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Measuring Dopamine Release in the Human Brain with PET

N.D. Volkow[ac], J.S. Fowler[b], G.-J. Wang[a], J. Logan[b],

[a]Medical and [b]Chemistry Departments Brookhaven National Laboratory, Upton, New York, NY 11973

[c]Department of Psychiatry, State University of New York at Stony Brook, Stony Brook, New York 11794-8101

INTRODUCTION

The dopamine system is involved in the regulation of brain regions that subserve motor, cognitive and motivational behaviors [1,2,3]. Disruptions of dopamine (DA) function have been implicated in neurological and psychiatric illnesses including substance abuse, as well as on some of the deficits associated with aging of the human brain [4,5,6]. This has made the DA system an important topic in research in the neurosciences and neuroimaging as well as an important molecular target for drug development.

Dopamine cells reside predominantly in the mesencephalon in three neuronal groups, the retrobulbar, the Substantia Nigra, and the Ventral Tegmental area [7,8,9,10,11]. The Substantia Nigra projects predominantly to the dorsal striatum and is mainly concerned with initiation and execution of movements. The Ventral Tegmental area projects to nucleus accumbens, orbital and cingulate cortices, amygdala and hippocampus and is involved with reinforcement, motivation, mood and thought organization. From within the DA cells dopamine is released into the synapse in response to an action potential and interacts with postsynaptic DA receptors. The concentration of DA in the synapse is regulated primarily by its reuptake by the DA transporters, to maintain low (nanomolar) steady-state concentrations [12].

Positron Emission Tomography (PET), was the first technology that enabled direct measurement of components of the DA system in the living human brain [13]. Imaging studies of DA in the living brain have been indirect, relying on the development of radiotracers to label DA receptors, DA transporters, precursors of DA or chemical compounds which have specificity for the enzymes which degrade synaptic DA [14]. Additionally, through the use of tracers that provide information on regional brain activity (ie brain glucose metabolism and cerebral blood flow) and of appropriate pharmacological interventions, it has been possible to assess the functional consequences of changes in brain DA activity. DA specific ligands have been useful in the evaluation of patients with neuropsychiatric illnesses as well as to investigate receptor blockade by antipsychotic drugs [15,16,17,18].

A limitation of strategies that rely on the use of DA specific ligands is that the measures do not necessarily reflect the functional state of the dopaminergic system and that there use to study the effects of drugs is limited to the investigation of receptor or transporter occupancy. Newer strategies have been developed in an attempt to provide with information

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