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BOSTON UNIVERSITY

ANNOUNCEMENT OF FINAL ORAL EXAMINATION
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

CANDIDATE:	**Maripierre Surpris**
DEPARTMENT OR PROGRAM:	**Neuroscience**
TITLE OF DISSERTATION:	**"Optogenetic Dissection of Striatopallidal Circuitries in Control of Motor Activity"**
DATE, TIME, AND PLACE:	**Thursday, July 16, 2015 at 1:00p.m.** **Boston University** **24 Cummington Mall (Room L 103)** **Boston, MA 02215**

EXAMINING COMMITTEE

FIRST READER:	**Dr. Jiang-Fan Chen**	
SECOND READER:	**Dr. Benjamin Wolozin**	
THIRD READER:		
CHAIRMAN OF THE EXAMINING COMMITTEE:	**Dr. Shelley Russek**	**Email: srussek@bu.edu**
ADDITIONAL COMMITTEE MEMBERS:	**Dr. Xue Han**	
	Dr. Richard Myers	
	Dr. Jun Lu	

Members of the committee are asked to confirm attendance by replying directly to the Chairman of the Examining Committee.

ALL MEMBERS OF THE SCHOOL OF MEDICINE FACULTY ARE INVITED TO ATTEND.

OPTOGENETIC DISSECTION OF STRIATOPALLIDAL CIRCUITRIES IN CONTROL OF MOTOR ACTIVITY

MARIPIERRE PAYEN SURPRIS

Boston University School Medicine, 2015

Major Professor: Jiang-Fan Chen, M.D., Ph.D., Professor of Neurology & Pharmacology

ABSTRACT

The striatopallidal (indirect) pathway is considered as the main modulatory locus for the basal ganglia control of motor functions. According to the classic basal ganglia model, the striatopallidal pathway inhibits motor activity mainly via its projection to globus pallidus (GPe). However, striatopallidal medium spiny neurons (MSNs) form extensive feedback and lateral inhibitory networks via their collaterals. Thus, the striatopallidal pathway may control motor activity either through its projections onto GPe or through the striatal collaterals.

To further define the circuit mechanism whereby the striatopallidal pathway controls motor activity, we have developed two new optogenetic transgenic mouse lines expressing channelrhodospin-2 (ChR2) or archaerhodopsin-3 (Arch) selectively in the striatopallidal neurons under the Adora2a gene promoter. Consistent with previous optogenetic studies, we found that ChR2 activation and Arch silencing of the striatopallidal neurons in dorsolateral striatum (DLS) suppressed and increased motor activity, respectively. However, contrary to the prediction from the classical model, we

found that selective activation of the striatopallidal axon projections in GPe increased locomotor activity. Thus, light stimulation of MSN cell bodies and collaterals in DLS, versus stimulation in GPe axon projections, produced opposite motor responses.

This led us to reassess the function of the striatopallidal collaterals and to test the hypothesis that the profuse projections and collaterization within the striatum may contribute to striatopallidal pathway control of motor activity. We found that ChR2-mediated activation of the striatopallidal neurons in DLS induced c-Fos expression in ChR2/GFP-positive MSNs. Conversely, Arch-mediated silencing of the striatopallidal neurons induced c-Fos expression and MAPK phosphorylation in Arch/GFP-negative MSNs surrounding the Arch/GFP-positive MSNs. This c-Fos/pMAPK expression pattern in MSNs is consistent with the suppression of GABA release in GFP-positive cells, resulting in the induction of c-Fos in GFP-negative cells having collateral connections with the GFP-positive cells.

Together, our findings revealed a previously unrecognized complexity and novel motor control mechanism of the striatopallidal pathway: activation of striatopallidal projections to GPe increases motor activity while activation of striatopallidal neurons and collaterals in the DLS may contribute to motor suppression. These findings call for a revisit of GPe as a potential locus for deep brain stimulation in Parkinson's disease.