Progress in Neuro-Psychopharmacology & Biological Psychiatry 48 (2014) 149–154

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp

No sex differences in neuropsychological performance in first episode psychosis patients ☆

Rosa Ayesa-Arriola [a,b,*], Jose Manuel Rodriguez-Sanchez [a,b], Elsa Gomez-Ruiz [a], Roberto Roiz-Santiáñez [a,b], Lauren L. Reeves [c], Benedicto Crespo-Facorro [a,b]

[a] Department of Psychiatry, Marqués de Valdecilla University Hospital, IFIMAV, School of Medicine, University of Cantabria, Santander, Spain
[b] CIBERSAM, Centro Investigación Biomédica en Red Salud Mental, Madrid, Spain
[c] Department of Psychology, Temple University, Philadelphia, PA, USA

ARTICLE INFO

Article history:
Received 19 June 2013
Received in revised form 16 September 2013
Accepted 17 September 2013
Available online 25 September 2013

Keywords:
Neuropsychology
Psychosis
Sex

ABSTRACT

Objective: The purpose of this study was to verify whether male patients with psychosis have greater neurocognitive impairment than female patients at illness onset.
Method: Participants with a first episode of psychosis (74 women/86 men) and healthy controls (62 women/97 men) were assessed with an extensive neuropsychological test battery.
Results: Women in the clinical group were older at illness onset and had achieved higher formal education than men. This trend was the same for the control group. The patient group presented with lower premorbid IQ compared to healthy controls, and performed below for most neuropsychological tests. Women scored higher than men on a test of verbal memory, whereas men scored higher than women on a test of reaction time, visual memory, and a planning task. There were no group-by-sex interactions for any of the neuropsychological tests.
Conclusion: The present study shows that at the onset of psychosis there are no differences between males and females in neuropsychological performance. The differential pattern of cognitive performance observed is similar to that in healthy males and females. Furthermore, females with a late onset of psychosis may represent a subgroup with specific visuospatial and problem solving impairments.
Significant outcomes:

1- The present study does not give support to the hypothesis that male have worse neurocognitive functioning than female patients at illness onset.
2- The neuropsychological profile of sex differences observed among patients is consistent with that observed among controls.
3- We identified a subgroup of female patients with late onset that differed in their degree and pattern of cognitive impairment with regard to their male counterparts.

Limitations:

1- Factors other than neurocognitive functioning may underlie the more severe impairment observed in the onset and course of illness in men.
2- Although the study used a broad battery of well established tests, this battery may lack sensitivity to detect sex differences.
3- A longitudinal study is required to further explore whether sex specific deficits require special rehabilitation programs for patients with schizophrenia.

Abbreviations: BPRS, Brief Psychiatric Rating Scale; CASH, Comprehensive Assessment of Symptoms and History; CDSS, Calgary Depression Scale for Schizophrenia; CI, Confidence interval; CPT, Continuous Performance Test; DAS, Disability Assessment Scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; DUI, Duration of untreated illness; DUP, Duration of untreated psychosis; FEP, First episode psychosis; GP, Grooved Pegboard; GNI, General neurocognitive impairment; GCF, Global cognitive functioning; MANCOVA, Multiple analysis of covariance; NOS, Not otherwise specified; IQ, Intelligence quotient; SAPS, Scale for the Assessment of Positive symptoms; SANS, Scale for the Assessment of Negative symptoms; SCID, Structured Clinical Interview for DSM; SD, Standard deviation; SPSS, Statistical Package for Social Science; OR, Odds ratio; PAFIP, Program of attention and intervention first-episode psychosis; RAVLT, Rey Auditory Verbal Learning Test; TMT, Trail Making Test; ToL, Tower of London Test; YMRS, Young Mania Rating Scale.

☆ Funding: Instituto de Salud Carlos III (FIS CP07/00008), Fundacio Seny, Fundación Marqués de Valdecilla.

* Corresponding author at: Department of Psychiatry, Marqués de Valdecilla University Hospital, Avda. Valdecilla s/n, 39008, Santander, Spain. Tel.: +34 942 202537; fax: +34 942 203447.
E-mail address: rayesa@humv.es (R. Ayesa-Arriola).

0278-5846/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pnpbp.2013.09.009

1. Introduction

Over the last two decades it has been reported that males have a worse course of psychosis compared with female patients under all diagnostic classifications (Grossman et al., 2008; Harrison et al., 1996). Men have a more severe form of the illness characterized in part by higher incidence and earlier onset (Abel et al., 2010), they tend to deteriorate more rapidly (Larsen et al., 1996), and they exhibit greater functional impairments that are not related to the development of symptoms (Hafner and an der Heiden, 1997). These lines of research support the hypotheses regarding the importance of biological processes in the onset and course of schizophrenia, suggesting that slowed neurodevelopment may be associated with male schizophrenia and may contribute to earlier age of onset and fewer years of education (Guerguerian and Lewine, 1998).

The less severe course of schizophrenia in women, relative to men, may be attributable to higher neurocognitive function in early stages of illness. Lewine (2004) found that female status predicted higher neuropsychological scores in schizophrenia patients. Additionally, some studies have noted that male patients with schizophrenia are more impaired than female patients on measures of language and verbal memory, executive functioning, attention and visuospatial ability (Goldstein et al., 1998; Han et al., 2012). However, others have found no significant sex differences in cognitive functioning (Goldberg et al., 1995). Furthermore, studies with fist-episode psychosis (FEP) patients show mixed results (Albus et al., 1997; Hoff et al., 1998).

