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Gender Differences in Cognition and Social Cognition in Patients Affected by Psychosis in the Process of Psychosocial Rehabilitation

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Abstract

Objectives: to explore gender differences in cognition and social cognition in patients affected by psychosis in processes of psychosocial rehabilitation, and to establish a model of the relationship between psychopathology, cognition and social cognition as a function of gender, attending to relevant clinical, sociodemographic and outcome factors.

Methodology: a cross-sectional observational study of 124 non-affective schizophrenia spectrum patients included consecutively in a community rehabilitation program at Corporaciò Sanitària Parc Tauí (Sabadell, Barcelona), assessed through PANSS (using Wallwork's factors) and MATRICS Cognitive Consensus Battery.

Results: participants had a mean age of 40.2 years, 57.3% men and mainly schizophrenia (71.0%). We found gender differences favouring men in attention (p=0.045), working memory (p=0.013), and reasoning/problem solving (p=0.002) domains. No differences in social cognition was found. A linear regression model shows different participations for different domains, with a predominance of the influence of the cognitive/disorganized Wallwork's factor and patient's age. In the subsample of men, the model was quite similar to that of the total sample, but the influence of the disorganized factor decreases while that of age remains. In the women subsample, the model had even less influence of the disorganized factor or age. In general, the women's models described less variance.

Conclusions: Men affected by schizophrenia and included in the community rehabilitation program of our sample, present better attention, working memory and reasoning/problem solving than women, without differences in social cognition. In general, the models describe less variance in women.

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Psychosis, MATRICS, MCCB, social cognition, emotional processing, gender

Diferencias de género en cognición y cognición social en pacientes afectos de psicosis en proceso de rehabilitación psicosocial

Resumen

Objetivos: Explorar diferencias de género en cognición y cognición social en pacientes afectos de psicosis en proceso de rehabilitación psicosocial y establecer un modelo de relación entre psicopatología, cognición y cognición social en función del género y de factores clínicos, sociodemográficos y evolutivos relevantes.

Metodología: Estudio observacional transversal con 124 pacientes del espectro de la esquizofrenia incluidos en el Programa de Rehabilitación Comunitaria de la Corporaciò Sanitària Parc Taulí (Sabadell, Barcelona), evaluados mediante PANSS (factores de Wallwork) y la batería cognitiva MATRICS.

Resultados: Edad media 40.2 años, 57.3% hombres, principalmente esquizofrenia (71.0%). Encontramos diferencias de género a favor de los hombres en la atención (p = 0.045), memoria de trabajo (p = 0.013) y razonamiento/resolución de problemas (p = 0.002). No se encontraron diferencias en la cognición social. El modelo de regresión lineal muestra diferentes participaciones para diferentes dominios, con un predominio de la influencia del factor de Wallwork cognitivo/desorganizado y la edad del paciente. En la submuestra de hombres, el modelo fue bastante similar al de la muestra total, pero la influencia del factor desorganizado disminuye y la de la edad permanece. En la submuestra femenina, el modelo tuvo, incluso, menos influencia del factor desorganizado o la edad. En general, los modelos de mujeres explican menos varianza.

Conclusión: Los hombres afectos de esquizofrenia e incluidos en el Programa de Rehabilitación Comunitaria de nuestra muestra presentan mejor atención, memoria de trabajo y razonamiento/resolución de problemas que las mujeres, sin diferencias en la cognición social. En general, los modelos explican menos varianza en las mujeres.

Palabras clave

Psicosis, MATRICS, MCCB, cognición Social, procesamiento emocional, género.

INTRODUCTION

Cognitive deficit is a central feature in schizophrenia that can be observed along the continuum of the disease. It has been reported in advanced and chronic stages (Asarnow & MacCrimmon, 1978; Nuechterlein et al., 1992; Reichenberg, 2010), in patients with a first psychotic episode (Addington, Brooks, & Addington, 2003; McCleery et al., 2014; Mesholam-Gately, Giuliano, Goff, Faraone, & Seidman, 2009), in high-mental risk subjects (Keefe et al., 2006; Keshavan et al., 2012; Lam et al., 2018), and in first-degree relatives (Kuha et al., 2007; Torniainen et al., 2011). Cognitive impairment appears to be generalized, with deficits between 1 and 1.5 standard deviations below the mean compared to healthy subjects (Green, 2006; Heinrichs & Zakzanis, 1998). Factors such as gender and symptomatology could affect these results.

The neurotoxicity hypothesis has suggested that the duration of untreated psychosis (DUP) could affect abilities cognition. However, the outcome of the studies investigating the relationship between DUP and cognitive domains remains inconclusive. A recent meta-analysis (Bora, Yalincetin, Akdede, & Alptekin, 2018), which included 27 studies including 3,127 patients with a first-episode psychotic, only found a very small but significant association between longer DUP and reduced performance in planning/problem-solving ability. Although the meta-analysis did not investigate the social cognition domain, another recent study showed that DUP was not associated with social cognitive performance in first-episode psychotic patients (On, Cotton, Farhall, Killackey, & Allot, 2016).

These deficits are associated with alterations for the activities of daily life (Green, Kern, & Heaton, 2004), functional results (Feet et al., 2011; Green, Kern, Braff, & Mintz, 2000) and the quality of life of the patients (Tolman & Kurtz, 2010).

