

**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*

(Received February 12, 2008, accepted April 4, 2008)

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^{1,2)}, but are not monoamine-related ones except of catechol-O-methyltransferase (COMT)³⁾. Epigenetics, i.e., modulation of gene expression without changing genomic arrangement, of monoamine-related genes should further be examined⁴⁾.

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 cord⁵⁾, and then classified into 14 groups from the spinal cord to bed nucleus of stria terminalis according to their localization (D1~D14)⁶⁾. We also reported the neuron group in the human striatum in 1997 (D15)^{7,8)}. 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

池本桂子

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/>

amines⁸⁾.

In our postmortem brain materials, schizophrenic cases contained reduced number of D-neurons in the striatum, especially in the nucleus accumbens⁹⁾. This might be in accordance with a recent report showing the decreased proliferation of neural stem cells (NSCs) in schizophrenia⁹⁾. 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-dopa¹⁰⁾. 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)¹¹⁾, and this fact made us to suspect that the striatal D-neurons might be derived from NSCs of the SVZ¹¹⁾. 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.

ACKNOWLEDGEMENTS

This study was supported by Grants-in-Aid for Scientific Research from Japan Society for the Promotion of Science (JSPS).

REFERENCES

1. Tamura Y, Kunugi H, Ohshima J, Hohjoh H. Epigenetic aberration of the human REELIN gene in psychiatric disorders. *Mol Psychiatry*, **12**: 593-600, 2007.
2. Duan X, Chang JH, Ge S, Faulkner RL, Kim JY, Kitabatake T, Liu XB, Yang CH, Jordan JD, Ma DK, Liu CY, Ganesan S, Cheng HJ, Ming GL, Lu B, Song H. Disrupted-In-Schizophrenia 1 regulates integration of newly generated neurons in the adult brain. *Cell*, **130**: 1146-1158, 2007.
3. Opgen-Rhein C, Neuhaus AH, Urbanek C, Hahn E, Sander T, Dettling M. Executive attention in schizophrenic males and the impact of COMT Val108/158Met genotype on performance on the attention network test. *Schizophr Bull*, Jan 16, 2008.
4. Tsankova N, Renthal W, Kumar A, Nestler EJ. Epigenetic modulation in psychiatric disorders. *Nat Rev Neurosci*, **8**: 355-367, 2007.
5. Jaeger CB, Teitelman G, Joh TH, Albert VR, Park DH, Reis DJ. Some neurons of rat central nervous system contain aromatic-L-amino-acid decarboxylase but not monoamines. *Science*, **219**: 1233-1235, 1983.
6. Jaeger CB, Ruggiero DA, Albert VR, Joh TH, Reis DJ. Immunohistochemical localization of aromatic-L-amino-acid decarboxylase. *In*: Bjorklund A, Hokfelt T, eds. *Classical Transmission in the CNS: Part I. Handbook of Chemical Neuroanatomy. vol 2.* Elsevier, Am-

- sterdam, 387-418, 1984.
7. Ikemoto K, Kitahama K, Jouvet A, Arai R, Nishimura A, Nishi K, Nagatsu I. Demonstration of L-dopa decarboxylating neurons specific to human striatum. *Neurosci Lett*, **232**: 111-114, 1997.
 8. Ikemoto K. Significance of human striatal D-neurons: implications in neuropsychiatric functions. *Prog Neuropsychopharmacol Biol Psychiatry*, **28**: 429-434, 2004.
 9. Reif A, Fritzen S, Finger M, Strobel A, Lauer M, Schmitt A, Lesch KP. Neural stem cell proliferation is decreased in schizophrenia, but not in depression. *Mol Psychiatry*, **11**: 514-522, 2006.
 10. Mura A, Jackson D, Manley MS, Young SJ, Groves PH. Aromatic L-amino acid decarboxylase immunoreactive cells in the striatum: a possible site for the conversion of exogenous L-DOPA to dopamine. *Brain Res*, **704**: 51-60, 1995.
 11. Jin K, Galvan V. Endogenous neural stem cells in the adult brain. *J Neuroimmune Pharmacol*, **2**: 236-246, 2007.