Single-Photon Emission Computed Tomography Findings in a Patient With Fahr Disease Associated With a Schizophrenia-Like Psychosis

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Fahr disease is a rare sporadic or familial idiopathic basal ganglia calcification associated with neurologic disorders, such as movement disturbances and dementia.[1,2] More rarely, schizophrenia-like psychosis characterized by paranoia, hallucinations, and delusions has also been reported to be associated with Fahr disease.[3–7] This second type of case associated with Fahr disease may help clinicians better understand the mechanisms underlying neuropsychiatric symptoms that are critical for future rational drug discovery in schizophrenia.[8] While dysregulated striatal dopaminergic function has been implicated in schizophrenia,[9] pathophysiology of schizophrenia-like psychosis in Fahr disease remains largely unknown.[6,10] We describe here clinical and single-photon emission computed tomography (SPECT) findings of a patient displaying Fahr disease with schizophrenia-like psychosis.

Case report. Mr A was a 53-year-old man with a 33-year history of persistent auditory hallucinations and delusions of persecution. In 2012, brain magnetic resonance imaging revealed symmetrical calcifications in the basal ganglia without other brain abnormalities, suggesting Fahr disease with schizophrenia-like psychosis (Figure 1). He complained that he heard inner self-deprecating and insulting voices, always the same since the beginning of his disease. He considered that these voices were a divine penetration of his body, and that God was testing him. The absence of family history of psychotic disorders and family/personal history of calcium metabolism disorders did not support a genetically determined neuropsychiatric disease. During the course of his illness, he experienced numerous hospitalizations, always for exacerbations of auditory hallucinations and delusions of persecution, without intervals of complete symptomatic remissions. None of the antipsychotics utilized as monotherapy or combination, tried over time, had significant influence on symptoms, eg, haloperidol (up to 20 mg/d), clozapine (up to 400 mg/d), olanzapine (up to 65 mg/d), risperidone (up to 10 mg/d), amisulpride (up to 1,200 mg/d), and, currently, quetiapine (800 mg/d). During all the courses of medications and whatever the dose, the patient presented extrapyramidal side effects (tremors, dystonia, oculogyric crisis, akathisia) that needed the indefinite treatment of an anticholinergic drug (tropatepine 10 mg/d or trihexyphenidyl 3 mg/d). Finally, auditory hallucinations were also refractory to 3 courses of 10 sessions of low-frequency (ie, 1 Hz) repetitive transcranial magnetic stimulation over the left temporal parietal cortex and to electroconvulsive therapy.

At the time of admission in our hospital, Mr A presented mixed symptomatology associating auditory hallucinations, delusions of persecution, anxiety, depression, and lack of judgment. On the Positive and Negative Syndrome Scale,[11] his positive score was 22 (range, 7–49), negative score was 21 (range, 7–49), general psychopathology score was 32 (range, 16–112), and total score was 75 (moderately ill) (30–210); his score on the Auditory Hallucinations Rating Scale[12] was 28 (range, 0–41). When the Extrapyramidal Symptom Rating Scale[13] was used, a mild dystonia (score = 3) and a very mild tardive dyskinesia (ie, involuntary movements of the tongue) (score = 2) were evidenced. Neuropsychological assessment revealed moderate cognitive impairments, mainly on attention, concentration, and verbal episodic memory. In particular, Mini-Mental State Examination[14] revealed a score of 24/30, and results of a Wechsler Adult Intelligence Scale-Revised[15] showed a full-scale intelligence quotient of 86. The examination did not reveal any other diagnostic criteria. Laboratory tests, including especially serum calcium, phosphorus, and parathyroid hormone levels, were within normal limits (eg, thyroid stimulating hormone, 2.32 mIU/L; vitamin B_{12}, 389 pmol/L). Using version 8 of Statistical Parametric Mapping (SPM8) software (Wellcome Trust Centre for Neuroimaging, University College London, London, United Kingdom), we performed a ([123]I) FP-CIT (I 123-radiolabeled 2_-carbomethoxy-3_-[4-iodophenyl]-N-[3-fluoropropyl] nortropane) SPECT analysis to explore the movement disorders, which identified left posterior putamen decrease of dopamine transporter binding in comparison to 23 healthy subjects (mean [SD] age = 52.5 [7.1] years ($P < .005$, uncorrected (Figure 1A).[16] Using SPM8, we also performed a brain perfusion SPECT analysis (Figure 1B); in comparison to 23 healthy subjects (mean [SD] age = 52.5 [7.1] years), the patient exhibited bilateral frontotemporal hypoperfusions, also involving the cerebellum and the midbrain ($P < .005$, uncorrected).[17]

