Schizophrenia Research 159 (2014) 36–42

Contents lists available at ScienceDirect

Schizophrenia Research

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

Cortical thinning and caudate abnormalities in first episode psychosis and their association with clinical outcome

Cathy Scanlon [a,b], Heike Anderson-Schmidt [a,c], Liam Kilmartin [d], Shane McInerney [a], Joanne Kenney [a,b], John McFarland [a], Mairead Waldron [a,b], Srinath Ambati [a,b], Anna Fullard [a], Sam Logan [a], Brian Hallahan [a], Gareth J. Barker [e], Mark A. Elliott [f,b], Peter McCarthy [g], Dara M. Cannon [a,b], Colm McDonald [a,b,*]

[a] Clinical Neuroimaging Laboratory, Department of Psychiatry and Anatomy, College of Medicine, Nursing and Health Sciences, National University of Ireland Galway, Galway, Ireland
[b] NCBES Galway Neuroscience Center, National University of Ireland Galway, Galway, Ireland
[c] Department of Psychiatry and Psychotherapy, Section of Psychiatric Genetics, University Medical Centre Goettingen, Georg-August University, Goettingen, Germany
[d] College of Engineering and Informatics, National University of Ireland Galway, Galway, Ireland
[e] King's College London, Institute of Psychiatry, Department of Clinical Neuroscience, Centre for Neuroimaging Sciences, London, UK
[f] School of Psychology, National University of Ireland Galway, Galway, Ireland
[g] Department of Radiology, College of Medicine, Nursing and Health Sciences, National University of Ireland Galway, Galway, Ireland

ARTICLE INFO

Article history:
Received 7 October 2013
Received in revised form 6 July 2014
Accepted 14 July 2014
Available online 11 August 2014

Keywords:
First episode psychosis
MRI
Cortical thickness
Volume
Shape
Superior temporal gyrus
Caudate

ABSTRACT

First episode psychosis (FEP) has been associated with structural brain changes, largely identified by volumetric analyses. Advances in neuroimaging processing have made it possible to measure geometric properties that may identify subtle structural changes not appreciated by a measure of volume alone. In this study we adopt complementary methods of assessing the structural integrity of grey matter in FEP patients and assess whether these relate to patient clinical and functional outcome at 3 year follow-up.

1.5 Tesla T1-weighted Magnetic Resonance (MR) images were acquired for 46 patients experiencing their first episode of psychosis and 46 healthy controls. Cerebral cortical thickness and local gyrification index (LGI) were investigated using FreeSurfer software. Volume and shape of the hippocampus, caudate and lateral ventricles were assessed using manual tracing and spherical harmonics applied for shape description.

A cluster of cortical thinning was identified in FEP compared to controls; this was located in the right superior temporal gyrus, sulcus, extended into the middle temporal gyrus (lateral temporal cortex — LTC). Bilateral caudate volumes were significantly lower in FEP relative to controls and the right caudate also displayed regions of shape deflation in the FEP group. No significant structural abnormalities were identified in cortical LGI or hippocampal or lateral ventricle volume/shape. Neither LTC nor caudate abnormalities were related to change in symptom severity or global functioning 3 years later.

LTC and caudate abnormalities are present at the first episode of psychosis but do not appear to directly affect clinical or functional outcome.

1. Introduction

Studying psychosis at the first episode is optimal for examining the underlying neurobiology of the illness, as it removes confounders associated with the illness and its treatment, such as long-term medication use (Ho et al., 2011). Abnormalities such as ventricular enlargement and hippocampal and basal ganglia volume reduction have been reported in first episode schizophrenia (Ellison-Wright et al., 2008; Vita et al., 2006). However, patients experiencing the less specific first episode of psychosis (FEP) appear to have more subtle deficits, with a recent meta-analysis identifying reduced grey matter volume in the right superior temporal gyrus (STG), bilateral insula and cerebellum (Fusar-Poli et al., 2011b).

Whilst the majority of previous studies have focused on brain tissue volumes, advances in neuroimaging data processing have made it possible to measure further geometric properties such as cortical thickness, cortical folding (gyrification) and shape of brain structures, which may identify more subtle structural changes than volume alone (Ong et al., 2012; Scanlon et al., 2011). With advances in methodology, it is also possible to separate volume into its subcomponents of thickness and surface area on the cerebral cortex, properties that do not necessarily track each other (Dickerson et al., 2009). Cortical thinning has previously been identified in FEP in the superior temporal gyrus and prefrontal and occipital cortices (Janssen et al., 2009).

* Corresponding author at: Clinical Neuroimaging Laboratory, Department of Psychiatry, Clinical Science Institute, National University of Ireland, Galway, Galway, Ireland. Tel.: +353 91 495465; fax: +353 91 494563.
E-mail address: colm.mcdonald@nuigalway.ie (C. McDonald).

http://dx.doi.org/10.1016/j.schres.2014.07.030
0920-9964/

Gyrification is the measure of the amount of cortex buried within the sulcal folds as compared with the amount of visible cortex. Gyrification of the brain undergoes substantial development during foetal life and as such can be a useful marker of cortical development later in life (Rajagopalan et al., 2011) and may reflect disturbances in connectivity (Ronan et al., 2011). A recent study in FEP patients identified hypogyrification across multiple brain regions and found that patients with poor treatment response displayed more prominent abnormalities (Palaniyappan et al., 2013).

Abnormalities of subcortical structures have been reported in FEP, with caudate nucleus volume loss being a consistent finding in first episode schizophrenia (Ellison-Wright et al., 2008). Conversely, hippocampal volume loss has been more often implicated in chronic schizophrenia rather than at the first episode (Ellison-Wright et al., 2008). Quantifying an overall measure of brain structure volume however may not be sensitive to local regional changes in structural integrity which may be better detected by analysis of shape (Ong et al., 2012).

