Premorbid functioning by gender and its relationship with duration of untreated phychosis in first psychotic episode

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Funcionamiento premórbido por género y su relación con la duración de la psicosis no tratada (DPNT) en el primer episodio psicótico

Summary

Introduction. *There are two phenotypes proposed for the psychotic disorders based on premorbid functioning and probably related with the duration of untreated psychosis (DUP). The aim of this study was to compare the clinical features, premorbid functioning and its relationship with DUP by gender in a group of first episode psychosis patients.*

Methods. *We included 77 patients in their first admission to a psychiatric facility. A clinical evaluation was performed with the PANSS, Calgary Depression Scale, Hamilton Depression Scale and Mania Rating Scale. Premorbid functioning was rated with the Premorbid Adjustment Scale.*

Results. *There were no clinical differences between men and women. Men had greater impairment in their premorbid functioning. Patients with short DUP (< 28 weeks) showed better premorbid functioning compared to those with long DUP (>28 weeks).*

Conclusion. *Duration of untreated psychosis is determined by premorbid functioning and it is possible that male patients, who show a higher frequency of poor premorbid functioning, have a longer delay in seeking treatment, that conditions a longer duration of untreated psychosis.*

Key words: *First episode psychosis. Gender. Premorbid functioning. Duration of untreated psychosis.*

Resumen

Introducción. *Existen dos fenotipos para los trastornos psicóticos sustentados en el funcionamiento premórbido y probablemente relacionados con la duración de la psicosis no tratada (DPNT). El objetivo del estudio fue establecer las diferencias de género en las características clínicas, el funcionamiento premórbido y su relación con la DPNT en pacientes con primer episodio psicótico.*

Métodos. *Se incluyeron 77 pacientes en su primera admisión a un servicio de psiquiatría. Se realizó una evaluación clínica con la PANSS, Escala Calgary de Depresión, Escala de Hamilton de Depresión y Escala de Evaluación de Manía y la Escala de Ajuste Premórbido para evaluar el funcionamiento premórbido.*

Resultados. *No hubo diferencias entre hombres y mujeres en la severidad clínica. Los hombres mostraron mayor deterioro en su funcionamiento premórbido. Los pacientes con DPNT corta (<28 semanas), en comparación con los que tuvieron DPNT larga (>28 semanas), presentaron un mejor funcionamiento premórbido.*

Conclusión. *La DPNT está determinada por el nivel de funcionamiento premórbido y es posible que los hombres, al presentar con mayor frecuencia un bajo funcionamiento premórbido, tarden más en buscar atención especializada para recibir un tratamiento específico prolongando la DPNT.*

Palabras clave: *Primer episodio psicótico. Género. Funcionamiento premórbido. Duración de la psicosis no tratada.*

INTRODUCTION

Onset of a schizophrenia episode has been based on the appearance of the first psychotic symptoms[1] during late adolescence or early adulthood. However, it has been established that there are functioning changes that precede the onset of the prodromic and psychotic phases of the disease.

Present evidence regarding early deterioration in the functioning of the individual suffering schizophrenia comes from investigations focused on the premorbid functioning study[2]. Premorbid functioning is defined as psychosocial adjustment of the individual in the school, labor, social and interpersonal relations area prior to the appearance of psychotic symptoms such as hallucinations, delusions, thought disorders or behavior disorders

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in which the symptoms do not have an organic cause[3]. Low premorbid functioning refers to deterioration in the individual adaptation in these areas. Premorbid functioning includes a 6 month period before the appearance of the psychotic symptoms or 6 months before the first hospitalization or contact with a specialized psychiatry service[3]. One of the major methodological problems when premorbid functioning is determined is that it is evaluated with scales that only assess late adolescence or early adulthood[4-6], stages in which the psychotic symptoms that condition low functioning are generally observed. Thus, evaluation of early stages of the vital cycle, as childhood and early adolescence, is important to determine premorbid functioning[2].

