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World Journal of Psychiatry (*World J Psychiatr*, *WJP*, online ISSN 2220-3206, DOI: 10.5498) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJP covers topics concerning behavior and behavior mechanisms, psychological phenomena and processes, mental disorders, behavioral disciplines and activities, adjustment disorders, anxiety disorders, delirium, dementia, amnestic disorders, cognitive disorders, dissociative disorders, eating disorders, factitious disorders, impulse control disorders, mental disorders diagnosed in childhood, mood disorders, neurotic disorders, personality disorders, schizophrenia and disorders with psychotic features, sexual and gender disorders, sleep disorders, somatoform disorders, and substance-related disorders. Priority publication will be given to articles concerning diagnosis and treatment of psychiatric diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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CASE REPORT

Cognitive correlates of neuroimaging abnormalities in the onset of schizophrenia: A case report

Silvia Grassi, Giulia Orsenigo, Marta Serati, Elisabetta Caletti, Alfredo Carlo Altamura, Massimiliano Buoli

Silvia Grassi, Giulia Orsenigo, Marta Serati, Elisabetta Caletti, Alfredo Carlo Altamura, Massimiliano Buoli, Department of Psychiatry, University of Milan, Fondazione IRCCS Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, 20122 Milan, Italy

Author contributions: Grassi S and Orsenigo G collected data; Serati M revised report; Caletti E performed neuropsychological tests; Altamura AC designed the report; Buoli M wrote the paper.

Institutional review board statement: This case report was exempted from IRB standards of University of Milan.

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Abstract

Increasing evidence shows that cognitive impairment and brain abnormalities can appear early in the first episodes of schizophrenia, but it is currently debated how brain changes can correlate with clinical presentation of schizophrenic patients. Of note, this report describes the case of a young schizophrenic male presenting parietal magnetic resonance/positron emission tomography abnormalities and cognitive impairment, documented by specific neuropsychological tests. In our knowledge only few studies have investigated if neuropsychological abnormalities could be concomitant with both structural and functional neuroimaging. This case shows that impairment in specific cognitive domains is associated with structural/functional brain abnormalities in the corresponding brain areas (frontal and parietal lobes), supporting the hypothesis of disconnectivity, involving a failure to integrate anatomical and functional pathways. Future research would define the role of cognitive impairment and neurodegeneration in psychiatric nosography and, in particular, their role in the early phases of illness and long-term outcome of schizophrenic patients.

Key words: Positron emission tomography; Magnetic resonance; Schizophrenia; Neuropsychology

Core tip: Schizophrenia is associated with impairment in executive function, verbal memory, verbal fluency and attention. Neuropsychological tests are associated with structural and functional brain alterations. This

case report is an example of the potential correlation between clinical symptoms (*e.g.*, cognitive impairment) and brain changes. These data may help in the prediction of possible outcome of schizophrenia patients.

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INTRODUCTION

A number of data would indicate schizophrenia as a progressive neurodegenerative disorder[1] whose outcome is influenced by many biological and clinical factors[2]. Of note, recent literature shows that neuropsychological deficits at onset may predict the clinical course of illness[3] being often associated with frontal and parietal lobe dysfunctions[4-6]. Moreover, a recent trial found that brain abnormalities of schizophrenic patients change according to age at onset. In particular, early onset patients show parietal abnormalities, while adult onset patients exhibit frontal and temporal ones[7].

To our knowledge there are few studies[8-10] associating cognitive frontal and parietal deficits with structural [magnetic resonance (MR)] and functional neuroimaging [positron emission tomography (PET)] and the anatomical and functional relationships underlying this deficit remain to be elucidated. Dysconnectivity, a failure in functional integration, is considered a key mechanism in the pathophysiology of cognitive impairments (in particular working memory performance) in individuals with schizophrenia[11].

The present paper deals with a recent diagnosed schizophrenic patient showing frontal and parietal lobe MR/PET abnormalities clinically associated with deficits in the corresponding cognitive domains.

