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Depressive Syndromes in Schizophrenic Patients after Discharge from Hospital

B. Bandelow, P. Müller, W. Gaebel, W. Köpcke, M. Linden, F. Müller-Spahn, A. Pietzcker, F. M. Reischies, and J. Tegeler – ANI Study Group Berlin, Düsseldorf, Göttingen, Munich

Department of Psychiatry, University of Göttingen, von-Siebold-Strasse 5, W-3400 Göttingen, Federal Republic of Germany

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Summary. A total of 364 schizophrenic outpatients who were stabilized for 3 months on continuous neuroleptic therapy after discharge from the hospital were rated according to three different scales for depressive syndromes (Brief Psychiatric Rating Scale anxious depression factor, AMDP/depression, and the self-rating PD-S depression scale). Between 19.5% and 27.5% of the patients were rated as depressed, or 35.7%–42.8%, when mild depressive syndromes were included. There were low, but significant correlations between demographic or life-event data and depression scores on the self-rating scale, whereas fewer correlations were found on the observer ratings. No associations were found between social adjustment and depression. Moderate correlations were found between measures of the apathetic syndrome and depression ratings, while observer ratings showed higher correlations than the self-rating. High depression scores, especially in the observer ratings, correlated with scales for global psychopathological assessment (CGI, GAS). There were significant correlations between extrapyramidal rigidity and observer rating depression scores, whereas the total amount of neuroleptics given had no influence. These results are interpreted on the basis of hypotheses about depressive syndromes in schizophrenia.

Key words: Schizophrenia – Depression – Neuroleptics

Introduction

Suicide is common in schizophrenia [1, 2, 9, 14, 39, 50, 56, 67] and may be due not only to the influence of auditory hallucinations, but also to depression. Depressive syndromes may occur in every phase of schizophrenic disease: in the foreground of acute psychosis, during inpatient treatment and in the post-remission phase. The origin of these syndromes is still unclear. The following hypotheses about their aetiology can be differentiated.

Offprint requests to: B. Bandelow

In the "natural course" hypothesis, depressive syndromes are considered to occur during the natural course of a schizophrenic episode – independently of drug therapy. Bleuler [10], Conrad [11] and Kraepelin [33] described these symptoms long before the neuroleptic era. In a recent view of depressive syndromes, Bartels and Drake [3] found that depression in schizophrenia is not a favourable sign of beginning remission, but rather is associated with an increased relapse rate or longer duration of hospitalization. Barnes et al. [2] showed that a greater number of auditory hallucinations were accompanied by higher depression scores in their study.

The "revealed depression" hypothesis postulates that depressive syndromes may accompany an acute psychotic episode, but are not revealed before remission of the acute episode [25]. 'Postpsychotic depression' might represent an already existing symptom complex that remits more slowly than the acute psychosis [38]. Some authors showed a decrease rather than an increase in depression scores when depression was investigated before and after a psychotic episode treated with neuroleptics [13, 27, 32, 40–42, 66].

In the "understandable reaction" hypothesis, described by McGlashan and Carpenter [38], it is assumed that postpsychotic depression may occur as a reaction to being ill, when insight returns during recovery from psychosis. Salama [56], investigating suicide among schizophrenic patients, had the feeling that depression was related to the patients' despair about their chronic disabling illness. Roy [55] found more unfavourable life events in the 6 months before the onset of depression. On the other hand, Johnson [30] found no correlation between depression and life events.

In the "wrong diagnosis" hypothesis it is assumed that presence of depressive symptoms calls the diagnosis of schizophrenia itself into question [14, 19]. Some authors included schizoaffective patients in their investigations about depression in schizophrenia [56].

A "coincidence by chance" hypothesis may be considered, because depression and schizophrenia could

occur together merely as a matter of chance. The lifetime risk of either depression or schizophrenia is high [21, 57], but the statistical probability that both diseases occur in the same period of time is very low [32].