These controversies may be due to the use of small and heterogeneous samples, the use of neuropsychological batteries that do not assess a wide array of cognitive abilities, and the lack of control groups (Goldstein et al., 1998; Roesch-Ely et al., 2009). Of particular importance is to examine whether differences found between male and female schizophrenia patients reflect differences observed between the two sexes in the general population (Longenecker et al., 2010). Moreover, it is critical to control for confounding factors on neuropsychological performance, such as education, age at testing, and illness severity (Zhang et al., 2012). The present study was designed to address such methodological weaknesses in previous studies in an attempt to elucidate sex differences in neurocognition.

1.1. Aims of the study

The aim of our study was to explore whether there is a difference in neurocognitive performance in male versus female FEP patients compared to healthy males and females. We hypothesized that FEP male patients would have lower performance than females on measures of verbal memory, executive functioning, and attention.

2. Methods

2.1. Subjects

The patient group consisted of 160 medication naïve subjects (age range: 16–60, mean: 32.11 years), 86 males and 74 females, included in the first episode psychosis program of Cantabria, Spain (PAFIP), from January 2005 to December 2010. The study was approved by the Marqués de Valdecilla University Hospital review board, and written informed consent was obtained from all subjects after complete description of the study (Pelayo-Teran et al., 2008). Referrals to the PAFIP come from the inpatient unit and emergency room at the University Hospital Marques de Valdecilla, community mental health services and other community health care workers in the entire region of Cantabria and there were no biases in the way patients were referred. The age-corrected incidence rate for schizophrenia spectrum disorder was of 1.38 per 10,000 reflects that mostly all new cases in the region are referred and included in our program. As a clinical program, PAFIP includes inpatient and outpatient care, and provides specific and personalized clinical attention, including psychotherapeutic and psychopharmacological treatment of patients and also family interventions, from the onset of the illness for up to three years. The patients met the following criteria: 1) 15–60 years of age; 2) living in the catchment area; 3) experiencing their first episode of psychosis; 4) no prior treatment with antipsychotic medication or, if previously treated, a total life time of adequate antipsychotic treatment of less than 6 weeks; and 5) DSM—IV criteria for brief psychotic disorder, schizophreniform disorder, schizophrenia, not otherwise specified (NOS) psychosis or schizoaffective disorder. The diagnoses were confirmed by the Structured Clinical Interview for DSM—IV (SCID—I) (First et al., 1996) conducted by an experienced psychiatrist, 6 months on from the baseline visit.

A group of 159 healthy volunteers (age range: 15–51 years, mean: 29.01 years), 97 male and 62 female, were initially recruited from the community through advertisements in key locations in the community. Control subjects were selected as much similar as possible to our clinical sample in relevant sociodemographic characteristics: age, sex distribution, educational and socioeconomic level. They had no current or past history of psychiatric, neurological or general medical illnesses, including substance abuse and significant loss of consciousness, as determined by using an abbreviated version of the Comprehensive Assessment of Symptoms and History (CASH) (Andreasen et al., 1992).

2.2. Baseline demographic, clinical and functional variables

Age, education, age of illness onset, socioeconomic, employment and marital status, and duration of untreated psychosis (DUP) was recorded from patients, relatives and medical records. Symptoms of psychosis were assessed with the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). The SANS and SAPS scores were used in generating dimensions of symptoms (negative, disorganized and psychotic) (Grube et al., 1998). Depressive and mania symptoms were assessed with the Calgary Depression Scale (CDS) (Addington et al., 1993) and Young Mania Rating Scale (YMRS) (Young et al., 1978), respectively. General psychopathology was assessed with the Brief Psychiatric Rating Scale (BPRS) (Flemenbaum and Zimmermann, 1973), and functioning with the Global Assessment of Functioning (GAF) (Hall, 1995) and the Disability Assessment Scale (DAS) Spanish version (Mañá et al., 1998).

2.3. Neuropsychological assessment

The neuropsychological evaluation was performed at any time between week-6 and week-13, as this time is considered optimal for patients' stabilization (Gonzalez-Blanch et al., 2007). All participants, FEP and healthy volunteers, completed the test in the following standardized sequence (scores considered in brackets): 1 — the Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1964) (trials 1–5, list recall, and list recognition discrimination subscores); 2 — WAIS—III digit symbol subtest (Wechsler, 1997) (standard total score); 3 — Grooved Pegboard Test (Lezak, 1995) (time to complete with dominant hand); 4 — Corsi Blocks (Wechsler, 1997) forward and backward subtest (span score); 5 — The Zoo Map Test (Evans et al., 1997) (first and second conditions); 6 — Tower of London Test (ToL) (Shallice, 1982) (total correct and total moves score); 7 — Rey Complex Figure (RCF) (Osterrieth, 1944) (copy figure and delayed recall); 8 — Trail Making Test (TMT) (Reitan and Wolfson, 1985) (trails A and B); 9 — WAIS—III digits forward and backward subtests (Wechsler, 1997) (standard total score); 10 — WAIS—III letter–number sequencing subtest (Wechsler, 1997) (standard total score); 11 — WAIS—III vocabulary subtest that was used as measure of premorbid IQ (Wechsler, 1997) (standard total score); 12 — Stroop Test (Golden, 1975) (color–word); 12 — letter (FAS) (Spreen, 1990) and semantic (animal) (Carew et al., 1997) fluency tests; 14 — Eyes Task (Baron-Cohen et al., 2001) (total correct score); 15- Continuous