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DO NEGATIVE SYMPTOMS INFLUENCE OUTCOME OF DEPRESSION?

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SUMMARY

Thirty four cases of endogenous major depression (RDC) have been studied in order to examine whether negative symptoms influence the outcome of depression, by comparing depressives with and without predominant negative symptoms, and by examining which negative symptoms have high percentage reduction in scores. Patients were rated on Scale for Assessment of Negative Symptoms (SANS) during their inclusion and later during one year followup. Complete recovery was seen in only 41% of the cases. Depression with predominant negative symptoms had poorer outcome and did not respond to tricyclic anti-depressants alone. The results indicate that negative symptoms adversely influence the clinical outcome in depressed patients and could have a role in producing chronicity.

Introduction

Negative symptoms should not be assumed to be specific to schizophrenia or pathognomonic of it. Many negative symptoms could be seen in patients with other diseases, particularly depression (Andreasen 1982, Andreasen and Oslen 1982, Andreasen 1979, Pogue-Geile and Harrow 1984, Chaturvedi and Sarmukaddam 1985, 1985a, Lewine 1983, Andreasen and Akiskal 1983). Though these studies have been conducted to examine negative symptoms in depression, symptoms which have been considered as 'negative' have also been dealt with in most phenomenological, nosological and outcome studies on depression. The frequency, nature and prognostic value of some negative symptoms have been examined though the symptoms were not termed as *'negative symptoms'*. Hamilton (1982), Nelson et al. (1984) and many other studies on cluster analysis have discovered a retarded-endogenous-psychotic cluster which is more likely to have negative symptoms (Grinker et al. 1961, Overall et al. 1966, Pilowsky et al. 1969, Fleiss et al. 1971, Paykel 1971, Byrne 1978, and Nelson and Charney 1981).

It is evident from the above mentioned studies that symptoms which are elicited using the Scale for Assessment of Negative Symptoms (SANS) by Andreasen (1981) are probably cardinal features of psychotic depression, atleast during the acute phase of the illness. But, it needs to be emphasised that these might be indistinguishable from negative symptoms in schizophrenia (Andreasen 1979, Chaturvedi and Sarmukaddam 1985).

The association of negative symptoms with poor prognosis is already appreciated in schizophrenic patients (Andreasen 1982, Andreasen and Oslen 1982), in depressive patients also negative symptoms have been found to predict poor prognosis (Chaturvedi and Sarmukaddam 1985a, 1986). Certain negative symptoms have been found to be persistent in depression, though to a different degree as compared to schizophrenia. Pogue-Geile and Harrow (1984) found poverty of speech, flat affect, psychomotor retardation and a mildly high total negative symptom score during followup after 1½ years. Similarly, Cassano et al. (1983) have described various types of residual states during recovery from depression, some of

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which are decreased affective under involvement in activities and loss of affective resilence.

The objectives of this study were to examine whether negative symptoms influence the outcome of depression by comparative evaluation of improvement in depressives with and without predominant negative symptoms, and studying the alteration in negative symptoms during the followup and their relationship with treatment given.

Material and Methods

Sample consisted of patients diagnosed as definite, endogenous major depressive disorder according to Research and Diagnostic Criteria (Spitzer 1978), between 16-55 years of age, either sex, presenting for the first time at the out patient clinic of National Institute of Mental Health and Neuro Sciences, Bangalore, India. Consecutive cases fulfilling the above criteria were included. Patients with associated organic problems, alcoholism or drug abuse, past history of non-affective psychotic disorder, and those who had received treatment elsewhere for the present episode were excluded. The cases were assessed using the Scale for Assessment of Negative Symptoms at the time of entry into the study. The scale has undergone inter-rater and test-retest reliability at this centre. Outcome was rated on a 5-point Clinical Global Improvement Scale (C.G.I. – recovered, moderate improvement, minimal improvement, no improvement, worsened). Outcome and repeat SANS were rated 'blind' at the end of treatment or one year period, whichever was earlier. Treatment was not controlled and patients were treated according to the clinical practice with tricyclic antidepressants (Imipramine commonly) to begin with and a combination of tricyclics with ECT or other psychoactive drugs in patients who did not show adequate response.