Previous studies have reported gender differences in schizophrenia related to clinical characteristics and functional outcomes (Ochoa, Usall, Cobo, Labad, & Kulkarni, 2012). In this sense, it has been reported that women have a later onset age than men (Arranz et al., 2015; Bertani et al., 2012; Coochi et al., 2014), better short and medium-term prognosis (Grossman, Harrow, Rosen, Faull, & Strauss, 2008; Häfner et al., 1998), and better social functioning (Cotton, Lambert, Schimmelmann, Foley, & Morley, 2009). Men present more severe negative symptoms (Koster, Lajer, Lindhart, & Rosenbaum, 2008; Torniainen et al., 2011; Torup et al., 2007) and disorganized symptoms (Galderisi, Bucci, Uçok, & Peuskens, 2012), while women show more positive and affective symptoms (Cotton et al., 2009; Morgan, Castle, & Jablensky, 2008).

Men and women present different cognitive patterns in healthy populations. In general, a greater effectiveness in mathematical and spatial tests is observed in men, although these aspects have been criticized and progressively it seems that new studies are reducing the differences (Hyde, 2016). Gender differences in verbal skills are also small and vary according to the type of verbal ability being assessed (eg., vocabulary, essay writing). The gender difference in 3D mental rotation shows a moderate advantage for men, but this gender difference only appears when these aspects are not included in the school curriculum (training in mental rotation skills eliminates these differences). The gender similarities hypothesis states that men and women are quite similar in most psychological variables, although not in all of them (Hyde, 2016). In fact, some cerebral and cognitive characteristics could be modulated by the environment, culture and practice (and many other influences) that interact with the menstrual cycle, the general level of hormones, and the current gender stereotypes (Jäncke, 2018).

In relation to cognitive performance in patients affected by schizophrenia, the results are still inconclusive (Krysta, Murawiec, Klasik, Wiglusz, & Krupka-Matuszczyk, 2013; Ochoa et al., 2012). Some studies have detected differences between men and women affected by schizophrenia in their cognitive functioning (Bozikas et al., 2010; Goldstein, Seidman, Santangelo, Knapp, & Tsuang, 1994; Hoff et al, 1998), while other studies have not been able to demonstrate them (Goldberg, Gold, Torrey, & Weinberger, 1995; Moriarty, Lieber, & Bennettetal, 2001; Salokangas, 1983). In samples of chronic patients, most studies show that men obtain worse results in attention tasks, language, and executive functions (Goldstein et al., 1994; Goldstein et al., 1998; Hoff et al., 1998; Seidman et al., 1997), and in late and immediate memory (Bozikas et al., 2012; Han et al., 2012). However, other studies have pointed out that women present worse cognitive results (Lewine, Walker, Shurett, Caudle, & Haden, 1996; Perlick, Mattis, Stastny, & Teresi, 1992). Conversely, other studies have not found gender differences in cognitive abilities or those differences are not clinically significant (Goldberg et al., 1995; Gogos, Joshua, & Rossell, 2010, Moriarty et al., 2001; Salokangas et al., 1983).

In samples of patients with a first psychotic episode, it has also been reported that women obtain better results in verbal learning and memory (Albus et al., 1997; Ayesa-Arriola et al., 2014; Hoff et al., 1998; Itting et al., 2015), while men obtain better results in executive functions (Ayesa-Arriola et al., 2014, Hoff et al., 1998). Zhang's study (2012) showed no sex differences in cognitive performance in first psychotic episodes using the neuropsychological battery RBANS, but did in chronic patients. Women afflicted with schizophrenia chronically had better scores in delayed and immediate memory (Zhang et al., 2012).

Considering social cognition skills, there are few studies that analyze gender differences (Navarra-Ventura et al., 2017). In samples of healthy controls, it has been pointed out that there would be gender differences in emotional processing (Gur et al., 2012; Kret & De Gelder, 2012) and in Theory of Mind (ToM) (Baron-Cohen, Kinickmeyer, & Belmonte, 2005; Christov-Moore et al., 2014).

The heterogeneity observed in these previous results could be attributable in part to methodological differences between the studies, such as the size of the samples, or to the different cognitive domains evaluated and the different tests used to assess each domain, making it difficult to interpret the results. It also makes research into cognitive dysfunctions related to the disease as well as the effect of drugs that can potentially act on cognitive dysfunction in schizophrenia difficult (Rodriguez-Jimenez et al., 2012). Therefore, it is important to advance our knowledge of influencing factors, such as gender, in these cognitive domains.

The objectives of our study are, on the one hand, to explore the gender differences in cognition and social cognition in patients affected by psychosis in the process of psychosocial rehabilitation and, on the other hand, to establish a model of the relationship between cognition and social cognition as a function of gender also considering clinical and evolutionary factors.

The main hypothesis of our analysis is that there are gender differences in cognition and social cognition, with a different pattern of psychopathological and clinical influences.

METHODOLOGY

Design, Population and Sample Selection

Cross-sectional observational study with consecutive patients included in the community rehabilitation program of Corporaciò Sanitària Parc Taui (Sabadell, Barcelona), between January 2014 and October 2017. The entity belongs to the public network and serves a reference population of 430,000 inhabitants, predominantly urban and in the economic, industrial, and services sectors. It is the only hospital center that treats serious mental pathology in the area. The outpatients treatment programs at our hospital attends approximately up to 1,800 people affected by non-affective psychosis.

Inclusion and exclusion criteria

We included 124 patients aged between 18 and 65 years, affected by any type of non-affective psychotic disorder according to criteria DSM-IV-TR (APA, 2002): schizophreniform disorder, schizophrenia (and subtypes), schizoaffective disorder (and subtypes), psychotic disorder not otherwise specified, and delusional disorder.

As exclusion criteria, we included the diagnoses of any affective psychoses, psychosis due to medical illness, due to the consumption of substances, and those patients with intellectual disabilities or difficulties in understanding or expressing themselves in the language. We also excluded patients with active drug or alcohol abuse. All the data were anonymized and analyzed separately from the researchers who collected them.