Recent evidence has suggested that volumetric abnormalities at the time of first episode may be used to identify those patients who will have the poorest clinical outcome (Lappin et al., 2013; Mourao-Miranda et al., 2012). In the current study we sought to determine if abnormal neuroimaging findings at FEP are predictive of clinical outcome 3 years later. Using a range of complimentary morphological Magnetic Resonance Imaging (MRI) analysis methods, this study aims 1) to identify the morphometric abnormalities in patients experiencing their first episode of psychosis and 2) to determine if identified abnormalities are related to clinical outcome 3 years later.

2. Methods

2.1. Subjects

Forty-six patients experiencing their first episode of psychosis and 46 healthy controls (HC) matched for age and gender participated in this study (Table 1). The baseline recruitment and clinical assessments have been described in detail previously (McFarland et al., 2012). Exclusion criteria for all participants included neurological disorders, learning disability, life-time substance dependency (as defined by DSM-IV-TR), a history of head injury resulting in loss of consciousness for over 5 min, oral steroid use in the previous 3 months and general contraindications to MRI. Healthy controls were also excluded if they had a personal history of any psychiatric illness, or a known family history of psychotic illness. Written informed consent was obtained from all participants. The study was approved by the Research Ethics Committees of the National University of Ireland Galway and Galway University Hospital.

2.2. Clinical assessment

Patients were diagnosed using the Structured Clinical Interview for DSM-IV-TR Research Version (First et al., 2002). FEP was defined as the presence of at least one psychotic symptom (e.g. delusions, hallucinations, disorder of thinking, disorganised/bizarre behaviour). Patients were diagnosed with schizophrenia (n = 15), schizoaffective (n = 4), schizophreniform (n = 5), delusional-disorder (n = 3), mania (n = 9), psychotic depression (n = 6), and psychosis not otherwise specified (n = 4). All patients were scanned as soon as was feasible after illness onset, and no more than 8 weeks after commencing any antipsychotic medication, with a median antipsychotic administration of 14 days. Seven patients were neuroleptic naïve and not taking any other medication at the time of scan; all other patients were taking an atypical antipsychotic. All patients underwent an assessment of symptomatology using the 0–6 point Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and a Global Assessment of functioning Score (GAF) (Hall, 1995). Duration of Untreated Psychosis (DUP) was measured using the Beiser Scale (Beiser et al., 1993). Total antipsychotic medication taken was recorded and converted to chlorpromazine (CPZ) equivalents (Lehman et al., 1998; Taylor et al., 2007; Woods, 2003) (Table 1).

Table 1
Demographic characteristics of FEP patients and healthy controls.

		Patients	Controls	p-Value
		Mean (SD)	Mean (SD)	t-test/χ^2
Age (years)		28.4 (8.8)	28.6 (8.5)	0.93
Gender (M/F)		n = 32/14	n = 33/13	0.82
Duration untreated (DUP) (months)		14 (17)		
Days on medication		18 (16)		
Medication:				
Total CPZ Equiv (mgs)	Cumulative	4937 (6820)		
	Daily dose	224 (198)		
Antipsychotic type:	Aripiprazole	4		
	Haloperidol	1		
	None	7		
	Olanzapine	19		
	Paliperidone	3		
	Quetiapine	5		
	Risperidone	7		
Symptoms: PANSS	Total	65 (15)		
	Positive	17 (4)		
	Negative	15 (7)		
	General	33 (7)		
Symptoms @ follow-up: PANSS	Total	43 (13)		
	Positive	9 (3)		
	Negative	11 (6)		
	General	22 (6)		
Functionality: GAF	Baseline	51 (11)		
	Follow-up	76 (14)		
Diagnosis: SCID	Non-affective	n = 31		
	Affective	n = 15		
Severity: USS @ follow-up	No further episodes	n = 11		
	Mild	n = 1		
	Moderate	n = 11		
	Severe	n = 11		

SD = standard deviation. DUP = duration of untreated psychosis, CPZ = chlorpromazine equivalents, PANSS = positive and negative symptom scale, GAF = global assessment of functioning, SCID = Structured Clinical Interview for DSM Disorders, USS = usual symptom severity.

PANSS and GAF were acquired 3.5 years later (SD = 0.9 years) in 28 patients. Additionally, clinical notes of 34 patients were reviewed 3 years later and usual symptom severity (USS) assessed using an amended version of the WHO Life Chart Schedule (WHO, 1992) and rated according to a Likert rating scale: 0 = no further episodes, 1 = mild, 2 = moderate, 3 = severe. Fig. 1 presents an overview of the patients re-recruited and lost to follow-up for each method.

2.3. MRI acquisition

All subjects underwent MR imaging at University Hospital Galway (UHG) in a 1.5 Tesla Siemens Magnetom Symphony scanner (Erlangen, Germany) equipped with a 4-channel head coil. A volumetric T1-weighted magnetization-prepared rapid acquisition of gradient echo

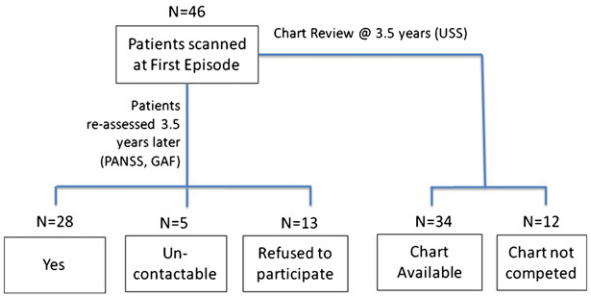

Fig. 1. Flow chart of patients followed-up 3.5 years later through interview and chart review and subjects lost to follow-up.