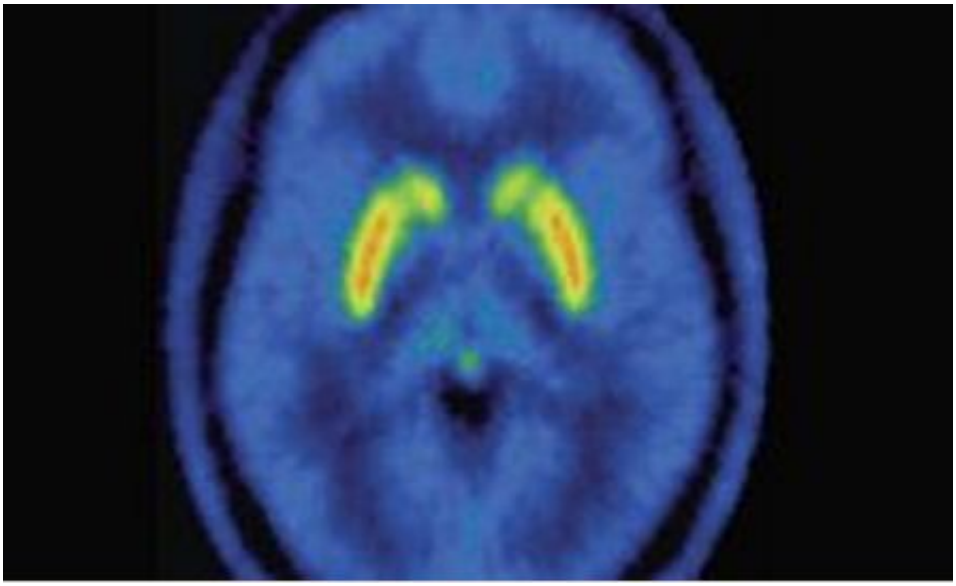
Research may explain why some people with schizophrenia do not respond to treatment

November 29 2012



PET scan showing dopamine uptake in the Striatum area of the brain. Credit: AJP 2012

(Medical Xpress)—New research suggests that the molecular mechanism leading to schizophrenia may be different in patients who fail to respond to anti-psychotic medication compared to patients who do respond.

The research, from King's College London's Institute of Psychiatry may help explain why up to one third of patients with schizophrenia do not respond to traditional anti-psychotic medication.

Schizophrenia is known to be associated with an overactive dopamine system, meaning that the brain processes abnormally high levels of dopamine. Traditional dopamine-blocking anti-psychotic medication attempts to normalise this process. However, approximately one third of patients with schizophrenia do not respond to this treatment, and until now, no study has examined whether dopamine abnormality is present in patients resistant to antipsychotic treatment.

The study was led by Dr Arsime Demjaha, Dr Oliver Howes, Professor Shitij Kapur, Professor Sir Robin Murray and Professor Philip McGuire from King's Institute of Psychiatry and published in the American Journal of Psychiatry.

Dr Arsime Demjaha and co-authors, say: 'Despite considerable scientific and therapeutic progress over the last 50 years, we still do not know why some patients with schizophrenia respond to treatment whilst others do not. Treatment resistance in such a disabling condition is one of the greatest clinical and therapeutic challenges to psychiatry, significantly affecting patients, their families and society in general.'

The authors conclude: 'Our findings suggest that there may be a different molecular mechanism leading to schizophrenia in patients who do not respond to anti-psychotic medication. Identifying the precise molecular pathway particularly in these patients is of utmost importance and will help inform the development of much-needed novel treatments.'

Researchers used PET scan imaging to investigate dopamine synthesis capacity in 12 patients with schizophrenia who did not respond to treatment, 12 who did, and 12 healthy controls. They found that schizophrenia patients whose illness was resistant to antipsychotic treatment have relatively normal levels of dopamine synthesis capacity which would explain why the dopamine blocking anti-psychotic medication was not effective in this group.

However, the authors add that the findings need to be replicated in larger samples before the research can affect clinical practice. They add that future research will need to focus on long-term prospective studies of patients who have never taken anti-psychotics to determine whether presynaptic dopamine synthesis capacity was normal in patients in the treatment-resistant group at the onset of their illness, and predates antipsychotic exposure.

More information: Demjaha, A. et al., Dopamine synthesis capcity in patients with treatment-resistant schizophrenia, *American Journal of Psychiatry* (Nov 2012) doi: 10.1176/appi.ajp.2012.12010144.

Provided by King's College London