

Visualized Dopamine Receptors in Schizophrenia

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The aberrant neurotransmission has been assumed in various neuropsychiatric disorders. However, the methods to evaluate the neurochemical brain functions are restricted to the non-invasive technique. Nuclear medicine technique is very powerful method with various radiolabeled ligands. We have investigated the dopamine receptors in the cerebral cortex since the symptoms of schizophrenia have been discussed with a functional impairment in dopaminergic transmission in the prefrontal cortex and mesolimbic system. To investigate the extrastriatal dopamine receptors *in vivo*, we have used positron emission tomography. [¹¹C]SCH23390 was used for the measurement of dopamine D1 receptors and [¹¹C]FLB 457 was used for dopamine D2 receptors. Eighteen healthy male subjects and 17 male schizophrenic patients were included in the study of dopamine D1 receptors. Ten patients were neuroleptic naive and seven patients were drug free. In the striatum, there were no significant differences between the patients and normal controls. But the bindings in

the prefrontal cortex were significantly lower in the schizophrenic patients. The bindings in the prefrontal cortex were negatively correlated with the BPRS negative symptom subscore. Although D1 receptors seemed to contribute to the pathophysiology of schizophrenia, the effects of antipsychotics mainly act on D2 receptor. We have measured the extrastriatal D2 receptor occupancy by risperidone and found curvilinear relationship between drug dose and occupancy. Eleven drug-naïve male patients with schizophrenia were examined in the study of dopamine D2 receptors. Unexpectedly, the binding was significantly lower in the anterior cingulate cortex in drug naïve patients with schizophrenia and significant negative correlation was observed between D2 receptor binding in the anterior cingulate cortex and the positive symptom score on BPRS. Alterations in D2 receptor function in the extrastriatal region may underlie the positive symptoms of schizophrenia whereas dysfunction of D1 receptors underlie the negative symptoms