Program description

The community rehabilitation program of Corporaciò Sanitària Parc Taui (Sabadell, Barcelona) emerges as a need for specific attention to people affected by serious disorders of the psychotic sphere with functional or clinical difficulties that cannot be resolved at the outpatient level. Specific attention is provided at both social and psychotherapeutic levels, with group and individual interventions, rehabilitation strategies, cognitive rehabilitation, and labour or educational reintegration when appropriate. Likewise, our program has a specific section for psychoeducation and family follow-up, as well as a usefulness of coordination between the different levels of care and devices. The community rehabilitation program attends approximately up to 160 people per year, 80% of them affected by non-affective psychosis.

Instruments

We designed a general questionnaire for the collection of sociodemographic data and personal and family psychiatric records. Likewise, we collected key clinical and evolutionary data, including the age at onset of the disease, the years of evolution, the consumption of toxins, or the diagnoses according to DSM-IV-TR criteria (APA, 2002).

For the psychopathological evaluation, the scale of the Positive and Negative Syndrome Scale (PANSS) for schizophrenia (Kay, Fiszbein, & Opler, 1987) was administered in the Spanish version validated by Peralta and Cuesta (Peralta & Cuesta, 1994), using the factorialization according to Wallwork et al. (Wallwork, Fortgang, Hashimoto, Weinberger, & Dickinson, 2012), which includes five factors: Positive, Negative, Disorganized/Cognitive, Excitative, and Affective/Depressive.

Cognitive functioning was assessed through the MCCB (Kern et al., 2008, Nuechterlein et al., 2008). The MCCB evaluates seven cognitive domains through ten standardized tests and provides a global composite score of cognitive performance. The tests that include each domain are:

1) Speed of processing: Symbol coding (brief assessment of cognitive processes in schizophrenia, BACS); Category fluency (animal naming); Trail making test A (TMT, Part A).
2) Attention/vigilance: Continuous performance test (identical pairs) (CPT-IP).
3) Working memory: Weschler-III memory scale spatial span subtest (WMSR-III); Letter-number span (LNS).
4) Verbal learning: Hopkins verbal learning test – revised version (HVLT-R).
5) Visual learning: Brief visuospatial memory test – revised version (BVMT-R).
6) Reasoning and problem solving: Neuropsychological evaluation battery (NAB) – Mazes.
7) Social cognition: Mayer-Salovey-Caruso emotional intelligence test (MSCEIT), subtest of Management of emotions (Sections D and H).

For more information about the MCCB, it is available on the website (www.matricsinc.org). The ten tests were administered following the order established by Kern et al. (2008). The test application time is approximately one hour. The Spanish translation and standardization of the MCCB was used for the computerized correction of the test (Rodriguez-Jimenez et al., 2012). For the analysis of results we obtained the T scores without correcting either by age or by gender.

Statistic analysis

Descriptive and comparative according to parametric and non-parametric tests, as indicated (student's T for continuous variables and Chi-square, or bilateral Fisher's exact test for categorical variables). We agree on a significance level of less than 0.05. Finally, we performed a regression analysis on the global sample and by gender considering the different variables of the equation step-by-step. We used the SPSS v.21 program for the analyses.

RESULTS

Characteristics of the sample

These are summarized in **Table 1**: a total of 124 patients participated, with an average age of 40.2 years; 57.3% are men, 68.5% are single, and 56.5% reside with their family of origin. Most have basic studies (65.3%) and belong to the diagnostic group of schizophrenias (71.0%). At the cognitive level, compared to other previous samples, they show a similar severity to other samples of chronic patients but worse results than samples from the first episodes. In general, the values of the domains are between 1 and 2 standard deviations below normal.

Gender differences

We found gender differences in the years of evolution of the disease, the level of studies, the diagnosis, and the drugs of abuse backgrounds (**Table 1**). However, we

Table 1. Characteristics of the sample (n = 124).

n (%)	TOTAL n = 124	WOMEN 53 (42.7)	MEN 71 (57.3)	p; df; es
Age (years): mean (s.d.)	40.2 (10.0)	41.91 (9.3)	39 (10.3)	0.118
Marital status: n (%)				0.133
Single	85 (68.5)	32 (60.4)	53 (74.6)	
Married/Stable couple	27 (21.8)	13(24.5)	14 (19.7)	
Separated/Divorced	12 (9.7)	8 (15.1)	4 (5.6)	
Cohabitation: n (%)				0.148
Origin family	70 (56.5)	27 (50.9)	43 (60.6)	
Own family	30 (24.2)	15 (28.3)	15 (21.1)	
Assisted apartment	3 (2.4)	3 (5.7)	0 (0.0)	
Alone	21 (16.9)	8 (15.1)	13 (18.3)	
Level of studies: n (%)				0.004; 1
Primary studies, ESO until 16 y. old or without studies	83 (66.9)	28 (52.8)	55 (77.5)	
Secondary studies or higher	41 (33.1)	25 (47.2)	16 (22.6)	
Years of Education mean (s.d.)	16.9 (3.6)	17.6 (4.2)	16.4 (3.0)	0.080
Age at onset of the illness: mean (s.d.)	27.6 (8.9)	27.3 (9.4)	27.9 (8.5)	0.717
Evolution of disease: mean years (s.d.)	12.4 (9.5)	14.6 (9.7)	10.8 (9.0)	**0.025**; 122; 0.216
Diagnostic: n (%)				**0.002**; 1
Schizophrenia	88 (71.0)	30 (56.6)	58 (81.7)	
Other psychosis	36 (29.0)	23 (43.4)	13 (18.3)	
Previous drugs/alcohol abuse, n (% si)	61 (49.2)	10 (18.9)	51 (71.8)	**>0.001**; 1
Familial psychiatric history, n (% yes)	43 (34.7)	16 (30.2)	27 (38.0)	0.364
Type of familial psychiatric history, n (% yes)				0.964
Schizophrenia	16 (39.0)	7 (43.8)	9 (36.0)	
Depressive disorder	12 (29.3)	5 (31.3)	7 (28.0)	
Drugs/alcohol abuse	7 (17.1)	2 (12.5)	5 (20.0)	
Personality disorder	3 (7.3)	1 (6.3)	2 (8.0)	
Bipolar disorder	3 (7.3)	1 (6.3)	2 (8.0)	
Classic PANSS factors: mean (s.d.)				
Total PANSS	53.4 (10.8)	52.7 (11.2)	53.8 (10.6)	0.586
Classic Positive	11.6 (3.2)	11.5 (3.2)	11.5 (3.1)	0.737
Classic Negative	16.3 (6.3)	15.1 (6.4)	17.2 (6.0)	0.076
General	25.4 (4.7)	25.8 (4.8)	25.1 (4.6)	0.385