CASE REPORT

The patient was a 19-year-old man admitted in our department. The patient showed nor psychiatric comorbidity with an Axis Ⅰ disorder neither personality disorders. A neurological exam, performed by a neurologist, was negative. Diagnosis of undifferentiated schizophrenia and exclusion of comorbid conditions were assessed through the administration of semi-structured interviews based on DSM-Ⅳ criteria (SCID Ⅰ and Ⅱ). Patient had family history for psychiatric disorders: The father was an alcohol abuser, one schizophrenic uncle (father's brother) committed suicide and the grandmother in mother line was affected by bipolar disorder. At the admission in our ward the patient was drug-naïve and showed persecutory delusion, auditory hallucinations, thought/behavioural disorganization and a duration of untreated psychosis of 9 mo[12]. Baseline score at Positive and Negative Syndrome Scale[13] was 84, while baseline score at Brief Psychiatric Rating Scale was 55[14]. In the first days of admission patient underwent to neuropsychological tests, cerebral MR and cerebral PET.

A neuropsychological battery was designed to encompass the areas believed to be affected by Schizophrenia[15]. Results and standard scores are summarized in Table 1. Patient's neurocognitive performances provided evidence for impairment in the following domains: Executive function (Cognitive Estimation, Verbal fluency, Trail Making Test), verbal memory, verbal ability (Boston Naming Test, phonemic Verbal Fluency) and attention (Visual Search, Trail Making Test). In addition, the patient failed in two Wechsler Adult Intelligence Scale[16] subscales: Verbal Comprehension Index and Perceptual Organization Index.

MR was performed using a circular polarized head coil and included Turbo Spin-Echo T1-weighted sequences, T2-weighted sequences and FLAIR. Imaging in three planes was performed using 5-mm slice thickness. MR revealed normal-sized ventricles, normal-sized subarachnoidal spaces, no abnormalities in gray matter, but bilaterally soft hyper-intensities in superior parietal lobe[4] periventricular white matter.

Fluorodeoxyglucose (FDG) was injected in condition of rest and fasting and after 30 min three-dimensional scan was performed. The images were compared to a cohort of normal ones. Fluoro-D-Glucose PET (Figures 1 and 2) showed glucose frontal and parietal lobes hypometabolism bilaterally. No further abnormalities in FDG distribution were observed.

MR and PET were performed by neuroradiologists collaborating within our department.

Of note, neuropsychological results are consistent with outlined MR abnormalities and PET images (fronto-parietal abnormalities)[17].

DISCUSSION

The present case report confirms data from literature of early cognitive deficits in the course of schizophrenia[18,19] and neuroimaging parietal abnormalities in early onset schizophrenic patients[7,20,21]. In addition, the correspondence between cognitive deficits and morphological/functional brain alterations[22] contributes to clarify the influence of brain changes in schizophrenia clinical presentation as well as to support the hypothesis of schizophrenia as a neurodegenerative disorder[23,24]. Recent trials found that brain abnormalities are more severe in patients with a longer duration of illness[25-27], novel antipsychotics are promising molecules for their efficacy in stopping the neurodegenerative process[28,29]. In this context cognitive and neuroimaging follow-up of our case can be useful to discriminate if neurodegenerative process of schizophrenia progresses in the course of illness or it is specific of early stages[24,30,31]. Finally, it would be important in the future to define the role of neuroimaging abnormalities in influencing outcome. MR

Table 1 Neuropsychological results

Test	Patient score	Normal value	Result	Z-score
Mini-mental state examination	27.19	24-29.19	Normal	0.45
Executive functions: Tower of London	25	20-36	Normal	-0.75
Frontal assessment battery	15.98	13.5-17.3	Normal	-0.95
Cognitive estimation task	19.97	0-18	Failed	2.43
Bizarreness	6	0-4	Failed	4
Problem solving: Raven's progressive matrices	29.05	18.6-33.05	Normal	0.89
Assessment of cognitive impairment in memory				
Verbal memory and learning				
Digit Span	5.75	3.75-8.75	Normal	-0.4
Verbal Learning	10.50	6.50-21.50	Normal	-0.93
Recall of prose: Immediate and after 10 min	3.50	8.00-27.50	Failed	-2.92
Spatial short-term memory (Corsi test)	4.50	3.50-8.50	Normal	-1.20
Attention and speed information processing				
Trail making test				
Part A	33	< 93 s	Normal	
Part B, dual task	161	< 282 s	Normal	
Part B-A	128	< 186 s	Borderline score	-1.36
Visual search	34.25	31-51.25	Borderline score	
Verbal fluency				
Phonemic	23	17-59	Borderline score	-1.43
Categories	32	25-58	Normal	-1.15
Language				
Boston naming test	31	43-60	Failed	-4.82
Token test	32	29-36	Normal	-0.29
Wechsler adult intelligence scale-revised	General IQ = 75 (verbal IQ = 81; performance IQ = 74) VCI = 5.5; POI = 6.25	80-120	Borderline score	-2.50

The standard scores, reported in the second column, are calculated considering a normal population. Our patient's scores, adjusted for age, sex and education are shown in the first column next to each test. A score is considered pathological when the score is present less than 5% of the normal population. Sometimes normal scores are considered pathological due to the clinical condition and the global performance. VCI: Verbal comprehension index; POI: Perceptual organization index.