Studies of patients who have their first psychotic episode facilitate assessment of premorbid functioning and its relationship with other clinical variables, since they allow for direct observation of the early disease phases.

It has been established that, compared to women, men present low premorbid functioning, associated to a greater index of negative symptoms and greater interval between onset of the psychotic symptoms and hospitalization[7-10,2]. On the other hand, it has been observed that some patients with schizophrenia present marked deterioration in premorbid functioning during late adolescence, which is probably conditioned by behavioral changes that are observed in childhood. These changes are not observed in patients with affective psychoses[11]. Two different phenotypes of schizophrenia have been proposed: the first is characterized by low premorbid functioning and the second by good premorbid functioning[12].

Recently, duration of untreated psychosis (DUP) has been established as a prognostic factor. DUP refers to the time interval between appearance of the psychotic symptoms and onset of an adequate treatment (equivalent to 5 mg/day of haloperidol for 4 weeks)[13]. Patients who present a long DUP (>54 weeks) more frequently tend to be men, to have negative symptoms and low premorbid functioning in late adolescence and the adulthood stage[14].

This study aimed to establish gender differences in the clinical characteristics and premorbid functioning, as well as their relationship with the untreated psychosis period in a group of Mexican patients with first psychotic episode.

METHOD

Sample

A total of 77 patients were included during a 36 month period. These patients came consecutively to out-patient, emergency and hospitalization services, with first psychotic episode defined as their first contact in life with a specialized psychiatry service due to their present psychotic picture[15]. The patients were grouped in non-affective psychosis (schizophreniform disorder, schizophrenia, schizoaffective disorder, brief reactive psychotic delusional disorder and unspecific psychosis) and affective psychosis (psychotic depression and bipolar disorder with psychotic symptoms) according to the diagnostic DSM-IV criteria[16] and with an age between 15 to 65 years. All the patients and one of their family members accepted to participate in the study by means of an informed and written consent. Patients who had received psychiatric care due to similar problems as the present ones as well as those who had received treatment with antipsychotics for more than one month prior to inclusion in the study were excluded.

The sample consisted of 40 men (51.9 %) and 37 women (48.1 %), with an average of 27.8 ± 9 years (range: 15-58). Most of the patients had no partner at the time of the study (n = 56, 72.7 %), with predominance of subjects belonging to the low and middle socioeconomic levels (49.4 % and 48.1%, respectively). More than half of the patients had some type of occupation (n = 48, 62.3 %). Averaging schooling was 11 years ± 2.82 (range: 6-19 years). At the onset of the study, 39 (50.6%) patients were hospitalized, the rest came to the out-patient service.

Instruments and procedure evaluation

The initial diagnosis was performed with the Schedules for clinical assessment in neuropsychiatry (SCAN)[17-19].

The sociodemographic data were recorded for each one of the patients, using a previously designed ad hoc instrument[20]. Data collection was performed by direct questioning of the patient and family.

After, clinical severity of each one of the diagnosed conditions included in the study was assessed by clinical scales validated in our environment[21].

Psychotic symptoms were assessed with the positive and negative symptoms of schizophrenia scale (PANSS)[21,22]. To examine the depressive symptoms in patients with non-affective psychosis, the Calgary depression scale for schizophrenia was used[23,24] and, for patients with affective psychosis, the Hamilton depression scale[25]. Severity of the mania symptoms of patients with bipolar disorder was quantified with the mania assessment scale[26].

For assessment of premorbid functioning, the premorbid adjustment scale (PAS)[3,27] was used. This scale was designed to assess functioning level in four features: *1.* socialization and isolation; *2.* relationships of friendship and companionship; *3.* capacity to function outside the family nucleus, and *4.* capacity for sociosexual link through four periods of the vital cycle: *a)* childhood (until 11 years); *b)* early adolescence (12-15 years); *c)* late adolescence (16-18 years), and *d)* adult age (19 years on). In the final section of the scale, there is an assessment of global features of general functioning that aims to estimate the highest level of functioning reached by the subject before the onset of the psychotic picture. The scale score goes from 0 to 1, in which 1 represents the lowest functioning. The mean score of the total gra-

ding of the PAS was 0.31, cut off that was used to divide the sample in low premorbid functioning and good premorbid functioning, definition proposed by Haas and Sweeney[2].