(continued)

n (%)	TOTAL n = 124	WOMEN 53 (42.7)	MEN 71 (57.3)	p; df; es
Wallwork PANSS factors: mean (s.d.)				
Positive	6.5 (2.2)	6.6 (2.5)	6.4 (2.0)	0.646
Negative	13.7 (6)	12.7 (6.4)	14.4 (5.7)	0.132
Cognitive/desorganized	6.0 (2.1)	6.3 (2.4)	5.8 (1.9)	0.203
Afective/Depressive	5.6 (2.5)	5.6 (2.6)	5.6 (2.5)	0.900
Excitative	5.1 (1.5)	5.3 (1.8)	4.9 (1.3)	0.263
MCCB domains: mean (s.d.), T values without correction				
Speed of processing	25.9 (10.8)	25.9 (11.7)	26.0 (10.2)	0.979
Attention/Vigilance	32.4 (10.8)	30.1 (10.4)	34.1 (10.9)	**0.045;** 119; 0.196
Working memory	36.3 (11.9)	33.2 (11.4)	38.5 (11.9)	**0.013**; 122; 0.221
Verbal learning	38.0 (9.8)	38.6 (10.2)	37.5 (9.6)	0.547
Visual learning	41.4 (13.6)	41.3 (13.1)	41.5 (14.0)	0.949
Reasoning and problem solving	40.4 (9.0)	37.5 (7.7)	42.5 (9.4)	**0.002**; 122; 0.296
Social cognition	34.1 (10.9)	33.3 (11.0)	34.6 (10.8)	0.500
Composite score	27.5 (11.9)	25.3 (12.0)	29.2 (11.7)	0.086

s.d.: Standard Deviation. **ESO**: Spanish compulsory secondary education (until 16 years of age). **PANSS**: Positive and Negative Symptoms Scale. **WALLWORK Factors**: PANSS factors following Wallwork et al., 2012. **MCCB**: MATRICS Consensus Cognitive Battery. p value calculated with corresponding test (Student t or Chi2). p: Level of signification. df: Degrees of freedom. es: Effect size. Signification if **p<0.05** (in bold).

did not observe gender differences in the age of onset of symptoms or in the psychopathological severity of symptoms according to the factors of the PANSS scale, whether using the three classical factors (positive, negative, and general), or the new Wallwork factors (positive, negative, disorganized, affective, and excitative) (Table 1). Despite multiple comparisons, we decided not to make corrections due to the characteristics of our study.

At the cognitive level, we found significant gender differences in the attention domains, in work memory and in reasoning and problem-solving, all in favour of men. There are no differences in the other domains, including that of social cognition or in the composite score (Table 1).

Association between cognition and clinical and evolutionary factors in the entire sample

Table 2 includes the bivariate correlations between the MCCB domains and psychopathological and evolutionary factors. In the total sample, the total PANSS score correlated negatively with all MCCB domains

Table 2. Pearson correlations between MATRICS and its domains with the psychopathological Wallwork PANSS factors, and other evolutional and sociodemographical factors.

MCCB Domains		Wallwork's PANSS Factors: TPANSS	Positive	Negative	Cognitive / Desorg.	Depressive	Excitement	EVO	Age	SCHO
Total n = 124	Speed of processing	-0.258**	-0.074	-0.175	-0.275**	-0.061	0.118	-0.268**	-0.472**	-0.186*
	Attention/vigilance	-0.280**	-0.214*	-0.152	-0.322**	-0.106	0.006	0.148	-0.196*	0.165
	Working memory	-0.130	-0.050	-0.048	-0.231**	0.055	-0.008	-0.281**	-0.382**	0.077
	Verbal learning	-0.250**	-0.148	-0.146	-0.236**	-0.010	-0.126	-0.053	-0.174	0.076
	Visual learning	-0.279**	-0.064	-0.126	-0.269**	-0.183*	-0.088	-0.197*	-0.303**	0.128
	Reasoning and problem-solving	-0.101	-0.032	-0.034	-0.037	-0.094	-0.039	-0.288**	-0.384**	0.012
	Social cognition	-0.198*	-0.047	-0.238**	-0.102	-0.038	-0.015	-0.001	-0.080	-0.004
	Composite score (overall)	-0.326**	-0.128	-0.222*	-0.277**	-0.115	-0.074	-0.262**	-0.402**	0.120

(continued)