The "negative symptoms" hypothesis maintains that the so-called depressive symptoms in the remission period are in fact negative symptoms like flatness of affect, psychomotor retardation, lethargia, lack of motivation, anhedonia [61]. Heinrich mentioned this possibility as early as 1967 [23]. McGlashan [37] coined the expression "aphanisis" for a pseudo-depressed syndrome more similar to the negative syndrome than to depression. House et al. [27] found that negative syndromes could be distinguished from depression. Barnes et al. [2] found no correlation between negative symptoms and the MADRS or the Beck Depression Inventory. In an investigation by Prosser et al. [51], only nonspecific items of the Hamilton Depression Scale showed an overlap with negative symptoms (decreased work and activities, motor retardation, and decreased libido).

The "pharmacogenic depression" hypothesis assumes that neuroleptic medication is responsible for the depressive syndromes. Early observations by Helmchen and Hippius [24] or Heinrich [23] pointed out this possibility. Other authors found no correlation between neuroleptic dose and depression [2]. Berrios and Bulbena [8] found that depot neuroleptic medication does not seem to be a significant factor in the precipitation of postpsychotic depression in a 10-year follow-up. The three double-blind studies on this issue show diverging results. Hogarty and Munetz [26] found no differences in the depression scores after chlorpromazine and placebo. Müller [43] found depressive syndromes in 19 of 25 (76%) neuroleptic-treated patients and only in 3 of 25 patients of the placebo control group (25%). Wistedt [72] found more depression in 6 non-remitted placebo patients than in 16 non-remitted neuroleptic-treated patients.

The "akinetic depression" hypothesis was coined when positive correlations were found between depression ratings and akinesia as a part of neuroleptic-induced parkinsonism [54, 69]. A mere statistical correlation between parkinsonism and depression could have two reasons. First, depression could be a real toxic drug effect, mediated by the blockade of dopaminergic receptors in the nigrostriatal system. Depression is common in patients with Parkinson's disease [28, 36]. Second, depression as observed by the psychiatrists could be a misinterpretation of akinesia. This may be named the "akinetic pseudo-depression" hypothesis. Some authors found no significant correlation between parkinsonism and depression [2, 30, 35]. House et al. [27] found that depressive syndromes can be reliably separated from akinesia and clinical poverty.

Because aetiological considerations show diverging results, it is not surprising that very controversial statements have been made about the frequency of depressive syndromes. Frequency data fluctuated between 0 and 76% [44], with an average of about 25%. Different depression scales were used and the cut-off scores for depression differ from scale to scale.

There are controversial opinions about the symptomatology of secondary depression. Becker et al. [6] found a symptom complex in secondary depression in schizophrenia which was separable from primary depression, whereas Weissman et al. [71] were not able to find differences in symptomatology.

Depending on their opinion about the origin of depression in schizophrenia, the authors made different recommendations about the treatment of these syndromes. Antidepressants were used by Siris and coworkers [59–62, 64] and Johnson [29], while some authors see the danger of exacerbations of hallucinatory symptoms or thinking disturbances by antidepressants [22, 34, 52]. Neuroleptics alone were used by Becker et al. [4, 5]. In Becker's opinion, the addition of antidepressants to the neuroleptic medication does not appear to enhance therapeutic efficacy [7]. Lithium was used in a small sample [68]. Fähndrich [16] recommended sleep deprivation. Following the "akinetic" or "pharmacogenic" depression hypothesis, many authors used anticholinergics [2, 17, 31, 35, 43, 53, 59] with diverging results. Müller [43] recommended reduction of neuroleptics.

In a German multicentre study concerning relapse prevention (psychiatric hospitals of the universities of Berlin, Düsseldorf, Göttingen, Munich) the effects of three different treatment strategies for remitted schizophrenic patients are being investigated. In the first therapy strategy, continuous neuroleptic medication is given in all cases. In the second strategy, neuroleptics are discontinued after stabilization and restarted only when a complete relapse occurs. In the third strategy (early intervention) neuroleptic treatment is discontinued and resumed as soon as the slightest prodromal syndromes of a relapse occur [49].