Clinical and demographic details were recorded on an interview proforma. Patients with predominant negative symptoms were compared with those depressives who had fewer negative symptoms. The relationship between percentage reduction of subscale scores with duration of treatment was examined.

Results

34 cases fulfilling the criteria were included into the study. The distribution of sample and its demographic and clinical characteristics have been given elsewhere (Chaturvedi and Sarmukaddam 1985). The duration of illness was less than 2 months in 41%, between 2 to 6 months in 35%, 6-12 months in 18% and more than one year in 6%.

Table 1
Clinical Details

Duration of Treatment		
Less than 2 months	7	20.6
2-6 months	18	52.9
6-12 months	9	26.5
Improvement (C.G.I)		
Nil or Mild	10	29.4
Moderate	10	29.4
Complete Recovery	14	41.2

Table 1 gives the duration of treatment of the cases and clinical improvement. Ten patients (29.4%) had minimal or no improvement and 14(41.2%) showed complete recovery. Ten cases (29.4%) had moderate improvement.

Table 2
Mean negative symptom scores during followup

Sub Scale	Initial	Followup***
Affective flattening	6.38 ± 5.72	2.47 ± 2.98
Alogia	3.97 ± 4.08	0.91 ± 2.12
Avolition-apathy	7.32 ± 4.33	1.47 ± 2.06
Anhedonia	9.79 ± 3.87	2.66 ± 3.10
Inattention	3.47 ± 3.12	0.41 ± 0.70
TOTAL SCORE	32.38 ± 14.82	7.53 ± 7.80

*** (Difference between initial and followup scores are highly significant $p < .001$.

Table 2 shows the initial and later, mean negative symptom scores. It can be observed that at one year followup mild negative symptoms persist.

Table 3
Relationship of improvement with treatment

Improvement	n	Imipramine	imipramine + ECT or other drugs
Complete	14	14	0
Mild or Moderate	20	9	11

Fisher's exact probability = 0.00006

Table 3 shows that of the 20 patients who did not achieve complete recovery 11 had to be given ECT or other psychoactive agents also. There is a highly significant difference between improvement with the treatment modalities. On examining the relationship between depression with predominant negative symptoms and certain clinical variables, it was observed that depression with negative symptoms significantly more often necessitated use of ECT or other psychoactive agents ($P = .013$), also the improvement was significantly poorer ($P = .053$) as compared to other depression categories (Table 4). In Table 5 the percentage reduction in negative symptom scores in those of who received treatment for more than or less than six months have been displayed. High reduction (> 75% of the score) in all sub-scales except alogia was significantly more associated with lesser duration of treatment (less than six months). Patients requiring treatment for more than six months also showed high reduction in negative symptoms, but only in very few cases.

Discussion

The study has tried to focus attention on two relatively uncommon themes related to depression, negative symptoms and clinical improvement. The results have shown lack of improvement or poor outcome in ten cases (29.4%), which is comparable to results of other studies (Kerr 1974, Murphy et al. 1974, Shobe et al. 1981), but is much higher than the figures reported by Toone (1979). Seven of these ten cases had very high scores on most subscales and also the total negative symptom score. Though the relationship between clinical improvement and duration of treatment or nature of treatment cannot be explicitly stated, it appears that the non-alleviation of symptoms has resulted in longer duration of treatment as well as use of a combination of tricyclics with ECT or other psycho-active agents as neuroleptics. Tricyclics were not combined with MAO inhibitors. Improvement has been poorer in those depression cases who had predominant negative symptoms. This corroborates our earlier reports that negative symptoms predict poorer outcome in depressive patients (Chaturvedi and Sarmukaddam 1985a).