Duration of the untreated psychosis (DUP) was evaluated according to the criteria proposed by Larsen[14] and was defined as the period between onset of the psychotic symptoms and onset of specific treatment with antipsychotics. Onset of the symptoms was defined as the presence of hallucinations, delusions, suspiciousness and though disorders graded with 3 or more points according to the P1, P2, P3, P5, P6 and G9 items of the PANSS scale. This information was obtained by a retrospective evaluation, using the patients and their family as information sources.

Statistical analysis

Description of the sociodemographic and clinical characteristics was performed with frequencies and percentages for the categoric variables and with means and standard deviations (±) for continuous variables. Chi squared (χ^2) for categoric contrasts and the Student's «t» test in continuous variables were used for comparison between men and women and diagnostic groups. The Cochran Mantel-Haenszel test with estimations of the common odds ratio for 3 way contingency tables (2 × 2 × 2) was used to evaluate the premorbid functioning level, diagnostic group and DUP by gender. Because the DUP does not have a normal distribution, the Mann-Whitney U test, a non-parametric test, was used to determine differences by gender. The sample was divided into long DUP and short DUP, using the median as cut off, a criterion proposed by other authors[2,13].

RESULTS

Demographic and clinical characteristics by gender

The differences in demographic and clinical characteristics by gender are shown in table 1.

Comparison of the premorbid functioning by gender

The averages in the PAS of the sample were the following: childhood, 0.22 ± 0.16; early adolescence, 0.25 ± 0.15; later adolescence, 0.33 ± 0.19; adult age, 0.39 ± 0.22; general, 0.40 ± 0.18, and total, 0.31 ± 0.15. A total of 40.3% of the sample reported low premorbid functioning. The women presented good premorbid functioning with greater frequency than the men (73% vs 47.5 %; $\chi^2 = 5.18$; gl 1, p = 0.02).

Significant differences were found in the assessment of premorbid functioning by gender, in which it was observed that men had lower functioning than women (fig. 1).

Results according to gender, diagnostic group and premorbid functioning level are shown in table 2. It was established that the groups (men-women) were not different based on the Breslow-Day Tarone homogeneity test ($\chi^2 = 0.18$; gl 1, p = 0.66) and it was determined that the risk of low premorbid functioning was different for diagnostic groups (estimated from the odds ratio = 6.4; p = 0.007).

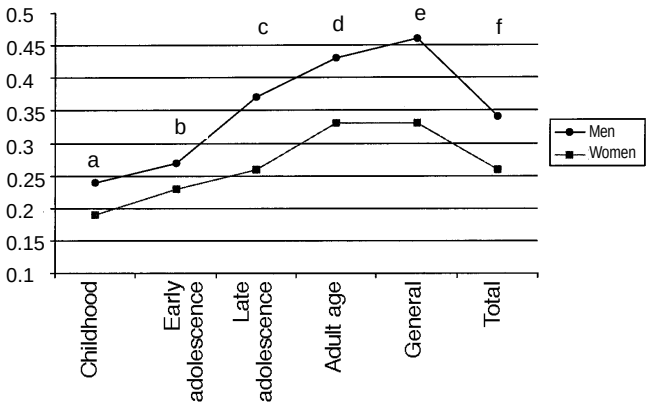
Duration of the untreated psychosis

The average of the untreated psychosis period of the sample was 60.5 ± 75.3 weeks, with a median of 28 weeks