So far, only preliminary results are available about the outcome of the study, which will be carried out in a 2-year follow-up design. Three hundred and sixty-five patients admitted to the above-mentioned psychiatric wards in an acute psychotic episode were discharged to outpatient treatment. After a stabilization period of 3 months under neuroleptic treatment, a number of investigations were performed, including rating scales for depression. These data make it possible to draw conclusions about the above-mentioned hypotheses. In this preliminary publication, results of the investigations 3 months after discharge from hospital are discussed. The results after a 2-year follow-up will be published in a subsequent paper.

Method

Details of the design of the German multicentre study on neuroleptic continuation therapy have been reported elsewhere [49]. Three-hundred and sixty-five patients diagnosed as schizophrenics according to ICD 9 and RCD criteria were derived from a series of patients admitted to the centres in Berlin, Düsseldorf, Göttingen and Munich for inpatient treatment and passed through a 3-month stabilization phase (outpatient treatment). All patients were treated with neuroleptics (haloperidol, fluphenazine, perazine, clozapine, benperidol, thioridazine, levomepromazine)

or depot neuroleptics (fluphenazine decanoate, flupenthixol decanoate, fluspirilene, haloperidol decanoate, perphenazine enanthate). Only biperiden was allowed as antiparkinson medication. Patients with a diagnosis of schizoaffective psychosis, according to ICD 9 or RDC criteria, were excluded from the study of depressive symptoms. Assessment took place after a 3-month stabilization phase on neuroleptics.

First Set of Variables. Among many other ratings, the following assessments were made concerning depressive syndromes in psychotic patients: (1) the BPRS factor anxious depression [46, 47], consisting of the items somatic concern, anxiety, guilt feelings, and depression; (2) the AMDP factor "depressive syndrome" (Arbeitsgemeinschaft für Methodik und Dokumentation in der Psychiatry – Assessment and Documentation of Psychopathology [18, 20, 48], consisting of the items worrying, feeling of loss of feeling, loss of vitality, depressed mood, hopelessness, self-depreciation, feeling of guilt, motor retardation, morning worst, interrupted sleep, shortened sleep, early waking, and appetite loss; (3) the D-scale of the PD-S (Paranoid Depression Scale) [70], a self-rating scale for the assessment of anxious/depressed mood. The results of these assessments were compared with the second set below.

Second Set of Variables. (1) Demographic data and life events (AMDP [20]); (2) AMDP factors "paranoid-hallucinatoric", "psychoorganic", "manic", "hostile", "autonomic", "apathic", "obsessive" [18]; (3) BPRS factors anergia, thought disturbance, activation, hostile-suspiciousness; (4) Clinical Global Impression (CGI [45]); (6) Global Assessment Scale (GAS [15]); (7) Outcome Scale of Strauss and Carpenter [65]; (8) EPS scale (Extrapyramidal Side Effects Scale of Simpson and Angus [58]).

Table 1. Mean values of depression ratings

PD-S/D (n = 346)		
Mean	11.4	(range 0–35)[a]
Score ≥ 15	27.5%	
Score ≥ 12	42.8%	
AMDP/D T values (n = 364)		
Mean	33.4	(range 31–58)[b]
Score ≥ 48	26.6%	
Score ≥ 46	37.1%	
BPRS/AD (n = 364)		
Mean	7.06	(range 4–18)
Score ≥ 10	19.5%	
Score ≥ 8	35.7%	

[a] Mean of healthy population: 5.46; mean of average psychiatric population: 18.75 [70]

[b] Mean of average psychiatric population: 54 [48]

Results

Depressed Mood

The mean values of the three depression ratings are shown in Table 1.

PD-S_D. PD-S was standardized in a healthy population. The mean value of the investigated patients (11.3) was between the mean of healthy population (5.46) and the mean of standard population of psychiatric patients, including all diagnoses (18.75). The differences were significant (P = 0.01). Ninety-five patients (27.5%) assessed themselves as depressed in the PD-S. Including also mild depressive syndromes, 42.8% rated themselves as depressed. The frequency distribution of the depression scores is shown in Fig. 1.