MCCB Domains		Wallwork's PANSS Factors								
		TPANSS	Positive	Negative	Cognitive / Desorg.	Depressive	Excitement	EVO	Age	SCHO
Men n = 71	Speed of processing	-0.306**	-0.020	-0.251*	-0.269*	-0.221	0.150	-0.362**	-0.508**	0.164
	Attention/vigilance	-0.262*	-0.117	-0.165	-0.324**	-0.238*	0.075	-0.162	-0.235	0.173
	Working memory	-0.215	-0.020	-0.178	-0.317**	0.184	0.049	-0.317**	-0.442**	0.082
	Verbal learning	-0.203	-0.099	-0.115	-0.139	-0.125	-0.069	-0.112	-0.238*	-0.173
	Visual learning	-0.276*	-0.095	-0.125	-0.295*	-0.228	0.065	-0.286*	-0.332**	0.151
	Reasoning and problem-solving	-0.182	-0.162	-0.107	-0.019	- 0.178	0.094	-0.211	-0.335**	0.154
	Social cognition	-0.316**	-0.147	-0.274*	-0.153	-0.173	-0.225	0.028	- 0.083	-0.044
	Composite score (overall)	-0.411**	-0.139	-0.308*	-0.325**	-0.298*	-0.005	- 0.277*	- 0.431**	0.124
Women n = 53	Speed of processing	-0.206	-0.166	-0.101	-0.284*	0.122	0.092	-0.175	-0.443**	0.211
	Attention/vigilance	-0.332*	-0.319*	-0.198	-0.297*	0.076	-0.020	-0.055	-0.076	0.241
	Working memory	-0.052	-0.069	0.040	-0.098	0.126	-0.019	-0.158	-0.240	0.156
	Verbal learning	-0.303*	-0.205	-0.169	-0.354**	0.176	-0.194	-0.011	0.109	0.284*
	Visual learning	-0.287*	-0.028	-0.133	-0.248	-0.120	-0.253	0.085	-0.263	0.116
	Reasoning and problem-solving	-0.022	0.167	-0.029	0.009	0.037	- 0.142	-0.306*	-0.414**	-0.051
	Social cognition	-0.061	-0.066	-0.221	-0.037	0.137	0.197	-0.002	-0.056	0.051
	Composite score (overall)	-0.256	-0.109	-0.182	-0.209	0.096	-0.111	-0.181	-0.315*	0.181

PANSS : Positive and Negative Symptoms Scale. **MCCB**: MATRICS Consensus Cognitive Battery. **WALLWORK Factors**: PANSS factors following Wallwork et al., 2012. **TPANSS**: Total PANSS. **EVO**: Years of evolution of the illness. **SCHO**: Years of school. $^{**}p \leq .01$; $^{*}p \leq .05$

except with working memory and reasoning and problem-solving. The Wallwork positive factor was negatively associated with the attention/surveillance domain. The negative factor was also negatively associated with social cognition and composite score. The disorganized factor was negatively associated with speed of processing, attention and vigilance, verbal learning, visual learning and composite score. The depressive factor was only negatively associated with visual learning. The years of evolution were negatively associated with the speed of processing, working memory, visual learning, reasoning and problem-solving and the composite score. Age was negatively associated with processing speed, attention, working memory, visual learning, reasoning and problem-solving and composite score. In contrast, the years of schooling were negatively associated only with the speed of processing. Social cognition was not associated with age or years of schooling.

All cognitive test and domains were not affected by diagnostic (schizophrenia vs. other psychosis). Previous drug/alcohol abuse is statistically more frequent in people affected by schizophrenia compared with people diagnosed with other psychosis.

Association between cognition and clinical and evolutionary factors according to gender

Taking into account gender (**Table 2**), we found quite similar results in each of the genres with respect to the total sample. However, we must emphasize how in men, the attention-surveillance relationship is lost with the positive factor, while the negative factor is gained in the processing speed domain. There are also small variations regarding the influence of the disorganized factor or the depressive factor. The same happens in the bivariate analysis with the influence of age and years of evolution.

The years of schooling do not significantly influence the cognitive domains in men. In contrast, among women, many of the relationships found in the total sample were lost. For example, the negative PANSS factor and the depressive no longer influence the cognitive domains. The years of evolution already only negatively influence reasoning and problem-solving. Age influences the domains less and, to the contrary, the years of schooling positively influence the dominance of verbal learning.

Association model for the entire sample and model by gender

The linear regression model shows different participations for the different domains, with a predominance of the influence of the disorganized factor and age (Table 3). The most powerful explanatory model (R2 of 0.288) involves the disorganized factor, age and years of schooling for the processing speed domain.

In the subsample of men, the model is quite similar to that of the total sample, but the influence of the disorganized factor decreases and that of age remains. The most powerful explanatory model in men (R2 of 0.288) is still for the domain of processing speed, but only implies age and years of schooling (**Table 3**).

In the subsample of women, the model has even less influence of the disorganized factor and age. In general, models for women explain less. The most powerful explanatory model in women (R2 of 0.240) is still for the processing speed domain, but, in this case, it only includes the disorganized factor and age (**Table 3**).

DISCUSSION

To our knowledge, this is the first analysis in our environment that explores gender differences in cognition and social cognition in a naturalistic sample of severe patients in the process of psychosocial rehabilitation. Our results show how significant differences are observed in MCCB domains of attention, in working memory, and in reasoning and problem-solving, all in favour of men. There are no gender differences in social cognition related to emotional management.

The relationships between cognitive domains, clinical factors, and certain key evolutionary factors, such as age, age at onset of illness and years of schooling, present very different relationships for each of them. Both age and the

Table 3. Lineal regressions of Pearson correlations between MATRICS and its domains with the psychopathological Wallwork factors, and other evolutional and sociodemographical factors.

