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Negative Symptoms in Chronic Schizophrenic Inpatients; Comorbidity with Late Involuntary Movements and Cognitive Deficits (A Cross Sectional Study)

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Abstract

Negative symptoms of schizophrenia have received increasing research attention in recent years especially after the emergence of new antipsychotic drugs which were found to be effective in some cases of schizophrenia with negative symptoms. The present work was designed to survey chronic schizophrenic inpatients as regards negative symptoms and to explore the relationships between these negative symptoms and tardive dyskinesia and cognitive deficits. 95 patients with predominant negative symptoms were assessed, matched with a control group of depressed patients. Results showed that unemployment was highly common among patients with negative symptoms. Those symptoms were also significantly and positively correlated with the age of patients, duration of hospitalization and negatively with education. Also, negative symptoms were significantly correlated with cognitive deficits and severity of tardive dyskinesia especially orofacial dyskinesia.

These results were discussed in the light of the possible lines of management so as to minimize the development of negative symptoms and how to manage them.

Introduction The heterogeneity of schizophrenic syndromes has long puzzled investigators who have attempted to identify components with different etiologies, prognosis and treatment responses. One of the oldest dichotomies is that of positive versus negative symptoms. Kraeplin noted this distinction one hundred years ago when he described a chronic deficit state more devastating than the acute psychotic episode. Since that time, interest in negative symptoms has waned with attention focused on the more florid first rank symptoms. Only in the past decade have researchers once again looked to negative symptoms to understand the processes underlying the schizophrenic syndrome.

The relationship between negative symptoms and tardive dyskinesia has been supported in more than one study, Barnes and Liddle, (1985) found that tardive dyskinesia is common in patients with negative features. Some results were reported by Jeste et al. (1984).

In a sample of chronic schizophrenic patients, a group of symptoms which included poverty of speech and lack of spontaneous movements was found to be associated with poor performance in tests of conceptual thinking, object naming and longterm memory and also with cortical neurological signs (Liddle, 1987). The aim of the present study was to explore the relationships of different negatie symptoms to each other, also it addresses its relationship with cognitive deficits, tardive dyskineaasia and depressive symptoms.

Methodology A sample of 95 patients diagnosed as chronic schizophrenia according to DSM-III-R criteria (APA, 1987) with prominant negative symptoms (Andresen et al, 1990) were selected ages ranging from 18-60 years. The sample consisted of 80 males and 15 fe-

male patients. A control group of 50 patients diagnosed as having depressive disorder were selected, matched for age, sex, marital status and education with a duration of illness more than five years.

Procedure All patients in the sample and control groups were clinically assessed by the use the of modified semistructured Ain Shams interview sheet. Diagnosis was carried out according to DSM-III-R criteria. The following scales were then applied to the sample and the control groups:

1-Scale for assessment of negative symptoms (SANS) (Andreasen, 1983).

2- Abnormal involuntary movement scale (Guy et al, 1976) for quantitative assessment of tardive dyskinesia.

3- Rockland scale (Simpson et al 1979) for assessment of tardive dyskineasia.

4- Beck inventory for depression (Beck, 1961).

5- Five subscales of Wechsler adult intelligence scale, namely digit span, arithmatic, picture completion, similarities and digit symbols for assessment of cognitive functions.

6- Ten question test for evaluation of the basic cognitive functions (Waddington et a.l 1986a).

Results Mean age of the sample was 40.5±11.1 years. Mean duration of education was 4.4±4.6 years. 80 patients (84.2%) were males and 15 (15.8%) were females. 63 (66.3%) were single, 23 (24.2%) married, 7 (7.4%) widows and 2 (2.1 %) were divorced. 11 (11.6%) patients were employed, while 84 (88.4%) were unemployed.

As regards clinical data, it was found that the mean age of onset 20.7±4.8 years ranging within 12-32 years. Duration of illness was 19.9±10.7 years. Frequency of admissions was 11.1±6.8 times. Mean duration of hospitalization was 8.8±10.1. Most of the patients were maintained on antipsychotic drugs with mean daily doses of 425.6 i 205.8 mg. Chloropromazine equivalents.

Interrater reliability for negative symptoms assessment scale were as follows: alogia 0.91, affective flattening 0.97, avolition apathy 0.91, anhidonia, asociality 0.92 and attentional impairment 0.95.

Negative symptoms scores Table (1) shows that more than 53% of patients got scores more than 20, i.e. had severe negative symptoms. Table (2) shows that the age of patients, duration of hospitalization, and duration of illness were positively correlated with negative symptoms scores, while the degree of education and current neuroleptic doses were negtively correlated with it.