$AMDP_D$. The mean score of our sample was 33.4%; 26.6% of the patients were rated as depressed by the psychiatrists, or 37.1%, when mild depressive syndromes were included.

$BPRS_{AD}$. The sample showed a mean anxious-depression score of 7.06. In this scale, 19.5% were diagnosed as depressed, or 35.7%, when mild depressive syndromes were included.

The intercorrelations between the three depression rating scales were: $PD\text{-}S_D$ with $AMDP_D$ 0.47, $PD\text{-}S_D$ with $BPRS_{AD}$ 0.45, and $AMDP_D$ with $BPRS_{AD}$ 0.69.

Demographic Data and Life Events

Tables 2 and 3 show findings concerning demographic data and a catalogue of significant life events which may

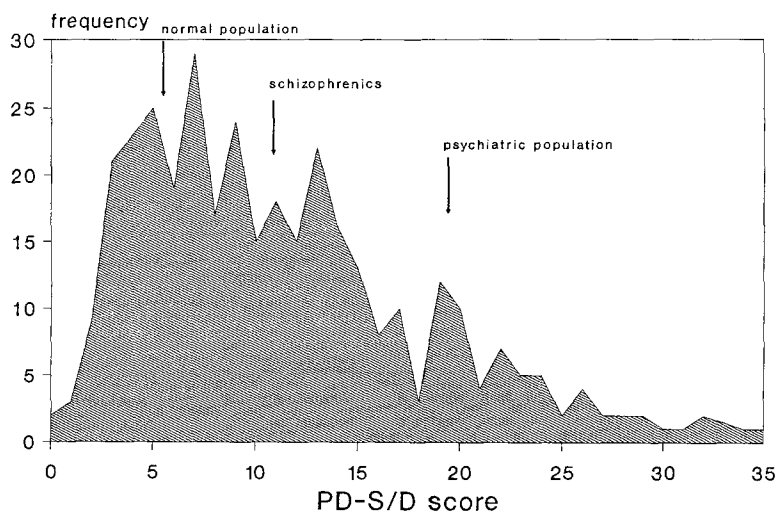

Fig. 1. Depression in schizophrenic patients (self rating)

Table 2. Demographic data (AMDP) and depression scales

	Depression scales		
	PD-S/D	AMDP/D	BPRS/AD
High depression score associated with:			
Female sex	$r = 0.23$ $P < 0.0001$	NS	NS
Marital status married	$r = 0.16$ $P < 0.007$	NS	NS
Number of children ≥ 1	$r = 0.14$ $P < 0.02$	NS	NS
High school education level	$r = 0.14$ $P < 0.05$	NS	NS
Level of employment	NS	NS	NS
Intensity of religious ties	NS	NS	NS

have occurred during the course of the patients' life. Low, but significant correlations were only found between some demographic data and the PD-S_D. Correlations with the two other scales were not significant. Almost no significant correlations could be found between the patients' life-event data and depression measured by the two observer ratings. The self-rating scale (PD-S_D) is more sensitive to the occurrence of certain life events.

Social Adaptation and Depression

The status of the patients' social adaptation 3 months after discharge from hospital, where the patients had been treated because of a psychotic episode, showed little association with depression (Table 4). The possible social sequelae of a psychotic relapse with some time spent in a psychiatric ward did not correlate with the depression scores, with one exception: the number of social contacts was positively related to the BPRS anxious-depression score, a finding which is difficult to interpret.

Apathy Syndromes and Depression

Significant, but only moderate correlations were found between rating scale factors representing the apathy syndrome, i.e. the AMDP "apathetic syndrome" factor and the BPRS anergia factor and the depression ratings. The highest correlation of 0.46 was found between the AMDP depressive syndrome factor and the apathetic syndrome factor. In the patients' ratings, this association was less marked. Only low, but still significant correlations were found between the PD-S depression dimension and the apathy factors (Table 5).