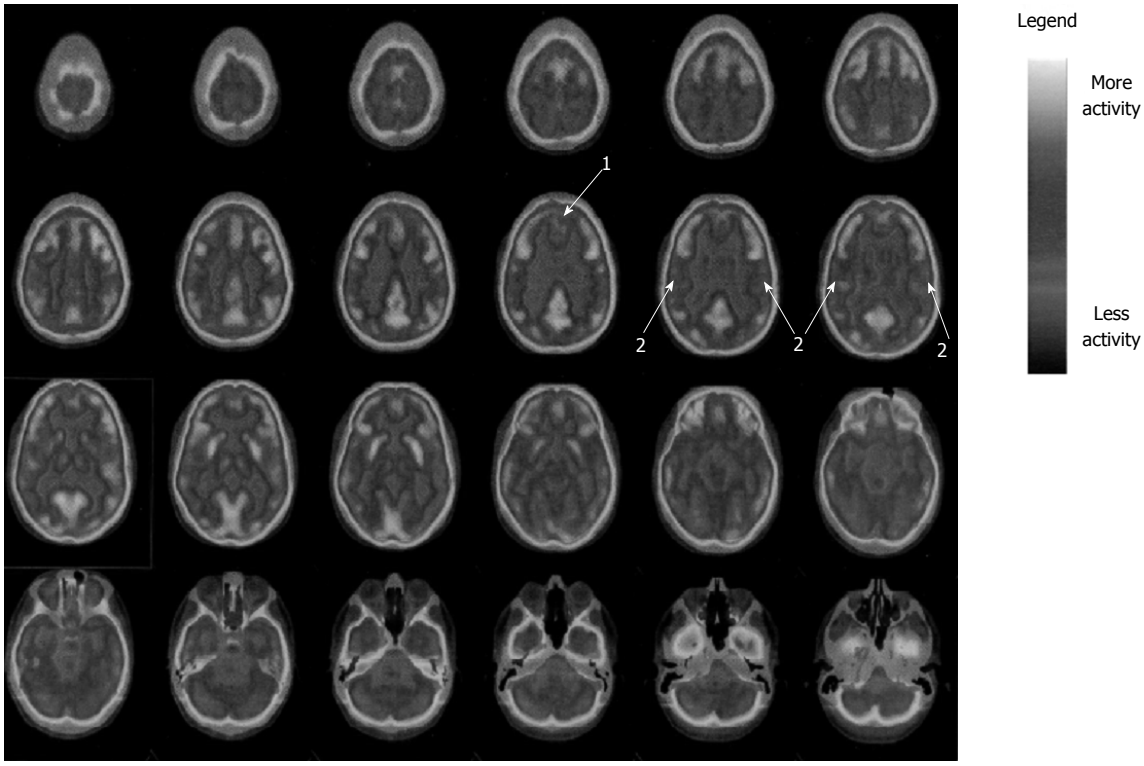

Figure 1 D-glucose (fluorodeoxyglucose) positron emission tomography, transversal sections. Pointer 1 displays the frontal lobe hypo-metabolism; pointer 2 displays the parietal lobe hypo-metabolism.