Negative symptoms in depression persist for a longer period of time, than do other symptoms and could possibly persist as residual features as observed by Pogue-Geile and Harrow (1983), and described in the review by Cassano et al. (1983). Mild symptoms were persisting in our cases also, as is evident from the negative symptom scores after treatment and at one year followup.

This study should raise interest regarding other related areas. Do negative symptoms continue as post-depressive personality changes? Mayer (1975) described features similar to the negative symptoms in post-depressive personality, but attributed them to the use of anti-depressants. The role of anti-depressants can neither be implicated nor ruled out by our results. It is worth mentioning that marked negative symptoms were present before anti-depressants were given and negative symptoms did not increase after the therapy, in any of the cases. The role of negative symptoms in

Table 4
Correlates of depression with predominant negative symptoms

	n	Depression without predominant negative symptoms (n_1 = 20)	Depression with predominant negative (n_2 = 14)	Fisher's exact probability
Duration of Illness				
Less than 6 months	26	17	9	P = 0.161
More than 6 months	8	3	5	
Duration of Treatment				
Less than 6 months	25	15	10	P = 0.560
More than 6 months	9	5	4	
Improvemen.				
Complete	14	11	3	P = 0.053
Mild or Moderate	20	9	11	
Medication Given				
Imipramine	23	16	6	
Imipramine + ECT or other drugs	11	3	8	P = 0.013

Table 5
Percentage reduction in negative symptom scores and duration of treatment

	(n)	High reduction (> 75%)	Low reduction (< 75%)	Fisher's Exact Probability
Affective flattening				
Less than 6 months	(21)	16	5	
more than 6 months	(9)	3	6	P = 0.0355
Alogia				
Less than 6 months	(19)	16	3	
Morelthan 6 months	(6)	4	2	P = 0.3430
Avolition-apathy				
Less than 6 months	(21)	19	2	
More than 6 months	(9)	5	4	P = 0.0492
Anhedonia				
Less than 6 months	(25)	23	2	
More than 6 months	(9)	2	7	P = 0.0002
Inattention				
Less than 6 months	(19)	18	1	
More than 6 months	(7)	4	3	P = 0.0468
Total Negative Symptom Score				
Less than 6 months	(25)	22	3	
More than 6 months	(9)	2	7	P = 0.0006

(Difference in (n) is because certain patients did not exhibit the symptom during their inclusion, hence their percentage reduction has not been examined).

causing or manifesting as chronicity needs to be examined.

It seems, negative symptoms influence the clinical outcome in depressed patients, but their exact etiopathogenesis is not clearly understood. They could have a role in production of post depressive personality and chronicity of depression. More research of these areas could clarify these issues.

The implications of studying negative symptoms could have other far reaching significance. Afterall, there still exist great disagreements concerning the definition and sub-typing of depressive disorders (Andreasen 1982a) and negative symptoms might help in evolving a new classification of depression, as in case of schizophrenia. Study of negative symptoms in depression open further avenues to study prognosis of depression, predictive ability of negative symptoms as regards long term prognosis, responses to drugs and physical treatments or studying etiological aspects of affective disorders. It also provides another dimension to examine the relationship between schizophrenic and affective disorders, or schizo-affective psychosis in terms of negative symptoms.

References

ANDREASEN, N. C. (1979), Affective flattening and the criteria for schizophrenia, *American Journal of Psychiatry*, 133, 944-947.

ANDREASEN, N. C. (1982), Negative symptoms in schizophrenia, Definition and reliability, *Archives of General Psychiatry*, 39, 784-788.

ANDREASEN, N. C. (1981), Scale for the assessment of negative symptoms (SANS), Iowa city, The University of Iowa.

ANDREASEN, N. C. (1982a), Concepts, diagnosis and classification, in Handbook of Affective disorders, Ed. E. S. Paykel, Churchill Livingstone, Edinburg.