Global Severity Assessment and Depression

Moderate to marked correlations were measured between all three depression ratings and two observer rating scales for the global psychopathological assessment of the severity of illness, the CGI and the GAS (Table 6). Note that the negative correlations with the GAS score show a positive association between global severity and depression. All symptoms, including depressive symptoms, are taken into account in the

Table 3. Correlation of life events with depression scales

High depression score associated with:	Depression scales					
	PD-S/D		AMDP/D		BPRS/AD	
Death of father	$r = 0.13$	$P < 0.05$	NS		NS	
Death of mother	NS		NS		NS	
Separation/divorce of parent(s) (1 year or more)	NS		NS		NS	
Out of home (e.g. in a foster home) 1 year or more	NS		NS		NS	
Marriage	$r = 0.17$		NS		NS	
Separation/divorce from spouse	$r = 0.12$	$P < 0.01$	NS		NS	
New spouse/mate	NS	$P < 0.05$	NS		$r = 0.11$	$P < 0.05$
Birth of child	$r = 0.14$		NS		NS	
School interruption	NS	$P < 0.02$	NS		NS	
Employment discontinuation	NS		$r = 0.13$	$P < 0.03$	NS	
Job relocation	NS		NS		NS	
Job abolished	NS		$r = 0.14$	$P < 0.02$	NS	
Suicide attempt	NS		NS		NS	
Alcoholism	$r = 0.13$		NS		NS	
First manifestation of illness	NS	$P < 0.05$	NS		NS	
Developmental retardation	NS		NS		NS	
Brain injury	NS		NS		NS	
Psychiatric illness in family	$r = 0.16$		NS		$r = 0.17$	$P < 0.5$
Previous successful treatment with neuroleptics	NS	< 0.05	NS		NS	
Number of psychiotic episodes	NS		NS		NS	
Number of hospitalizations	NS		NS		NS	
Triggering events for current psychotic episode	NS		NS		NS	

Table 4. Correlation of social adaptation items with depression scales (Outcome Scale, Strauss and Carpenter 1970)

	Depression scales		
	PD-S/D	AMDP/D	BPRS/AD
High depression score associated with:			
Daily work in hours	NS	NS	NS
Duration of non-hospitalization	NS	NS	NS
Number of social contacts	NS	NS	$r = 0.18$ $P < 0.01$
Usefully employed	NS	NS	NS
Sexual adaptation	NS	NS	NS
Social adaptation	NS	NS	NS
Social class	NS	NS	NS
Total score	NS	NS	NS

Table 5. Correlation of "apathy syndromes" with depression scales

	Depression rating scales		
	PD-S/D	AMDP/D	BPRS/AD
AMDP apathetic syndrome	0.22	0.46	0.33
BPRS anergia	0.18	0.28	0.37

Table 6. Correlation of global severity assessments with depression scales

	Depression rating scales		
	PD-S/D	AMDP/D	BPRS/AD
Clinical Global Impression (severity)	0.31	0.39	0.50
BPRS anergia	0.31	0.35	0.47

psychiatrists' assessment of severity. In the item "absence of psychotic symptoms in past month" of the Outcome Scale, high correlation coefficients were found between the presence of symptoms in the last month and depression ratings (PD-S_D 0.31, $AMDP_D$ 0.34, $BPRS_{AD}$ 0.42).

Neuroleptic Treatment, Extrapyramidal Symptoms, Antiparkinson Medication and Depression

The intercorrelations between neuroleptic treatment and depression ratings are listed in Table 7. No significant correlation was found between total amount of neuroleptic dose given in the 3-month period. Likewise there was no correlation with antiparkinson medication.

Correlations of depression scales with the EPS scale are listed in Table 8. Extrapyramidal symptoms (mild to severe) were found in 45.2% of the patients. Salivation was seen in 13.5%. Of all extrapyramidal symptoms checked in the EPS scale, significant correlations were found between the two observer ratings and rigidity symptoms (gait, arm dropping, shoulder shaking, elbow

Table 7. Correlation between neuroleptic and antiparkinson (AP) treatment and depression scales

	Depression rating scales		
	PD-S/D	AMDP/D	BPRS/AD
Cumulative dose of neuroleptic	NS	NS	NS
Cumulative dose of AP medication	NS	NS	NS
Last dose of AP medication	NS	NS	NS

rigidity and wrist rigidity). Tremor correlated significantly with the AMDP depression score, but only on the EPS scale.

