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A cross-sectional and longitudinal structural magnetic resonance imaging study of the post-central gyrus in first-episode schizophrenia patients

Adele Ferro [a,*], Roberto Roiz-Santiáñez [b,c], Victor Ortíz-García de la Foz [b,c], Diana Tordesillas-Gutiérrez [c,g], Rosa Ayesa-Arriola [b,c,d], Noemi de La Fuente-González [b,c], Lourdes Fañanás [c,e], Paolo Brambilla [a,f], Benedicto Crespo-Facorro [b,c]

[a] Department of Experimental Clinical Medicine, Inter-University Center for Behavioral Neurosciences (ICBN), University of Udine, Udine,Italy
[b] Department of Psychiatry, University Hospital Marqués de Valdecilla, School of Medicine, University of Cantabria-IDIVAL, Santander, Spain
[c] CIBERSAM, Centro Investigación Biomédica en Red Salud Mental, Madrid, Spain
[d] Psychosis Studies Department, Institute of Psychiatry, London, England
[e] Departament de Biologia Animal, Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain
[f] IRCCS "E. Medea" Scientific Institute, UDGEE, Udine, Italy
[g] Neuroimaging Unit, Technological Facilities, IDIVAL, Santander, Spain

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ABSTRACT

The post-central gyrus (PoCG) has received little attention in brain imaging literature. However, some magnetic resonance imaging (MRI) studies have detected the presence of PoCG abnormalities in patients with schizophrenia. Fifty-six first-episode schizophrenia patients, selected through the program of first-episode psychosis (PAFIP) and carefully assessed for dimensional psychopathology and cognitive functioning, and 56 matched healthy controls were scanned twice over 1-year follow-up. PoCG gray matter volumes were measured at both time-points and compared between the groups. Differences in volume change over time and the relationship between PoCG volume and clinical and cognitive variables were also investigated. The right PoCG volume was significantly smaller in patients than in controls at the 1-year follow-up; furthermore, it was significantly smaller in male patients compared with male controls, with no differences in female. Although there was no significant time by group interaction in the overall sample, a trend-level interaction was found for the right PoCG in males. This is the first study, as per our knowledge, to focus on PoCG in first-episode schizophrenia patients. The presence of PoCG abnormalities in the first year of schizophrenia suggests a possible contribution to the pathophysiology of the illness, probably as part of a more extensive network of abnormalities.

1. Introduction

Schizophrenia (SCZ) is a complex brain disease that affects thoughts, beliefs, perception of reality, volition, emotions, and behavior. Although abnormal functioning of the parietal lobe (PL) has been associated with psychotic experiences (Spence et al., 1997), involvement of the PL in SCZ remains unclear.

The main etiological models focus on the prefrontal cortices as prime candidates for cognitive disturbances in patients with SCZ. The possible role played by PL in the disorder has not been as extensively studied, although its implication in several neurocognitive processes, which are impaired in patients with SCZ (Sirigu et al., 1999; Blakemore et al., 2003; Bellani and Brambilla, 2008), has been suggested.

Moreover, in a three-year longitudinal study, we have previously demonstrated an association between cognitive deficits and progressive PL volume loss in schizophrenia spectrum disorder patients (Ayesa-Arriola et al., 2013), analyzing a sample partially overlapping with the present one.

Compared with other areas of the brain, PL has received little attention in the literature on brain imaging. Nevertheless, several magnetic resonance imaging (MRI) studies have found deficits in PL volumes or some of its subareas in SCZ patients (for a review, see Bellani et al., 2010), suggesting an involvement in the pathophysiology of the illness in a fronto-parietal network. PL consists of the post-central gyrus (PoCG), superior parietal lobule, and inferior parietal lobule (IPL), which is further subdivided into the

* Corresponding author.
E-mail address: adele.ferro@uniud.it (A. Ferro).

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supramarginal gyrus (SMG) and angular gyrus (AG), the precuneus, and the posterior cingulate gyrus (Crespo-Facorro et al., 2000).