This report describes decreased striatal dopamine transporter associated with frontotemporal hypoperfusions in Fahr disease with schizophrenia-like psychosis. These findings suggest a possible shared mechanism underlying schizophrenia-like psychosis in Fahr disease and schizophrenia. A substantial body of evidence implicates dopaminergic dysfunction in the etiology of psychotic disorder[18] involving, in particular, a striatal presynaptic dopamine dysfunction.[9] In line with our findings, a striatal dopamine transporter dysfunction has been described in dementia with Lewy bodies presenting neuropsychiatric symptoms such as hallucinations and delusions.[19,20] Although the data are inconsistent, a few studies have also reported an association between striatal dopamine transporter levels and hallucinations in schizophrenia.[21–23] However, a recent meta-analysis has rather suggested that striatal dopamine synthesis capacity was predominantly affected in schizophrenia without dopamine transporter dysfunction.[9] Moreover, our SPECT findings are in support of previous studies in schizophrenia-like psychosis[6,10] and schizophrenia[24] that have reported the impairment of a neural network involving frontotemporal regions, which are connected to the striata.

To conclude, psychiatrists must be aware of this presentation of schizophrenia-like psychosis in Fahr disease. This report emphasizes the importance of researching structural and functional brain causes in patients with atypical presentation. Clinicians

should be especially aware that these patients are prone to extrapyramidal symptoms or abnormal movement and that they should preferentially use atypical antipsychotics causing fewer extrapyramidal side effects. However, more studies need to be done, and future drug development should focus on the control of presynaptic dopamine dysfunction.

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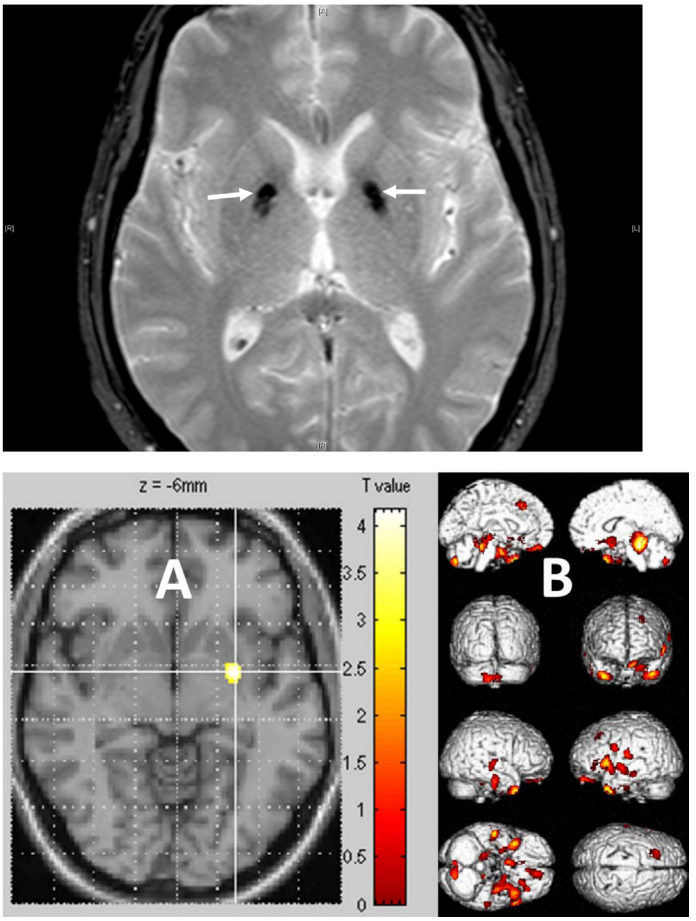
Figure 1. Neuroimaging Findings[a]



[a]Axial T2* brain magnetic resonance imaging shows symmetrical bilateral calcification in the basal ganglia (upper image; arrows show bilateral pallidal hyposignal); brain single-photon emission computed tomography findings in the patient are presented in comparison to 23 healthy subjects ($P < .005$, uncorrected) using SPM8. Panel A shows a decrease in dopamine transporter binding within the left posterior putamen; panel B shows bilateral frontotemporal hypoperfusions, also involving the cerebellum and the midbrain.

Drug names: clozapine (Clozaril, FazaClo, and others), haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel and others), risperidone (Risperdal and others).

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