At the same time negative symptoms subscales were found to be positively correlated with each other as shown in Table (3).

Negative symptoms and cognitive functions subscales of negative symptoms were found to be negatively correlated with scores of modified Rath Hopbins questionnaire as well as with other cognitive function tests as digit span, antithmatic, similarities picture completion and digit symboles ofWechsler test of intellegence results are shown in Table (4).

Negative symptoms and Tardive Dyskinesia Table (5) shows that negative symptom scores were positively correlated with the total scores of AIMS and Rockland tests, both of them measures tardive dyskinesia. Morever, negative

Table (1) : Negative symptoms summary scores of schizophrenic patients

NS Summary score	Number of patients with the score	%
25	21	22.1
24	8	8.4
23	3	3.2
22	5	5.3
21	7	7.4
20	7	7.4
19	8	8.4
18	6	6.3
17	10	10.5
16	5	5.3
15	3	3.2
14	2	3.1
13	5	5.3
11	4	4.2
8	1	1.1
Total	95	100

Table (2): Correlation of negative-symptoms with different clinical variables

Variable	Correlation
Age	0.41**
Education	-0.60**
Age of onset	-0.02
Duration of hospitalization	0.50**
Current neuroleptic dose (CPZ mg equivalent)	-0.21*
Duration of illness	0.42**
Frequency of admission	-0.02

*P<0.05

**P<0.001

Table (3) Correlation matrix for the scale of assessment of negative symptoms (SANS) subcales, suing Spearman correlation coefficient

	Affective flattening	Alogia	Avolition apathy	Anhidonia asociality	Attentional impairmant
Affective flattening	-	0.78**	0.63**	0.64**	0.66**
Alogia	0.78**	-	0.60**	0.67**	0.70**
Avolition-apthy	0.63**	0.60**	-	0.67**	0.57**
Anhidonia asociality	0.64**	0.67**	0.67**	-	0.67**
Attentional impariment	0.66**	0.70**	0.57**	0.67**	-

Table (4): Correlation of negative symptoms with cognitive function in schizophrenic inpatients

	Affective flattening	Alogia	Avolition apathy	Anhidonia asociality	Attentional impairmant	SANS Summury score
10 questionnaire scale	-0.71**	-0.71**	-0.65**	-0.75**	-0.72**	-0.79**
Digit span	-0.23*	-0.27*	-0.24*	-0.39**	-0.54**	0.44**
Arithmatic	-0.13	-0.06	-0.1	-0.26*	-0.40**	-0.28*
Similarities	0.21	-0.16	-0.6	-0.29*	-0.48**	-0.35**
Picture completion	0.35**	-0.34**	0.11	-0.5**	-0.49**	-0.45**
Digit symbol	0.12	-0.3	-0.06	-0.29*	-0.41**	-0.27*

*P<0.05 **P<0.001

Table (5): Correlation of negative symptoms with depression in schizophrenic patients

	Affective flattening	Alogia	Avolition apathy	Anhidonia asociality	Attentional impairmant	SANS Summury score
AMIS						
-Orofacial	0.09	0.15	0.09	0.19*	0.21*	0.17*
-Truncal	0.08	0.19	0.11	0.19*	0.28*	0.2*
-Total	0.09	0.17*	0.1	0.2*	0.25*	0.19*
Rockland						
-Orofacial	0.15	0.2*	0.16*	0.2*	0.26*	0.23*
-Truncal	0.01	0.12	0.9	0.19*	0.23*	0.14
-Total	0.1	0.17*	0.14	0.21*	0.26	0.21*

*P<0.05

Table (6): Correlation of negative symptoms with depression in schizophrenic patients

	Affective flattening	Alogia	Avolition apathy	Anhidonia asociality	Attentional impairmant	Summury score
Beck	-0.18*	-0.26*	-0.16	-0.41**	-0.38**	0-.34**

also positively and significantlycorrelated with orofacial dyskinesia specifically.

Negative symptoms and depression Table (6) shows high significant and negative corelation between different subscales of SANS and Beck inventory of depression except that of avoliation apathy subscale.

Discussion: Over the past few years there has been considerable interest in the positive/negative distinction in schizophrenia, which offers a means of reducing the heterogeneity of the disorder and a model for generating hypotheses about underlying pathophysiology. The present study highlights some points concerning the concept.