TABLE 1. Demographic and clinical characteristics by gender

Variable	*Men n = 40*	*Women n = 37*	*Statistics*	*95% confidence interval*	*p*
Age (years)	27.2 (8.4)	28.4 (9.7)	t = 0.58; gl 75	–5.3-2.9	0.56
Single*	77.5	67.6	χ^2 = 0.9; gl 1		0.32
Unemployed*	42.5	32.4	χ^2 = 0.8; gl 1		0.36
Schooling (years)	11.4 (3.0)	10.5 (2.4)	t = 1.38; gl 75	–0.38-2.1	0.17
Hospitalization*	37.5	64	χ^2 = 5.7; gl 1		0.01
Age of onset (years)	26 (8.4)	27.5 (9.8)	t = 0.75; gl 75	–5.7-2.5	0.45
Diagnosis*					
Non-affective P.	62.3	29.2	χ^2 = 7.2; gl 1		0.007
Affective P.	37.7	70.8			
PANSS					
Positive	24.2 (4.5)	24.1 (5.5)	t = 0.01; gl 75	–2.2-2.3	0.99
Negative	20.3 (7.8)	21.5 (7.4)	t = 0.71; gl 75	–4.7-2.2	0.47
General	44.4 (7.9)	47.5 (9.6)	t = 1.58; gl 75	–7.1-0.8	0.11
Total	89.5 (16.7)	93.3 (17.2)	t = 1.00; gl 75	–11.6-3.8	0.32
Calgary Scale	6.4 (4.3)	4.9 (4.0)	t = 1.20; gl 49	–0.9-3.9	0.23
Mania Scale	31.7 (7.7)	38.5 (7.0)	t = 1.44; gl 8	–17.5-4.0	0.18
Hamilton-D Scale	31.2 (5.4)	28.7 (5.7)	t = 0.81; gl 14	–4.1-9.0	0.43

* Percentages (SD).



a n = 77 0.24 *vs* 0.19; t = 1.12; gl 71, p = 0.043
b n = 77 0.27 *vs* 0.23; t = 1.16; gl 75, p = 0.041
c n = 73 0.37 *vs* 0.26; t = 2.50; gl 71, p = 0.002
d n = 61 0.43 *vs* 0.33; t = 1.85; gl 59, p = 0.011
e n = 77 0.46 *vs* 0.33; t = 3.39; gl 75, p = 0.000
f n = 77 0.34 *vs* 0.26; t = 2.73; gl 75, p = 0.001

Figura 1. Premorbid functioning by gender

(range: 1-312 weeks). No differences were found in the DUP between men and women (average = 70.8± 79.4 vs 49.4 ± 69.9, respectively; z=–1.66; p = 0.09). The DUP was greater in the patients with low premorbid functioning in comparison with those who presented good premorbid functioning (average in weeks = 96.1 ± 97.9 vs 36.5 ± 41.5, respectively; z = –2.5; p = 0.009). No differences were observed between the patients with long and short DUP in the comparison by gender and diagnostic group.

Results according to gender, diagnostic group and premorbid functioning level by DUP are shown in table 3. It was established that the groups (men-women) were not different based on the Breslow-Day Tarone homogeneity test ($\chi^2 = 0.86$, gl 1, p = 0.35) and it was determined that the risk of low premorbid function was different for the type of DUP (estimated from odds ratio: 2.6; p = 0.050).

DISCUSSION

In this study of patients with first psychotic episode, differences were observed between men and women in regards to some clinical variables and premorbid functioning. In our sample, men in the group of non-affective psychosis predominated, a finding reported in other studies[2,12]. However, other authors report greater frequency in women[28] and others a frequency of 1:1[29]. These differences are because only patients with schizophrenia were included in some studies while patients with different psychotic disorders were included in this study. No differences in other demographic and clinical characteris-tics were observed, which agrees with previous reports[2,10,12,30,31]. Women were hospitalized more frequently, which can be explained, in the first place, because the diagnosis of affective psychoses was more common in this gender. It has been proposed that affective symptoms are recognized more frequently by the families and the patient him/herself as part of a mental health problem, conditioning the search for psychiatric care[29,32,33].

