

Studies Of Neurotransmitters At The Synaptic Level: Editors E. Costa, L. L. Iversen And R. Paoletti



Dopamine-Induced Changes in $G\alpha_{olf}$ Protein Levels in Striatonigral and Striatopallidal Medium Spiny Neurons Underlie the Genesis of L-DOPA-Induced Dyskinesia in Parkinsonian Mice

Ryoma Morigaki^{1,2,3}, Shinya Okita^{1,2,3} and Satoshi Goto^{1,2,3*}

¹Department of Neurodegenerative Disorders Research, Institute of Biomedical Sciences, Graduate School of Medical Sciences, Tokushima University, Tokushima, Japan, ²Parkinson's Disease and Dystonia Research Center, Tokushima University Hospital, Tokushima, Japan, ³Department of Neurosurgery, Institute of Biomedical Sciences, Graduate School of Medical Sciences, Tokushima University, Tokushima, Japan

The dopamine precursor, L-3,4-dihydroxyphenylalanine (L-DOPA), exerts powerful therapeutic effects but eventually generates L-DOPA-induced dyskinesia (LID) in patients with Parkinson's disease (PD). LID has a close link with deregulation of striatal dopamine/cAMP signaling, which is integrated by medium spiny neurons (MSNs). Olfactory type G-protein α subunit ($G\alpha_{olf}$), a stimulatory GTP-binding protein encoded by the $GNAI3$ gene, is highly concentrated in the striatum, where it positively couples with dopamine D_1 (D_1R) receptor and adenosine A_{2A} receptor ($A_{2A}R$) to increase intracellular cAMP levels in MSNs. In the striatum, D_1R s are mainly expressed in the MSNs that form the striatonigral pathway, while D_2R s and $A_{2A}R$ s are expressed in the MSNs that form the striatopallidal pathway. Here, we examined the association between striatal $G\alpha_{olf}$ protein levels and the development of LID. We used a hemi-parkinsonian mouse model with nigrostriatal lesions induced by 6-hydroxydopamine (6-OHDA). Using quantitative immunohistochemistry (IHC) and a dual-antigen recognition *in situ* proximity ligation assay (PLA), we here found that in the dopamine-depleted striatum, there appeared increased and decreased levels of $G\alpha_{olf}$ protein in striatonigral and striatopallidal MSNs, respectively, after a daily pulsatile administration of L-DOPA. This leads to increased responsiveness to dopamine stimulation in both striatonigral and striatopallidal MSNs. Because $G\alpha_{olf}$ protein levels serve as a determinant of cAMP signal-dependent activity in striatal MSNs, we suggest that L-DOPA-induced changes in striatal $G\alpha_{olf}$ levels in the dopamine-depleted striatum could be a key event in generating LID.

Keywords: olfactory type G-protein α subunit, dopamine, striatum, Parkinson's disease, L-DOPA-induced dyskinesia

INTRODUCTION

Human pathology has shown that Parkinson's disease (PD) results from dopamine deficiency in the neostriatum, particularly in the putamen, due to degenerative loss of nigrostriatal dopaminergic cells (Kish et al., 1988; Goto et al., 1989). Treatments with the dopamine precursor, L-3,4-dihydroxyphenylalanine (L-DOPA), remain the gold standard of drug

OPEN ACCESS

Edited by:

Hansen Wang,

University of Toronto, Canada

Reviewed by:

Erminio Iversen,

Centre National de la Recherche

Scientifique (CNRS), France

Denis Hervé,

Institut National de la Santé et de la

Recherche Médicale (INSERM),

France

Veronique Spambato-Faure,

Centre National de la Recherche

Scientifique (CNRS), France

*Correspondence:

Satoshi Goto

sgoto@tokushima-u.ac.jp

Received: 01 December 2016

Accepted: 26 January 2017

Published: 10 February 2017

Citation:

Morigaki R, Okita S and Goto S

(2017) Dopamine-Induced Changes

in G-protein Levels in Striatonigral

and Striatopallidal Medium Spiny

Neurons Underlie the Genesis of

L-DOPA-Induced Dyskinesia in

Parkinsonian Mice.