The excess of men (84.2%) in our sample may be partly explained by the evidence that men with schizophrenia tend to be readmitted to the hospital (Goldstein, 1988), also, an association between male sex and negative symptoms has been reported by Tantam et al., (1991).

Most of the patients with NS (88.4o%) were unemployed. This would reflect the devastating effect of NS. It might be due to its effect on volition, interest, attention and the capability to work. This goes with other studies which found high prevalence of unemployment among schizophrenic patients with NS (Andreasen and Oslen,1982; Andreasen et al., 1990).

Ns were found to be significantly correlated with the duration of illness. Other studies reported that a longer duration of illness was usually associated with NS (Owens and Johnstone,1980; Pogine-Geile and Harrow,1984). On the other hand, some studies found that NS were not correlated with the duration of illness (Ring et al.,1991; Philips et al., 1991). Discrimination between primary negative symptoms as manifestations of an enduring deficit state, and secondary negative symptoms, which are essentially a behavioral presentation of positive psychotic symptoms and are likely to be transient and treatable, is essential (Carpenter, et al., 1988). The failure to distinguish between primary and secondary symptoms could account for some of the inconsistencies in research findings and the different responses to pharmacological and psychological treatments observed at different stages of the schizophrenic illness (Barnes, 1994). Also, the effect of prolonged hospitalization of our schizophrenic patients (8.8 10.1 years) may have great impact on the severity of negative symptoms as a result of institutionalization.

Feton and McGlashan (1991) in their follow up study for an average of 19 years on schizophrenic patients found that schizophrenia with high levels of enduring primary negative symptoms was associated with insidious onset, few remissions and a progressive course leading to permanent disability. Patients with particularly poor outcome showed rapid increases in negative symptoms early in their illnesses. Some of these findings are replicated in other studies reporting high levels of enduring primary negative symptoms in older schizophrenic patients (Mathai and Gopinath,1986; Kay and Singh, 1989; Harris et al.,1991). our findings also gave support to the effect of age on the severity of negative symptoms. Also, Hafner (1993) reported that negative symptoms occurring from the very beginning in about 90% of cases, constitute the core symptomatology in schizophrenia, and pointed to the weak association between negative symptoms, neuropsychological deficits and morphological brain findings that might indicate an increase in

the morbid risk rather than be of general etiologic relevance in the sense of a neurodevelopmental disorder.

The previously reported association between movement disorders and negative symptoms has been replicated in several studies (Davis et al.,1991; McGlashan and Fenton, 1992). Within our schizophrenic sample, patients with tardive dyskinesia had significantly higher negative symptom scores and more cognitive impairment than patients without tardive dyskinesia. Other studies support this notion; Waddington and Youssef, (1986b) found that almost 90% of their patients with tardive dyskineasia had one or more of negatives ymptoms, while only about one third ofthose without tardive dyskinesia were characterized in this way. Moreover, orofacial dyskinesia was found to be highly significantly correlated with negative symptoms. The reliability and prominence of the association between the presence of orofacial but not of limb-truncal movement disorders and cognitive dysfunction/ negative symptoms suggest that these varying topographies may not constitute a unitary syndrome (Waddington et al.,1987). A strong association between negative symptoms and cognitive impairment was reported. Several studies have examined the differential cognitive correlates of negative symptoms and supported the view (Tamlyn et al., 1992).

Clinically, there is an overlap between depressive symptoms and certain negative features such as anhedonia, anergia, feeling of emptiness and emotional withdrawal. Using standard instruments for the assessment of depression and negative symptoms, several studies have examined samples of schizophrenic patients to test whether negative symptoms are distinct from other schizophrenic symptoms including depressive features. Most of these studies concluded that in patients with schizophrenia, flattened affect was distinguishable from depressed affect, and depression and negative symptoms were distinct clinical phenomena (Kuck et al., 1992). The present study supports the same view. Hafner's opinion (1993) was that the nonspecific symptorns (e.g. depressive symptoms) represent age- and in part also sex- related responses to schizophrenic disorders.

Finally, why are negative symptoms so important ?. For long time more attention was paid to positive symptoms of schizophrenia, as they are more overt and easy to be measured. Positive symptoms were of some value in predicting future hospitalizations but were comparatively less powerfull and specific as indicators of differential illness history, course or long term functional incapacity (Fenton and McGlashan, 1992). Thoughnegative symptoms were difficult to be rated, they were considered as predictors of poor outcome. The renewed interest in negative symptoms stemmed from the findings of different studies relating them to structural changes, and the hope to identify homogenous entity with known pathophysiological etiology. Although Crow (1989) had repored that negative (type II) schizophrenia do not respond to neuroleptic drugs and that positive (type I) schizophrenia responds, recent literature claims that negative schizophrenia can respond to non classical neuroleptics specially those acting as 5HT2 antagonists e.g. risperidone and clozapine. This has altered the etiology, management and prognosis of schizophrenia. So, approaches to schizophrenia should include how to minimise the development of negative symptoms and how to manage them.