PoCG (Brodmann area 1,2,3) is the most anterior area and divides the anterior and posterior parietal cortices. The primary somatosensory cortex (SI) is located in this area. PoCG contains a somatotopic representation of information from the contralateral half of the body and is the main sensory receptive area for the sense of touch and kinesthesia.

To the best of our knowledge, only a few structural MRI studies have investigated PoCG in SCZ patients using a region of interest (ROI) method, with the results being inconclusive (Niznikiewicz et al., 2000; Nierenberg et al., 2005; Zhou et al., 2007). Zhou et al. (2007) reported a reduction of PoCG gray and white matter in patients with SCZ compared to healthy subjects.

Alterations in white matter connectivity may reflect abnormalities at the level of the gray matter (Brambilla and Tansella, 2007). Douaud et al. (2007) observed reduced white matter integrity in two of major ascending tracts of the SI and bilateral gray matter loss in SI in SCZ suggesting they may be closely related, possibly constituting a structural substrate of the disease.

Other studies using voxel-based morphometry (VBM) found a decrease in PoCG volume at the first-episode of schizophrenia (FES) (Job et al., 2002) and before the onset of the illness (Dazzan et al., 2012). Similarly, a recent meta-analysis (Glahn et al., 2008) on results from 31 VBM studies pointed out a decrease in gray matter density in a distributed network of regions, including PoCG, in patients with SCZ compared with controls.

Interestingly, some VBM studies suggested a correlation between PoCG volume and severity of hallucinations (Garcia-Marti et al., 2008; Nenadic et al., 2010).

The present study aimed to assess PoCG gray matter volume differences between FES patients and healthy subjects (at baseline and 1-year) and investigate whether patients would present different pattern-of-volume changes using MRI. Also, the possible relationships among PoCG measures and clinical (i.e., symptomatology) and several cognitive variables were considered to clarify the role of PoCG, as part of a more extended brain network, in possibly sustaining SCZ symptomatology and cognitive impairment. On the basis of the literature on PL and the few cross-sectional studies on PoCG, we hypothesized that there would be some abnormalities in PoCG morphometry in FES patients. To the best of our knowledge, this is the first longitudinal study focusing on PoCG volume in FES patients using a ROI method.

2. Methods

2.1. Study setting and financial support

Data for the present investigation were obtained from an ongoing epidemiological and three-years longitudinal intervention program of first-episode psychosis (PAFIP) conducted at the outpatient clinic and the inpatient unit at the University Hospital Marques de Valdecilla, Spain (Pelayo-Teran et al., 2008). Conforming to international standards for research ethics, this program was approved by the local institutional review board. Patients meeting inclusion criteria and their families provided written informed consent to be included in the PAFIP. The Mental Health Services of Cantabria provided funding for implementing the program.

2.2. Subjects

Patients were drawn from a large prospective longitudinal study on first-episode psychosis (PAFIP) conducted at the University Hospital Marques de Valdecilla, Santander, Spain. A detailed description of our program has been previously reported (Pelayo-Teran et al., 2008). Other MRI studies have been written based on PAFIP program. Patients referred to the program were selected if they met the following criteria: 1) age 15–60 years; 2) lived in the catchment area; 3) were experiencing their first-episode of psychosis; 4) had no prior treatment with antipsychotic medication or, if previously treated, a total life time of adequate antipsychotic treatment of less than 6 weeks; 5) and met DSM-IV criteria for schizophrenia, schizophreniform disorder, brief psychotic disorder, schizoaffective disorder or not otherwise specified psychosis. Patients were excluded for any of the following reasons: 1) meeting DSM-IV criteria for drug dependence (except nicotine dependence), 2) meeting DSM-IV criteria for mental retardation, 3) having a history of neurological disease or head injury. Our operational definition for a "first-episode of psychosis" included individuals with a non-affective psychosis (meeting the inclusion criteria defined above) who have not received previously antipsychotic treatment regardless of the duration of psychosis. Individuals who entered the study received extensive clinical and psychopathological assessments and went through MRI scan. The diagnoses were confirmed at 6 months using the Structured Clinical Interview for DSM-IV (SCID-I) (First et al., 2001). For the present longitudinal investigation only those patients with a DSM-IV diagnosis of schizophrenia who completed both a baseline and 1-year follow-up MRI scan were included in this study ($n=56$).

