

## DOCTORAL THESIS

### Localization of GABA receptors in the rat basal ganglia

Ng, Kwok Yan

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**Localization of GABA Receptors in the Rat Basal Ganglia**

**NG Kwok Yan**

**A thesis submitted in partial fulfillment of the requirements  
for the degree of**

**Doctor of Philosophy**

**Principal Supervisor: Dr. YUNG Kin Lam**

**Hong Kong Baptist University**

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## Abstract

Gamma-aminobutyric acid (GABA) is one of the most important inhibitory neurotransmitters in the rat basal ganglia. GABA<sub>B</sub> receptors are the first heteromeric metabotropic receptors found in the brain and it is one of the most important types of GABA receptor that mediate GABA neurotransmission. A functional GABA<sub>B</sub> receptor is known to be composed of two subunits, namely the GABA<sub>B</sub>R1 and GABA<sub>B</sub>R2 subunits. The novelty of the present study was to provide one of the first comprehensive studies about the precise cellular and subcellular localization of two subunits of the GABA<sub>B</sub> receptor in identified subpopulations of neurons in the normal rat basal ganglia. In the confocal microscope, immunoreactivity for GABA<sub>B</sub>R1 was detected in the neuropilar elements as well as in the perikarya of neurons in the neostriatum. Many of the GABA<sub>B</sub>R1-immunoreactive perikarya resembled the morphology of medium spiny neurons. In addition, other GABA<sub>B</sub>R1-immunoreactive neurons were characterized by double immunofluorescence. Over 90% of the parvalbumin- and choline acetyltransferase-immunoreactive striatal interneurons and about 80% of the nitric oxide synthase-immunoreactive interneurons displayed GABA<sub>B</sub>R1 immunoreactivity. In contrast, immunoreactivity for GABA<sub>B</sub>R2 was primarily found in the neuropil of the neostriatum. Double labeling revealed that those perikarya that expressed immunoreactivity for parvalbumin, choline acetyltransferase, nitric oxide synthase, glutamate receptor two, *N*-methyl-*D*-aspartate receptor one, or GABA<sub>A</sub>α1 receptor respectively, did not express GABA<sub>B</sub>R2 immunoreactivity. These results indicate that there is a differential expression of GABA<sub>B</sub>R1 and GABA<sub>B</sub>R2 immunoreactivity in different subpopulations of striatal neurons. The striatal neurons may therefore suggest to process less GABA<sub>B</sub> receptor in their fully functional assembly. In the normal rat substantia nigra, over 90% of tyrosine hydroxylase-immunoreactive dopaminergic neurons in the substantia nigra pars compacta were found to display immunoreactivity for GABA<sub>B</sub>R1. Less GABA<sub>B</sub>R1 immunoreactivity was detected in neurons of the substantia nigra pars reticulata. In addition, the tyrosine hydroxylase-immunoreactive dopaminergic neurons and the parvalbumin-immunoreactive GABAergic neurons in the substantia nigra pars reticulata were also found to display moderate GABA<sub>B</sub>R2 immunoreactivity. These results demonstrate that there is also a distinct pattern of localization of GABA<sub>B</sub>R1 and GABA<sub>B</sub>R2 immunoreactivity in different subpopulations of the rat substantia nigra. A functional GABA<sub>B</sub> receptor may be expressed by the dopaminergic neurons in the substantia nigra pars compacta. It is less clear whether neurons in the substantia nigra pars reticulata express a functional GABA<sub>B</sub> receptor. In the electron microscope, GABA<sub>B</sub>R1 and GABA<sub>B</sub>R2 immunoreactivity was found in dendritic elements as well as in axonal elements in the neostriatum and the globus pallidus. These results confirm that neurons in the neostriatum and the globus pallidus may display both GABA<sub>B</sub> receptor subunits, although neurons may express a much higher level of GABA<sub>B</sub>R1 than GABA<sub>B</sub>R2 subunit. Last but not least, immunoreactivity for GABA<sub>B</sub>R1 and GABA<sub>B</sub>R2 was found to be increased in the substantia nigra but not in the neostriatum of the 6-hydroxydopamine-lesioned rat, an animal model of Parkinson's disease. These results indicate that expression of GABA<sub>B</sub> receptors in the neostriatum and the substantia nigra is differentially affected by dopamine denervation. These findings may have important implications in treatment of Parkinson's disease.

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