Reference

American Psychiatric Association (1987): Diagnostic and statistical manual of mental disorders,3rd edition, revised (DSM III-R) Washington, DC.

Andreasen, N.C. and Oslen, S. (1982): Negative versus positive schizophrenia, definition and validation. Arch. Gen. Psychiat,39: 784-88.

Andreasen, N.C. (1983): The scale for the assessment of negative symptoms (SANS). Iowa city, Iowa. University of Iowa.

Andreasen, N.C., Flaum, M., Swayze, V.W., Tyrrel, G., Arndt,S. (1990): Positive and negative symptoms in schizophrenia: a critical reappraisal. Arch. Gen. Psychiat, 47: 615-21.

Barnes, T.R.E. and Liddle, D.F. (1985): Tardive dyskinesia: implications for schizophrenia ?. In " Schizophrenia, new pharmacological and clinical developments (eds. A A. Schiff, Sir Martin Roth and H.L. Freeman) Royal Society of Medicine. International Congress and Symposium Series. No. 94 p. 81-87.

Barnes, T.R. E. (1994): Issues in the clinical assessment of negative symptoms.Current Opin. Psychiat, 7: 35-38.

Beck, A.J., Ward, C.H., Mendelson, M., Mock, J. and Exbaught (1961): An inventory for measuring depression. Arch Gen. Psychiat, 4: 561-71.

Carpenter, W.T.Jr., Heinrighs,D.W., Wagman,A.M. (1988): Deficit and non deficit forms of schizophrenia: the concept. Am. J. Psychiat,145: S78-83.

Crow, T.J. (1980): Molecular pathology of schizophrenia, more than one disease process. Br. Med. J, 280: 66-68.

Crow, T.J. (1989): A recent view oftype II syndrome. Age of onset, intellectual impairment and the measuring of structural changes in the brain. Br. J. Psychiat, 155 (suppl 7): 15-20.

Davis, E.J.B., Borde, M. and Sharma, N. (1992): Tardive dyskineasia and type II schizophrenia. Br J Psychiat, 160: 253-56.

Fenton,W.S. and McGlashan, T.H. (1991): Natural history of schizophrenia subtype II. positive and negative systems and long-term course. Arch. Gen. Psychiat,48: 978-8S.

Fenton, W.S. and McGlasan, T.H. (1992): Testing systems for assessment of negative symptoms in schizophrenia. Arch Gen Psychiat, 149: 179-

Goldstein, J.M.(1988): Gender differences in the course of schizophrenia. Am. J. Psychiat, 14S: 684-89.

Guy, W., Ban, T.A and Wilson, W.H. (1976): The prevalence of abnormal involuntary movements among chronic schizophrenics. Inter. Clin Psychopharm,l: 134-44.

Jeste, D.V., Karson, C.N. and Wyatt, R.J. (1984): Movements disorders and psychopathology. In "Neuropsychiatric movements disorders. (eds. D.V. Jeste and R.J. Wyatt) Washington.

Harris,J.M.,Jeste,D.V.,Krull,A,Montague,J., Heaton,R.K. (1991): Deficit syndrome in older schizophrenic patients. Psychiat Res,39: 258-92.

Hafner, H. (1993): What is schizophrenia?. Neurology, Psychiatry and brain research, 2: 36 - 52.

Kay, S.R. and Singh,M.M.(1989):The positive-negatived is tinctionindrug-free

schizophrenic patients. Stability, response to neuroleptics and prognostic significance. Arch. Gen. Psychiat, 46: 711-18.

Kuck,J.,Zisook,S.,Moranville,J.T., Heaton,R.K., Braff,D.L. (1992): Negative symptomatology in schizophrenic outpatients. J. Ner. Ment. Dis, 180: 510-15.

liddle, P.F. (1987): The symptoms of chronic schizophrenia, an examination ofthe,positive-negative dichotomy. Br.. J Psychiat, 151: 145-51.

Mathai, P.J. and Gopinath, P.S. (1986): deficits of chronic schizophrenia in relation to long terM hospitalization. Br J Psychiat, 148: 509-16.