ANDREASEN, N. C. & AKISKAL, H. A. (1983), The specificity of Bleulerian and Schneiderian symptoms, a critical re-evaluation, *Psychiatric Clinics of North America*, 6, 41-51.

ANDREASEN, N. C. & OSLEN, S. (1982), Negative Vs Positive schizophrenia, Definition and validation, *Archives of General Psychiatry*, 39, 789-794.

BYRNE, D. G. (1978), Cluster analysis applied to self reported depressive symptomatology, *Acta Psychiatrica Scandinavica*, 57, 1-10.

CHATURVEDI, S. K. & SARMUKADDAM, S. (1985), Negative symptoms in depression, *Indian Journal of Psychiatry*, 27(2), 139-144.

CHATURVEDI, S. K. & SARKUKADDAM, S. (1985a), Negative symptoms as predictive factors in outcome of major depression, *NIMHANS Journal*, 3, 115-119.

CASSANO, G. B., MAGGINI, C. & AKISKAL, H. S. (1983), Short term, sub-chronic and chronic sequalae of affective disorders. *Psychiatric clinics of North America*, 6, 55-67.

FLEISS, J. L., LAWLOR, W., & PLATMAN, S. R. (1971), The use of inverted factor analysis for generating typologies, *Journal of Abnormal Psychology*, 77, 127-132.

GRINKER, R. R., MILLER, J., & SHABSIN, M. (1961), The phenomenon of depressions, Moeber, New York.

HAMILTON, M. (1982), Symptoms and assessment of depression. In Handbook of affective disorders. Ed. Paykel, E. S. Churchill Livingstone, Edinburgh.

KERR, T. A., ROTH, M. & SCHAPIRA, K. (1974), Prediction of outcome in anxiety states and depressive illness, *British Journal of Psychiatry*, 124, 125-133.

LEWINE, R. R. J., FOGG, L. & MELTZER, H. Y. (1983), Assessment of negative and positive symptoms in schizophrenia, *Schizophrenia bulletin*, 9(3), 368-376.

MAYER, D. Y. (1975), Psychotropic drugs and 'anti-depressed' personality, *British Journal of Medical Psychology*, 48, 349-357.

MURPHY, G. E., WOODRUFF, R. A., HERJANIC, M. & SUPER, G. (1974), Variability of the clinical course of primary affective disorder, *Archives of General Psychiatry*, 30, 757-761.

NELSON, J. C. & CHARNEY, D. S. (1981), The symptoms of major depressive illness. *American Journal of Psychiatry*, 138, 1-13.

NELSON, J. C., MAZURE, C., QUINLAN, D. M., JATLOW, P. I. (1984), Drug responsive symptoms in melancholia, *Archives of General Psychiatry*, 41, 663-668.

OVERALL, J. E., HOLLISTER, L. E., JOHNSON, M. & PENNINGTON, V. (1966), Nosology of depression and differential response to drugs, *Journal of American Medical Association*, 195, 946-950.

PAYKEL, E. S. (1971). Classification of depressed patients, a cluster analysis derived grouping, *British Journal of Psychiatry*, 118, 275-288.

PILOWSKY, I., LEVINE, S., BOTTON, D. M. (1969), The classification of depression by numerical taxonomy, *British Journal of Psychiatry*, 115, 937-945.

POGUE-GIELE, M. F. & HARROW, M. (1984), Negative and positive symptoms in schizophrenia and depression, a followup. *Schizophrenia Bulletin*, 10, 371-387.

SHOBE, F. O. & BRION, P. (1971), Long term prognosis in manic depressive illness, *Archives of General Psychiatry*, 24, 334-337.

SPITZER, R., ENDICOTT, J. & ROBINS, E. (1978), Research Diagnostic Criteria, New York and State Psychiatric Institute, New York.

TOONE, B. K. & RON, M. (1977), A study of predictive factors in depressive disorders of poor outcome, *British Journal of Psychiatry*, 131, 587-591.