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Author(s)	Ikemoto, Keiko
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**STRIATAL D-NEURONS : IN NEW VIEWPOINTS FOR  
NEUROPSYCHIATRIC RESEARCH USING  
POST-MORTEM BRAINS**

KEIKO IKEMOTO

*Department of Neuropsychiatry, Fukushima Medical University School of Medicine, Fukushima,  
960-1295, Japan*

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**Key words** : neural stem cell, subventricular zone, epigenetics, Parkinson's disease, schizophrenia

*Epigenetics of monoamine-related genes and psychoses*

It is well known that the monoamine neuronal systems, especially the dopamine (DA) and noradrenaline systems are well developed in humans and that the dysfunctions of monoamine neuronal systems are seen in mental illnesses including schizophrenia and mood disorders. The recent studies have indicated that the most of susceptible genes for schizophrenia are related to development or formation of neuronal circuits<sup>1,2)</sup>, but are not monoamine-related ones except of catechol-O-methyltransferase (COMT)<sup>3)</sup>. Epigenetics, i.e., modulation of gene expression without changing genomic arrangement, of monoamine-related genes should further be examined<sup>4)</sup>.

*Striatal D-neurons and neurological and neuropsychiatric diseases*

At 1983, Jaeger CB *et al.* reported non-monoaminergic aromatic L-amino acid decarboxylase (AADC)-containing neurons (D-neurons) in the spinal cord<sup>5)</sup>, and then classified into 14 groups from the spinal cord to bed nucleus of stria terminalis according to their localization (D1~D14)<sup>6)</sup>. We also reported the neuron group in the human striatum in 1997 (D15)<sup>7,8)</sup>. These neurons have not yet been confirmed exactly to meet the definition as "neurons", i.e., synthesizing, transporting and releasing neurotransmitter(s), and having neurotransmitter(s) that act(s) on the receptor(s), and their functions and nature have not yet been clarified. However, these neurons may have multi-functions, i.e., conversion of L-dopa into DA and exogenous droxidopa (L-threo-DOPS) into noradrenaline, and biosynthesis of trace

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Corresponding author : Keiko Ikemoto, MD, PhD E-mail : ikemoto@fmu.ac.jp  
<http://www.fmu.ac.jp/home/lib/F-igaku/> <http://www.sasappa.co.jp/online/>

amines<sup>8)</sup>.

In our postmortem brain materials, schizophrenic cases contained reduced number of D-neurons in the striatum, especially in the nucleus accumbens<sup>9)</sup>. This might be in accordance with a recent report showing the decreased proliferation of neural stem cells (NSCs) in schizophrenia<sup>9)</sup>. Interaction between DA hyperactivity and reduction of D-neurons in pathophysiology of schizophrenic striatum remain to be elucidated.

It has been reported that parkinsonian model rats contained increased number of AADC cells, most of which were D-neurons, and they synthesized DA after administration of L-dopa<sup>10)</sup>. Such DA synthesis via D-neurons or AADC-containing glial cells must also be studied in the human parkinsonian striatum, and reinforcement of this system might be essential for the treatment of Parkinson's disease.

#### *Relation between neural stem cells in subventricular zone*

The localization of these striatal D-neurons were apparently similar to that of NSCs of the subventricular zone (SVZ)<sup>11)</sup>, and this fact made us to suspect that the striatal D-neurons might be derived from NSCs of the SVZ<sup>11)</sup>. If such a relation between these two cell populations were clarified, stimulation of the differentiation and proliferation of endogenous NSCs, for example via brain-derived neurotrophic factor, might be a new strategy for Parkinson's disease therapy.

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