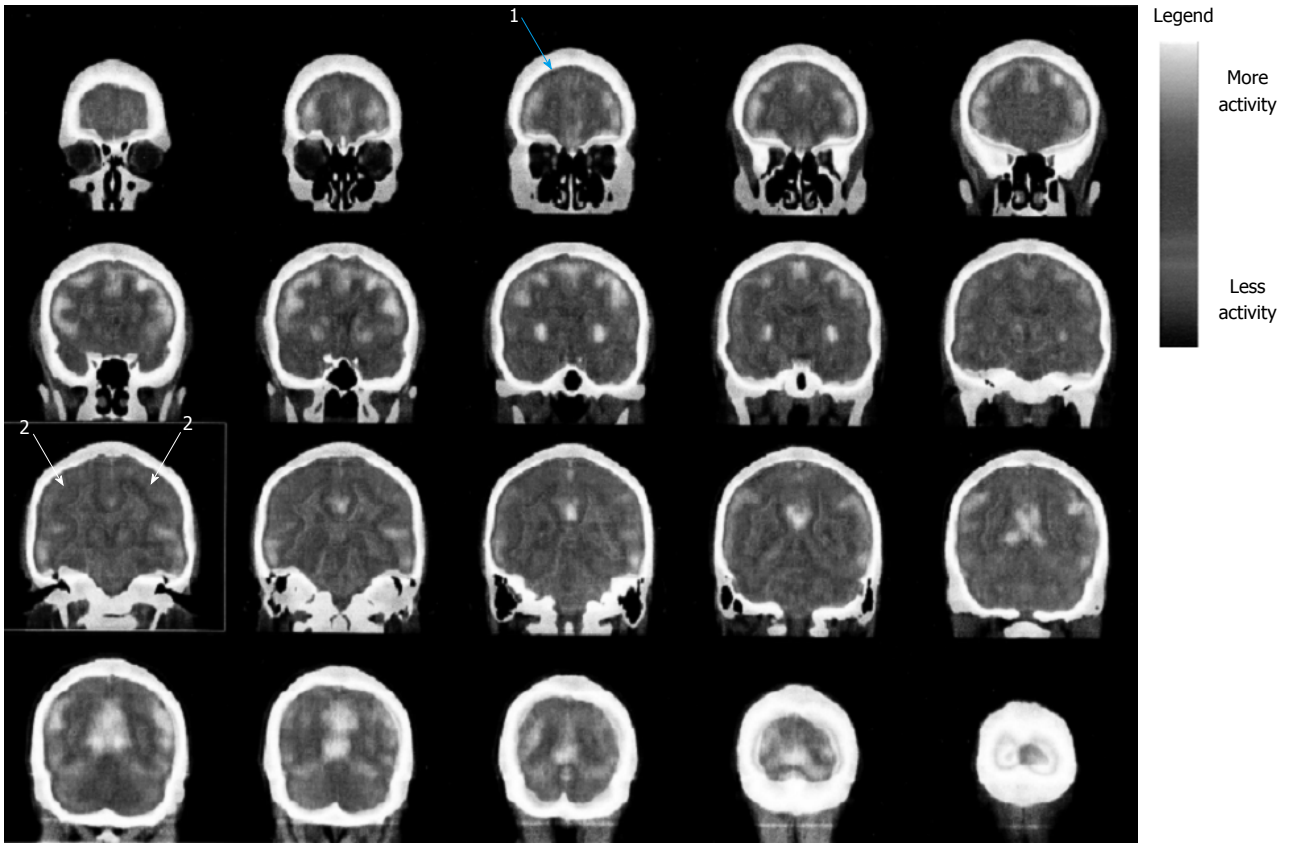

Figure 2 Fluoro-D-glucose (fluorodeoxyglucose) positron emission tomography, coronal sections. Pointer 1 displays the frontal lobe hypo-metabolism; Pointer 2 displays the parietal lobe hypo-metabolism.

and PET could be useful tools to make diagnosis and to predict long-term course of schizophrenic illness.

COMMENTS

Case characteristics

A 19-year-old male patient with severe schizophrenia presentation.

Clinical diagnosis

Patient was hospitalized because of prominent persecutory delusion, auditory hallucinations, aggressiveness and thought/behavioural disorganization.

Differential diagnosis

Bipolar disorder, substance use disorder.

Laboratory diagnosis

Routine blood tests were resulted within normal limits.

Imaging diagnosis

At magnetic resonance imaging bilaterally soft hyper-intensities in superior parietal lobe periventricular white matter were detected, while positron emission tomography showed glucose parietal lobes hypo-metabolism bilaterally.

Pathological diagnosis

Schizophrenia, acute episode.

Treatment

Ziprasidone 80 mg × 2 and Gabapentin 300 mg × 3.

Related reports

Severe cognitive impairment as showed by neuropsychological tests.

Term explanation

Dysconnectivity means abnormal functional integration among brain regions resulting in impaired modulation of neurotransmitters.

Experiences and lessons

It is important to perform imaging evaluation and neuropsychological tests to better define long-term outcome of schizophrenia patients.

Peer-review

This case report is novel and well designed.

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