		Wallwork's Positive	Wallwork's Negative	Wallwork's Desorganized / Cognitive	Wallwork's Depressive	Wallwork's Excitement	Age	EVO	SCHO	R^2
TOTAL n = 124	MCCB Domains	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	
	Speed of processing			-0.186, *0.019* (-1.724/-0.161)			-0.461, *0.000* (-0.669 / -0.335)		0.194, *0.014* (0.120 / 1.040)	0.288
	Attention/ vigilance			-0.323, *0.000* (-2.509/-0.762)						0.097
	Working memory			-0.182, *0.031* (-1.930/-0.281)			-0.363, *0.000* (-0.634/-0.238)			0.169
	Verbal learning			-0.236, 0.*009* (-1.888/-0.281)						0.048
	Visual learning			-0.234 *0.007* (-2.550/-0.415)			-0.272, *0.002* (-0.601/-0.141)			0.131
	Reasoning and problem-solving						0.378, *0.000* (-0.492/-0.191)			0.136
	Social cognition		-0.241, *0.007* (-0.746/-0.118)							0.050
	Composite score (overall)			-0.237, *0.006* (-2.344/-0.392)			-0.379, *0.000* (-0.685/-0.262)			0.205

(continued)

		Wallwork's Positive	Wallwork's Negative	Wallwork's Desorganized / Cognitive	Wallwork's Depressive	Wallwork's Excitement	Age	EVO	SCHO	R^2
	MCCB Domains	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	B *p* (CI)	
Men n = 71	Speed of processing						-0.534, *0.000* (-0.733/-0.328)		0.228, *0.029* (0.081/1.476)	0.288
	Attention/ vigilance			-0.325, *0.007* (-3.192/-0529)						0.092
	Working memory			-0.233, *0.033* (-2.764/-0.116)			-0.408, *0.000* (-0.718/-0.224)			0.236
	Verbal learning						-0.243, *0.043* (-0.445/-0.007)			0.045
	Visual learning			-0.241, *0.038* (-3.417/-0.104)			-0.284, *0.015* (-0.696/-0.078)			0.141
	Reasoning and problem-solving						-0.328, *0.006* (-0.506/-0.090)			0.094
	Social cognition		-0.283, *0.018* (-0.974/-0.093)							0.066
	Composite score (overall)			-0.268, *0.022* (-2.969/-0.236)			-0.398, *0.001* (-0.749/-0.202)			0.235
Women n = 53	Speed of processing			-0.271, *0.030* (-2.507/-0.136)			-0.435, *0.001* (-0.850/-0.241)			0.240
	Attention/ vigilance	-0.319, *0.021* (-2.448/-0.207)								0.084
	Working memory									—
	Verbal learning			-0.354, *0.009* (-2.633/-0.388)						0.108
	Visual learning									—
	Reasoning and problem-solving						-0.414, *0.002* (-0.555/-0.131)			0.155
	Social cognition									—
	Composite score (overall)						-0.315, *0.026* (-0.799/-0.053)			0.080

PANSS : Positive and Negative Symptoms Scale. **MCCB**: MATRICS Consensus Cognitive Battery. **WALLWORK Factors**: PANSS factors following Wallwork et al., 2012. **EVO**: Years of Evolution of the Illness. **SCHO**: Years of School. **B**: Beta. **CI**: B 95% Confidence Interval.

disorganized factor of the PANSS were the factors that most influenced the cognitive domains. In addition, the explanatory models also presented some significant gender differences. The most powerful explanatory model in men was for the domain of speed of processing, but it only included age and years of schooling. By contrast, explanatory models in women showed even less influence of the disorganized factor and age and, in general, explanatory models explain less the cognitive domains. For example, the most powerful explanatory model in women is the same as in men (domain of speed of processing), but the influencing factors are different.

Social cognition correlates only with the negative symptoms and only in men. In the final model in men, the negative symptoms come back in, although the resulting R2 is very small.

The MATRICS initiative and total averages

The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative of the USA's National Institute of Mental Health (NIMH) had as one of its objectives the development of a cognitive consensus battery, and led to the design of the MATRICS Consensus Cognitive Battery (MCCB) (Kern et al., 2008, Nuechterlein et al., 2008) to be used in clinical trials. The battery has been translated into several languages including Spanish, with standardization and normative data of the MCCB in Spain (Rodriguez-Jimenez et al., 2012). Several studies that have used the MCCB show that patients with schizophrenia obtain lower scores compared to healthy controls in each of the seven cognitive domains (August, Kiwanuka, McMahon, & Gold, 2012; Fonseca et al., 2017; Keefe et al., 2011; Kern et al., 2011; Lystad et al., 2014; McCleery et al., 2014; Rajii et al., 2103; Rodríguez-Jimenez et al., 2015; Shamsi et al., 2011; Wu et al., 2016), showing a general deterioration pattern of the order of 1-2 standard deviations below the healthy controls.

There is some variability between which are the most altered domains in patients affected by schizophrenia using the MATRICS battery. For example, the study by Kern et al. (2011), concluded that the most affected domains in a sample of patients with schizophrenic and schizoaffective disorder compared to healthy controls, were processing speed and working memory, while the least affected domain was problem-solving/reasoning. The study by Rodríguez-Jiménez et al. (2015) concluded that the most affected domains in patients suffering from schizophrenia in Spain were verbal learning and visual learning, while those less affected were reasoning/problem-solving and social cognition. The authors point out that the differences with the Kern study (2011) in the most altered domains could be in part due to the selection of patients (the sample of North American patients was composed of patients with schizophrenia and schizoaffective disorder, whereas in the Spanish sample only patients affected by schizophrenia were included).