Front. Cell. Neurosci. 11:26.

doi: 10.3389/fncel.2017.00026

Studies of Neurotransmitters at the Synaptic Level (Advances in Biochemical Psychopharmacology) [E., L. L. Iversen, and R. Paoletti (editors) Costa] on.Studies of neurotransmitters at the synaptic level / editors, E. Costa, L. L. Iversen, R. Paoletti. Format: Book; Language: English; Published/Created: New York.E., L. L. Iversen, and R. Paoletti (editors) Costa Studies of Neurotransmitters at the Synaptic Level (Advances in Biochemical Psychopharmacology).lemeilleurnettoyantducolon.com: Studies of Neurotransmitters at the Synaptic Level / Advances in Biochemical Book by Costa, E., L. L. Iversen, and R. Paoletti (editors).Studies of Neurotransmitters at the Synaptic Level (Advances in Biochemical Psychopharmacology). Costa, E., L. L. Iversen, and R. Paoletti (editors). 0 ratings .Studies of Neurotransmitters at the Synaptic Level (Advances in Biochemical Psychopharmacology). by Costa, E., L. L. Iversen, and R. Paoletti (editors).Studies of Neurotransmitters at the Synaptic Level: Advances in Biochemical Find all books from E., L. L. Iversen, and R. Paoletti, editors Costa.[pdf, txt, ebook] Download book Studies of neurotransmitters at the synaptic level. Editors: E. Costa, L. L. Iversen, R. Paoletti. online for free.Mechanisms of synaptic transmission: bridging the gaps () / Joseph D . Robinson. Author / Creator Subject, Neural transmission -- Research -- History -- 20th century. Synapses Neurotransmitter Release; Studies of neurotransmitters at the synaptic level.: Editors: E. Costa, L. L. Iversen [and] R. Paoletti.Author(s): Costa,Erminio; Iversen,Leslie L; Paoletti,Rodolfo Title(s): Studies of neurotransmitters at the synaptic level. Editors: E. Costa, L. L. Iversen [and] R.Results 1 - 20 of Studies of neurotransmitters at the synaptic level: Editors: E. Costa, L.L. Iversen [and] R. Paoletti. Costa, Erminio (Editor). New York.Studies of neurotransmitters at the synaptic level.: Editors: E. Costa, L.L. Iversen [and] R. Paoletti . by Costa, Erminio, editor and Ebadi, Manuchair S., editor.Studies of neurotransmitters at the synaptic level. Editors: E. Costa, L.L. Iversen [and] R. Paoletti(Book) 13 editions published between and in.Studies of neurotransmitters at the synaptic level. editors, E. Costa, L.L. Iversen [and] R. Paoletti. The dynamical systems approach to cognition concepts.Studies of natural vegetation characteristics at different environments and range improvement practices at Southern West Bank / al-Joaba, Studies of neurotransmitters at the synaptic level. editors, E. Costa, L.L. Iversen [and] R. Paoletti.biographical notes on, 84, ., Costa, E., Iversen, L. L. &Paoletti, R. (editors). Studies of neurotransmitters at the synaptic level, synaptic terminal, function in central nervous system, . Paoletti, R., see Costa, E., Paramecium. [\[PDF\] Proceedings Of The Boston Area Colloquium In Ancient Philosophy](#) [\[PDF\] First International Conference On E-Science And Grid Computing: Proceedings Melbourne, Australia, De](#) [\[PDF\] Basic Concepts In Information Theory And Statistics: Axiomatic Foundations And Applications](#) [\[PDF\] Adequacy Of Laws And Regulations Governing Rail Transportation Of Hazardous Chemicals: Hearing Befor](#) [\[PDF\] Lessons For A Sunday Father](#)

[\[PDF\] Things I See At Easter](#)

[\[PDF\] Sticky Situations: 365 Devotions For Kids And Families](#)