparison of antidepressant medications in neurotic and psychotic patients. *Arch Gen Psychiatry* 32:1172–1176
- Woggon B (1980) Veränderungen der psychopathologischen Symptomatik während 20tägiger antidepressiver oder neuroleptischer Behandlung. *Psychiatr Clin* 13:150–164
- Woggon B (1983) Prognose der Pharmakotherapie. Klinische Untersuchungen zur Voraussagbarkeit des Kurzzeitherapieerfolges von Neuroleptika und Antidepressiva. Enke, Stuttgart
- Zerssen D v (unter Mitarbeit von Koeller D-M) (1976) Klinische Selbstbeurteilungsskalen (KSb-S) aus dem Münchner Psychiatrischen Informationssystem (PSYCHIS München). a) Allgemeiner Teil; b) Paranoid-Depressivitäts-Skala; c) Befindlichkeits-Skala; d) Beschwerden-Liste. Beltz, Weinheim
- Zerssen D v (1980) Psychopathometrische Verfahren und ihre Anwendung in der Psychiatrie. In: Peters U-H (ed) Die Psychologie des 20. Jahrhunderts, Bd. X. Kindler, Zürich, pp 149–169
- Zerssen D v (1982) Personality and affective disorders. In: Paykel ES (ed) Handbook of affective disorders. Livingston, Edinburgh, pp 212–228
- Zerssen D v (1986) Clinical self-rating scales (CSRS) of the Munich psychiatric information system (PSYCHIS München). In: Sartorius N, Ban TA (eds) Assessment of depression. Springer, Berlin Heidelberg New York, pp 270–303
- Zerssen D v, Cording C (1978) The measurement of change in endogenous affective disorders. *Arch Psychiatr Nervenkr* 226:95–112
- Zerssen D v, Pfister H, Koeller D-M (1988) The Munich Personality Test (MPT) – a short questionnaire for self-rating and relatives' rating of personality traits: formal properties and clinical potential. *Eur Arch Psychiatr Neurol Sci* 238:73–93