Tardive dyskinesia was found in 7.7% of the patients. No correlations were found between this item and depression ratings.

Discussion

This study contains only preliminary results of the German multicentre study. The origin of depressive syndromes in neuroleptic-treated schizophrenic patients remains unclear. It is possible that these symptoms represent a complex phenomenon which cannot be explained by only one of the existing hypotheses. It must always be kept in mind that the possible aetiological causes for depressive syndromes in schizophrenia can overlap, thus making for considerable confusion.

Depressed Mood

Depression in schizophrenia is not rare. Moderate to severe depression was found in 19.5–27.5% of all patients, in the observer scales as well as in the self-ratings. When mild depressive syndromes are included, the proportion of depressive syndromes after hospital admission and neuroleptic treatment was 35.7%. This is in accordance with many other authors, even when the variance is very high in the literature.

The correlations of the self-rating PD-S_D and the psychiatrists' ratings $AMDP_D$ and $BPRS_{AD}$ are only moderate, whereas the correlation between the two psychiatrists' ratings is sufficient. The lower correlation between self- and observer ratings may be due to the different forms of depression rated by these scales. In a comparison of self-report vs observer rating of depressed mood in patients with various diagnoses, Craig and van Natta [12, 53] found that schizophrenics showed no correlation on these instruments, whereas patients with other diagnoses showed significant correlations, suggesting disturbances in communication between the patient and observer in schizophrenia.

The sufficient correlation between $AMDP_D$ and $BPRS_{AD}$ shows that the depression factor of the European AMDP system can be cross-validated by the anxious depression dimension of the widely accepted BPRS scale.

Table 8. Analysis of variance: correlations of extrapyramidal symptoms with depression scales (EPS Scale, Simpson and Angus 1970)

	Frequency	Depression scales				
		PD-S/D	AMDP/D		BPRS/AD	
Gait	15.4%	NS	$u = 5276$	$P = 0.0000$	$u = 5976$	$P = 0.003$
Arm dropping	11.3%	NS	$r = 0.2$	$P = 0.0001$	$u = 4046$	$P = 0.0002$
Shoulder shaking	7.4%	NS	$r = 0.14$	$P = 0.009$	$r = 0.17$	$P = 0.0009$
Elbow rigidity	17.3%	NS	$u = 7442$	$P = 0.04$	$u = 7253$	$P = 0.02$
Wrist rigidity	12.1%	NS	$r = 0.17$	$P = 0.001$	$u = 4485$	$P = 0.0004$
Leg pendulousness	6.9%	NS	$r = 0.22$	$P = 0.0000$	$u = 2506$	$P = 0.002$
Head dropping	5.0%	NS	$r = 0.15$	$P = 0.004$	$u = 1908$	$P = 0.01$
Tremor	21.7%	NS	$r = 0.11$	$P = 0.03$	NS	
Salivation	13.5%	NS	NS	NS		
Total EPS	45.6%	NS	$r = 0.16$	$P = 0.0009$	$r = 0.29$	$P = 0.0001$

Demographic Data and Life Events

Low, but significant correlations between demographic data and depression were observed in the self-rating in some items: women reported more depression. Patients who are married, those having their own children or having a higher school education level may have suffered more distress caused by the psychotic episode, because communicative limitations were more easily noticeable by these patients. No associations were found between the psychiatrists' ratings and demographic data.

Life events do not seem to have a significant influence on the development of depression in the sample. The self-rating PD-S_D is somewhat more sensitive to the influence of life event data.

The data do not show a clear relation between depression in treated patients and their demographic data and life events. All correlations are very low and are not important for the explanation of depressive syndromes in this sample.

Social Adaptation

The fact that there are almost no correlations between data concerning the present social adaptation and depression scores may refute the hypothesis of depression as an understandable reaction after a psychotic episode. The negative social sequelae of psychotic episodes do not seem to induce depression in schizophrenic patients.