Low premorbid functioning presented in 40% of the patients included and deterioration was progressive through the vital cycle stages evaluated with the PAS, as was expected, because the subjects possibly would present the psychotic picture. The late adolescent and adult age stages were those that showed greater deterioration in premorbid functioning, suggesting the presence of the prodromic symptoms or the onset of the first psychotic symptoms, because of the acceleration of the physiopathological process expressed, in the last place, as a psychotic picture.

Premorbid functioning was lower in the men, deterioration being greater during late adolescence or adult age. This supports the observations of greater premorbid functioning reported in women[10,12,34,35]. Diagnosis of non-affective psychosis was related with low premorbid functioning in which gender did not interact in this association, since the risk of low premorbid functioning in the presence of non-affective psychosis is similar between men and women. The findings of this study are consistent with the association of low premorbid functioning and non-affective psychosis reported by other authors[11,36,37].

Some reports suggest a probable association between female gender with good premorbid functioning and short DUP and the male gender with low premorbid functioning and long DUP[38,39]. Similarly to previous stu-

TABLE 2. Distribution by gender and diagnostic group in the premorbid functioning level

Gender	*Low premorbid functioning n (%)*	*Good premorbid functioning n (%)*	*Odds ratio*	*95% confidence interval*
Men				
Non-affective psychosis	20 (64.3)	13 (28.3)	9.23	0.99-85.77
Affective psychosis	1 (3.2)	6 (13.0)		
Women				
Non-affective psychosis	8 (25.8)	12 (26.1)	5.00	0.89-28.7
Affective psychosis	2 (6.5)	15 (32.6)		

$\chi^2 = 8{,}53$; gl 1, p = 0,003.

TABLE 3. Distribution by gender and premorbid functioning level by DUP

Gender	*Long DUP > 28 weeks n (%)*	*Short DUP < 28 weeks n (%)*	*Odds ratio*	*95% confidence interval*
Men				
Low functioning	13 (34.2)	8 (20.5)	1.80	0.51-6.36
Good functioning	9 (23.6)	10 (25.6)		
Women				
Low functioning	7 (18.4)	3 (7.6)	4.66	0.96-22.46
Good functioning	9 (23.6)	18 (46.1)		

χ^2 = 3,99; gl 1, p = 0,046.

dies[10,40,41], the results of this study did not replicate the association between DUP and premorbid functioning level by gender; the association found was related with long DUP and low premorbid functioning, in which the gender did not represent a significant influence on this finding. On the other hand, when the sample was divided into low premorbid functioning and good premorbid functioning, it was observed that the patients with a DUP greater than 28 weeks had low premorbid functioning. Generally, DUP has been evaluated as a variable with normal distribution, when, in fact, it does not have this distribution, which generates inconsistencies in the different reports[42]. The results of our study support the heterogeneity in the DUP, converting it into a dependent variable that is determined by the premorbid functioning level. Consequently, low premorbid functioning conditions prolonged duration of untreated psychosis and inversely, good premorbid functioning conditions a short DUP.

In summary, the period prior to the appearance of the psychotic symptoms is heterogeneous in its duration and is influenced by several factors, among which gender is found. The evaluation of premorbid functioning, dividing it into low and good functioning, in order to have a more homogeneous description of the premorbid period, is useful to establish the different characteristics of the different phenotypes proposed for the psychotic disorders[12,43]. In conclusion, the duration of untreated psychosis is determined by premorbid functioning level and it is possible that men, as they have low premorbid functioning more frequently, take longer to look for specialized care to receive specific treatment, prolonging the duration of the untreated psychosis.

The results of this study seem to support the hypothesis that the duration of the untreated psychosis has no influence on the prognosis, but rather that it is the result of the premorbid functioning level regardless of gender[44].

The hypothesis that must be proven according to our findings is that the prognosis is determined by premorbid functioning and not by influence of the duration of untreated psychosis. The principal limitation of this study was the number of patients included and that it was cross-over, so that it is proposed to perform follow-up studies to determine the influence of the duration of untreated psychosis and the premorbid functioning in the prognosis.

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