Also, a group of healthy comparison subjects were recruited from the community through advertisements. They had no past or present psychiatric, neurological, or general medical illness, including substance abuse or significant loss of consciousness, as determined by using an abbreviated version of the Comprehensive Assessment of Symptoms and History (Andreasen et al., 1992). They were selected to have a similar distribution in age, gender, laterality index, drug history and years of education to the patients. Thus, 56 control subjects were included in this study. The absence of psychosis in first-degree relatives was confirmed by clinical records and family interview.

2.3. Clinical assessment

Clinical symptoms were assessed by using the Brief Psychiatric Rating Scale total (BPRS) (Overall and Gorman, 1962), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1984). We also divided psychopathology into three dimensions of symptoms: positive (scores for hallucinations and delusions), disorganized (scores for formal thought disorder, bizarre behaviour and inappropriate affect) and negative (scores for alogia, affective fattening, apathy and anhedonia) (Grube et al., 1998). Duration of untreated illness (DUI) was defined as the time from the first unspecific symptoms related to psychosis (for such symptom to be considered, there should be no return to previous stable level of functioning) to the date of initiation of an adequate dose of antipsychotic drug taken regularly. Duration of untreated psychosis (DUP) was defined as the time from the first continuous (present most of the time) psychotic symptom to initiation of adequate antipsychotic drug treatment. Duration of prodromic period (DPP) was defined as the period from the first unspecific symptoms related to psychosis (as defined above) to the first continuous (present most of the time) psychotic symptom.

2.4. Medication assessment

The amount and type of medication being prescribed during the 1-year follow-up period was thoroughly recorded. At intake patients were randomly assigned to Haloperidol ($N=10$, 17.9%), Olanzapine ($N=10$, 17.9%), Risperidone ($N=10$, 17.9%), Quetiapine ($N=10$, 17.9%), Ziprasidone ($N=11$, 19.6%) and Aripiprazole ($N=5$, 8.9%). At 1-year follow-up patients were on: Haloperidol ($N=4$, 7.1%), Olanzapine ($N=10$, 17.9%), Risperidone ($N=10$, 17.9%), Quetiapine ($N=10$, 17.9%), Ziprasidone ($N=4$, 7.1%), Aripiprazole ($N=6$, 10.7%), Amisulpride ($N=2$, 3.6%), Clozapine ($N=1$, 1.8%) and Risperidone depot ($N=9$, 16.1%). Additional information about concomitant medications is available under request. To derive total antipsychotic dose, each antipsychotic was converted to chlorpromazine (CPZ) milligram equivalent units (Andreasen et al., 2010).

2.5. Neuropsychological assessment

Cognitive functioning was evaluated at baseline (13.2 weeks after inclusion) and 1-year after recruitment. Forty-five patients and 43 healthy subjects were evaluated at baseline. Thirty-nine patients and 42 healthy subjects were evaluated at 1-year follow-up. A detail description of cognitive battery has been described elsewhere (Gonzalez-Blanch et al., 2007). For this investigation, baseline, 1-year follow-up, and differences between baseline and 1-year follow-up measures of 6 cognitive domains comprising 8 cognitive tests were utilized, with outcome measures in parenthesis: 1. Verbal memory: Rey Auditory Verbal Learning Test (RAVLT) (two measures were obtained: total number of words recalled over learning trials and number of words recalled from the list after delay period); 2. Visual memory: Rey Complex Figure test (RCFT) (long-term recall measure); 3. Executive functions: Trail Making Test B (TMT-B) (time to complete) and FAS fluency test (number of words in time limit); 4. Working memory: WAIS III-Backward Digits (BD) (total score); 5. Speed of processing: WAIS III-Digit Symbol (DS) (standard total score); 6. Attention: Continuous Performance Test Degraded-Stimulus (CPT-DS) (total number of correct responses). Handedness was assessed by the Edinburgh Inventory (Oldfield, 1971). The WAIS III subtest of vocabulary (number of words generated) was used as pre-morbid IQ.