Apathy Syndromes and Depression

The hypothesis that depressive syndromes are sometimes diagnosed in schizophrenics because the "negative syndrome" has some features that overlap with depression [27, 28] can partly be supported by the fact that correlations were found between AMDP and BPRS factors representing the apathetic syndrome, i.e. the AMDP "apathetic syndrome" factor and the BPRS anergia factor and the depression ratings. The highest correlation was found between the AMDP depressive and apathetic syndrome factor. Only low but significant correlations were found between the self-rating PD-S depression dimension and the apathy factors, showing that the observer ratings may carry a higher risk of misinterpretation.

Global Severity Assessments and Depression

The moderate to high correlations between all depression ratings and two observer rating scales for the global severity assessment (CGI and GAS) show that observers tend to take depressed mood into account when they have to assess the overall severity of schizophrenic illness. Patients still suffering from symptoms in the past month showed more depression in all scales.

Neuroleptic Treatment, Extrapyramidal Side-Effects, Antiparkinson Medication and Depression

A correlation of depression scores with extrapyramidal side effects (EPMS) could have two reasons: (a) neuroleptics could cause depression directly, due to the blockade of dopaminergic or adrenergic receptors ("pharmacogenic depression" hypothesis), or (b) akinesia is misinterpreted as depression by psychiatrists. We found significant correlations between rigidity symptoms and observer ratings of depression ($AMDP_D$ and $BRPR_{AD}$). However, the self-report scale PD-S_D does not show such a relation. This could support the theory of misinterpretation of akinetic symptoms as depression by psychiatrists. As only extrapyramidal rigidity symptoms (EPS: gait, arm dropping, shoulder shaking, elbow rigidity and wrist rigidity; DOTES: rigidity) correlate with depression, the "akinetic depression" hypothesis [37, 38] receives some support from these findings.

The neuroleptic dose did not correlate with depression. The therapeutic implication of these results could be that the total amount of neuroleptic medication given is not responsible for the development of depressive syndromes, but the degree in which the individual patient reacts with extrapyramidal symptoms. Only guarded inferences can be made about the influence of neuroleptic therapy, because all patients obtained neuroleptics in the stabilization phase of our study. In the near future, we will report on the comparison of treated with non-treated subjects after a 2-year follow-up.

Nothing can be said about the positive effect of antiparkinson medication on depressive symptoms, because very few patients obtained such medication. No correlation was found between tardive dyskinesia and depression. This is consistent with the findings of Barnes et al. [8].

Conclusions

Depressed mood is not rare in schizophrenic patients after an acute episode. After inpatient treatment and subsequent treatment with neuroleptics, between 19.5 and 42.8% were found to be depressed, depending on the cut-off scores of the rating scales. Our results should be interpreted with caution, because the origin of depressive syndromes seems to be complex and cannot be explained by the single hypotheses. It is possible that the self-assessment by the patient measures a different kind of depression from rating by psychiatrists. In the self-rating, depression correlates with some demographic data and life events, but not with extrapyramidal side-effects, while in observers' ratings depression correlates with EPS and less with life events and demographic data.

The missing correlation between self-rating and EPS could support the "akinetic pseudo-depression" hypothesis, but the statistical evidence is not strong enough to clearly separate this effect from the possibility that depression and EPS develop at the same time due to toxic effects on the same neurotransmitter system. Further information will be available when we can compare patients with or without neuroleptics over a longer period of time. Because of the high therapeutic range of neuroleptics, it is plausible that no correlation was found between neuroleptic dose and depression. The lacking influence of antiparkinson medication on depression may be due to the rare prescription of such medication in our study.

Furthermore, it may be worthwhile separating a real "postpsychotic depression" from depressive mood existent simultaneously with overall psychopathological severity scores or with the apathy syndrome. These effects might support the "revealed depression" or "understandable reaction" hypothesis or could be due to misinterpretation. The statistical relevance of the findings is not very marked. This underlines the fact that depressive syndromes in schizophrenia may be due to a complex interaction of many different aetiological factors. The evaluation of all data of this large sample after a 2-year period may be very helpful in these issues.

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