McGlashan,T.H.,andFenton,W.S.(199) :The postive-negative distinction in schizophrenia : review of natural history validators. Arch. Gen. Psychiat, 49: 63-72.

Owens, D.G.C. and Johnstone, E. C. (1980): The disabilities of chronic schizophrenia. Their nature and the factors contributing to their development. Br. J. Psychiat, 136: 384-95.

Philips, M.R., Zlao,Z., Xiong X-9, Chang, X, Sun,G. and Wu,N. (1991): Changes in the positive and negative symptoms of schizophrenic inpatients in China. Br. J. Psychiat, 159: 226-31.

Pogue Geile, m. F. and Harow,M. (1984): Negative and positive symptomsin schizophrenia and depression: afFollow up study. Schiz. Bulletin, 10: 371-87.

Ring, N.,Tantum P., Montague L., Morris,J. (1991) : Negative symptoms in chronic schizophrenia. Relationship to duration of illness. Br. J. Psychiat, 159: 495-99.

Simpson, G.M., Lee, J.H., Zoubok,B. (1979) : A rating scale for tardive dyskinesia. Psychopharmacology, 64: 171-79.

Sommers, A A.(1985): "Negative Symptoms" conceptual and methodological problems. Schiz. Bulletin, 11: 364-79.

Tamlyn,D., McKenna,P.J., Mortimer,A M., Lund,C.E., Hammond,S., Baddeley,A. D.(1992): Memory impairment in schizophrenia: its extent, affiliations and neuropsychological character. Psychol. Med, 22:101-15.

Tantam,D., Montague,L., Newby,D., Black,D., Morris,J.(1991): Gender differences in the incidence of definite schizophrenia and atypical psychosis, focus on negative symptoms of schizophrenia. Acta. Psychiat. Scand,84: 489-96.

Waddington,J.L.,Yossef,H.A.,Dolphin, C., Kinsella,A.(1987): Cognitive dysfunction, negative symptoms and tardive dyskineasia in schizophrenia. Their association in relations topography of involuntary movements and criterion oftheir abnormality. Arch. Gen. Psychiat, 44:907-12.

Waddington, J.L., Youssef,H.A. (1986a): An unusual cluster of tardive-dyskineasia in schizophrenia: association with cognitive dysfilnction and negative symptoms. Am J Psychiat, 143: 1162-6S.

Waddington J.L., and Youssef, H.A. (1986b): Late onset involuntary movements in chronic schizophrenia. Relationship of tardive dyskinesia to intellectual impairment and negative symptoms. Br. J. Psychiat, 149: 616-20.

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الأعراض السلبية لدى مرضى الفصام المزمنين :الترابط المرضى مع الحركات اللاارادية و التدهور المعرفى (دراسة مستعرضة)

لقيت الأعراض السلبية لمرضى الفصام اهتماما كبير من قبل الباحثين فى الآونة الأخيرة وذلك بعد ظهور أنواع جديدة من مضادات الذهان التى وجد أنها تفيد فى بعض هذه الحالات. و قد صمم البحث لمسح حالات الفصام المزمن المقيم بالمستشفى من حيث وجود الأعراض السلبية و دراسة علاقتها بعسرالحركة الآجل والتدهور المعرفى. تم فحص ٩٥ مريضا ممن يعانون من الأعراض السلبية و مقارنتهم بعينة مماثلة من مرضى الإكتئاب وأظهرت النتائج انتشار البطالة فى هذه العينة و كذلك وجدت علاقة ذات دلالة أحصائية مع تقدم السن ومدة الإحتجاز بالمستشفى مع وجود الأعراض السلبية إلا أن درجة التعليم كانت مترابطة معها إرتباط عكسى. كذلك وجدت علاقة ذات دلالة أحصائية بين تقدم السن و مدة الإحتجاز بالمستشفى و بين وجود الأعراَض السلبية إلا أن درجة التعليم كانت ذات إرتباط عكسى. كذلك وجدت علاقة ذات دلالة أحصائية مع التدهور المعرفى و درجة الإصابة بعسر الحركة الآجل خاصة حركات الفم اللاإرادية. و قد نوقشت هذه النتائج فى ضوء الأساليب المختلفة للعلاج بهدف التقليل من الأعراَض السلبية.

The Diagnosis Of Epilepsy Is Largely Based On

Medical History

Neurological history

Psychiatric history

History of possible causative scndition (e.g.ead injury, cerebral and development history)

Pernatal and development history

Family history