The study by McCleery et al. (2014) also showed that the most altered domain in patients affected with schizophrenia and patients with a first psychotic episode was the speed of processing. In addition, McCleery et al. (2014) showed that patients with a first psychotic episode had a pattern of impairment similar to that of chronic patients, but they had preserved the cognitive skills of working memory and social cognition.

In our sample, the most altered domains were speed of processing and attention/vigilance. By contrast, visual learning and reasoning and problem-solving were more preserved, but equally altered. In any case, our cognitive results would present certain differences with previous studies (Kern et al., 2011; McCleery et al., 2014; Rodriguez-Jimenez et al., 2015). Although in general there are worse results in speed of processing (Kern et al., 2011; McCleery et al., 2014) and better results in reasoning and problem-solving (Kern et al., 2011; McCleery et al., 2014; Rodriguez-Jimenez et al., 2015), the different previous studies included different types of patients and settings, which could affect the results.

Relationship between psychopathology and cognition

So far, different previous articles have attempted to find an explanatory model of the relationships between cognitive domains and psychopathological factors in psychosis, but few of them take into account the MATRICS initiative.

In the August et al. (2012) sample, the performance of MCCB was minimally related to the type of clinical symptom or severity. The total SANS scores correlated significantly with the speed of processing, working memory, or the general composite score. The disorganized syndrome factor (according to the BPRS) was negatively correlated with the overall total score of MCCB, speed of processing, verbal learning, visual learning ($rs = -0.21$, $p = 0.027$) and, more robustly, with social cognition. In our sample, the disorganized factor also has a very important relationship with the different cognitive domains. However, we have to highlight how social cognition in our total sample, measured by the MSCEIT, was not influenced by any clinical variables.

In the study by Bagney et al. (2015) of a sample of Spanish patients suffering from schizophrenia, the results indicated that the relationship between psychopathology and cognition measured by MATRICS depends above all on the PANSS elements related to cognitive functioning (grouped under the cognitive/disorganized factor), more than with those related to negative symptoms. In fact, in the partial correlations, the disorganized PANSS factor following the factorialization of Wallwork et al. (2012) was the only one with significant relationships. In the final models, in addition, only the disorganized factor is included in the models, together with certain clinical factors (age, gender, and antipsychotic dosage) but with a very low explanatory power (adjusted R2). According to these last authors, their results support a cognitive independence between cognitive performance and negative symptoms in patients with schizophrenia.

Finally, the study by Wu et al. (2016) analyzes a sample of controls, first episode psychosis (FEPs) never treated (drug-naïve) patients, and a third sample of chronic patients affected by schizophrenia with at least five years of evolution of the disease. In FEPs, education (years of education), total PANSS score and negative symptom scores (according to the classic PANSS factorialization of three factors) contributed independently to the total score of the MCCB, with a variance of 30%. On the other hand, in chronic patients, years of education and classic PANSS negative symptoms represented 20.2% of the variance in the total score of MCCB.

In our sample, final models are quite robust, especially for speed of processing. The Wallwork cognitive PANSS factor appeared as the main factor explaining the results for the different cognitive domains (except in reasoning/problem-solving and in social cognition). Our own results also support the independence of most of the cognitive domains in psychosis and the negative symptoms grouped into the negative factor of the factorialization of Wallwork et al. (2012), except in the case of social cognition, and in this last case also with a very low R2 (0.050). In our model, not only age but also years of schooling are shown as relevant factors in the models.

Gender differences in MATRICS

Gender differences in the MCCB have been reported in the normative samples of healthy volunteers from different countries. In the North American normative sample (Kern et al., 2008), healthy male participants obtained better results than healthy women in reasoning/problem-solving and working memory. Women had better results than men in verbal learning, and there were no significant gender differences in the other four cognitive domains nor in the composite score. In the Spanish normative sample (Rodriguez-Jimenez et al., 2012), the effects of gender were seen in four cognitive domains: men performed better in attention/vigilance, reasoning/problem-solving, and working memory. In contrast, women scored better in social cognition. There were no differences in the other three cognitive domains or the composite index. Subsequently, the authors find that the effects of gender on cognitive functioning are independent of the diagnosis and, therefore, conclude that these differences are also observed in patients affected by schizophrenia (Rodriguez-Jimenez et al., 2015).

In data obtained from 250 healthy Norwegian subjects aged 12-59 years (Mohn, Sundet, & Rund, 2012), the group of adult women scored higher than men in speed of processing, verbal learning and social cognition; while men scored higher in reasoning/problem-solving and attention/vigilance.

Moreover, in a sample of healthy Chinese volunteers (Shi et al., 2015), men had better scores in working memory tests (WMS-III and Spatial Span) and in reasoning (NAB-Mazes). On the other hand, women had better scores in speed of processing tests (BACS Symbol Coding) and social cognition (MSCEIT). Therefore, except for some differences between these studies, the different authors coincide in pointing out for healthy men better results in visual spatial tasks, and for women better results in verbal tasks and social cognition.

Few studies have specifically addressed the effects of gender on MCCB administered in psychiatric populations. In a sample of FEPs García et al. (2016) found that women had a better cognitive profile in tasks related to speed of processing and verbal learning. Radjji et al. (2013) reported the effects of gender on the subtests of MCCB in a sample of healthy controls and patients with schizophrenia. Women in their total sample had better results in a speed of processing test (DSC-Digit Symbol Coding), a verbal learning test (HVLTR-Hopkins Verbal Learning Test Revised), and in social cognition (measured by the MSCEIT, Mayer-Salowey-Caruso Emotional Intelligence Test). Men had better scores in tests that measure reasoning and problem-solving (Mazes), and in working memory (SSP, Spatial Span). Recently, Zhang et al. (2017), using MATRICS, found that male patients suffering from schizophrenia performed significantly worse than women in speed of processing, verbal learning, visual learning, and social cognition.

In the cited study by Bagney et al. (2015), gender, along with the cognitive/disorganized factor but also with other clinical factors (age and antipsychotic dosage), appeared in explanatory models for all MCCB domains, but, as we have also mentioned, the explanatory power of the models were low.

Our sample showed a significantly better level of education in women but higher evolution of the disease (years). Historically these are aspects that the literature has associated with a worse cognitive performance. On the other hand, cognitive performance in women is significantly lower in at least three domains. As we pointed out in the introduction, previous studies have reported gender differences in schizophrenia related to clinical characteristics and functional outcomes (Ochoa, Usall, Cobo, Labad, & Kulkarni, 2012). In this sense, it has been reported that women have a later onset age than men (Arranz et al., 2015; Bertani et al., 2012; Coochi et al., 2014), better short and medium-term prognosis (Grossman, Harrow, Rosen, Faull, & Strauss, 2008; Häfner et al., 1998), and better social functioning (Cotton, Lambert, Schimmelmann, Foley, & Morley, 2009). It is possible that later onset women could reach better educative levels than men. It is also possible that women in psychosocial rehabilitation were more severe than their male counterparts, but both aspects were hard to find out with transversal analysis.

Moreover, our study showed explanatory models including different factors differentiated by gender, and these analyses allow us to show a quite different behavioural models after splitting the data. While in women speed of processing was influenced by the disorganized factor, in the subsample of men it was not (but it was by current age and years of schooling). Likewise, social cognition in men was influenced by the negative PANSS factor, but it was not in women. Other small differences (Table 3) show how gender analysis can bring greater understanding (and complexity) to these relationships.

Social cognition, MCCB and gender differences

As we have mentioned, there are few studies that analyze gender differences in emotional processing and ToM (Baron-Cohen et al., 2005; Christov-More et al., 2014; Gur et al., 2012; Kret and De Gelder, 2012; Navarra-Ventura et al., 2017).

Gur et al. (2010), in a sample of 3,500 young people between 8 and 21 years of age, finds that women outnumber men in attention, memory of words and faces, speed of reasoning, and in all tests of social cognition used (Penn Emotion Identification Test, Penn Emotion Differentiation Test, and Penn Age Differentiation Test). Men outperform women in spatial and sensorimotor processing and in motor speed.

In another healthy population, Pardeller et al. (2014) did not find gender differences in any of the MSCEIT domains, including the MCCB emotions management tests.

On the other hand, in clinical samples with patients suffering from schizophrenia, gender differences in emotional processing have been pointed out. For example, Scholten et al. (2005) found worse performance in samples of patients with schizophrenia compared with controls, but in addition, there were also gender differences within the group of patients, since female patients obtained better results in the Benton and Allen facial recognition test. Likewise, in the study by Erol et al. (2013), also with samples of controls and schizophrenia patients, male patients performed worse than females in the facial emotion identification test (FEIT, total and negative scores).

To the contrary, other studies did not find gender differences in emotional processing. The meta-analysis of Kohler et al. (2010) finds gender differences in emotional processing in normal populations, with worse results among men. However, in clinical samples with schizophrenia, these differences were lost and the authors suggest that the effects of the disease on patients conceal any possible gender-related difference.

In this sense, a recent study by Navarra-Ventura et al. (2017), very exhaustive, did not find significant gender differences using the POFA (pictures of facial affect test) as a measure of emotional processing.

Moreover, focusing now on the MSCEIT of the MCCB, in a sample of DeTore et al. (2018), including not only patients with schizophrenia but also some with other severe mental disorders, negative symptoms (measured with the factorialization of White et al., 1994), were correlated with the emotional management scale of the MSCEIT.

In another clinical samples, as reported by Radjji and colleagues (2013), women obtained better results in social cognition, using the same test as in our study (MSCEIT). Similar results in terms of social cognition using the MSCEIT were replicated in Zhang et al. (2017).

In our sample, we did not obtain significant gender differences in emotional management. Consequently, it would support the hypothesis of Kohler and collaborators (2010): gender differences in social cognition in normal populations could be lost after the onset of the disease. Obviously, a series of prospective and broader studies would be necessary to validate this hypothesis.

Limitations and strengths of the study

The main limitations of the study are its transversal design, which is also very specific for patients undergoing rehabilitation. Another limitation is the lack of control of cognitive evaluation by drug dosage, drug treatment, or changes/stability in the last three months. Gender differences in our sample could be related too to the sample size. We also did not control by DUP, IQ, or inclusion in cognitive rehabilitation programs. Rehabilitation treatment could also affect cognitive outcomes.

As the main strengths, we had the naturalistic characteristic of the sample, the adequacy of the selection of the sample (since our program is the only provider of psychosocial rehabilitation in the services area), as well as the specific analysis of gender.

CONCLUSIONS

There were gender differences in some of the different MCCB domains but not in all. In our sample of patients who have undergone psychosocial rehabilitation, men have better performance in attention-vigilance tasks, working memory, and in reasoning and problem-solving. No differences were observed in social cognition (emotional management) or in other cognitive domains.

The explanatory models for the different cognitive domains, according to clinical (psychopathological) and evolutionary variables, were partially different depending on gender. In general, cognitive domains were better explained in the men than in women.

Gender analysis of cognitive function in patients affected by a psychotic disease could provide useful information for the approach in the process of rehabilitation. It could help us to understand the different pathways of cognitive deterioration evolving in people affected by a psychotic disease.

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Conflict of interest

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