Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2016-2017

Project Nº 34

Title: Stereological estimates of GABA-A receptor gamma 2 subunit-immunoreactive neurons in the pedunculopontine and laterodorsal tegmental nuclei in the rat

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Summary

The basal ganglia are a set of interconnected subcortical structures that in close association with the cerebral cortex play a key role in goal-directed behavior. Alterations in basal ganglia circuits lead to diverse pathologies, such as Parkinson's disease (PD). The projections from the output nuclei of the basal ganglia to the pedunculopontine tegmental nucleus (PPTg) are particularly implicated in gait and posture, as shown by the partial benefits rendered to PD patients with severe gait disorders, by deep brain stimulation of the PPTg. Despite this, the postsynaptic targets of pallidotegmental fibers in PPTg and the associated laterodorsal tegmental nucleus (LDTg) have not been determined yet. Pallidotegmental projections are GABAergic, and GABA-A receptors (GABA-A Rs) mediate neural transmission in these nuclei. As a first step to identify potential sites of pharmacological intervention in PPTg and LDTg in relation to gait disorders, we aim to determine whether GABA-A receptors are localized in cholinergic or non-cholinergic cells of PPTg and LDTg, or in both, and also estimate the density and regional distribution of cells expressing GABA-A Rs.

The GABA-A R gamma 2 subunit is the most widely expressed subunit in the rat brain. Thus, dual immunocytochemistry will be carried out in sections containing PPTg and LDTg in order to label 1) the cholinergic neurons which identify these nuclei, and 2) the cells expressing the gamma 2 subunit. An stereological estimation of the density of neurons expressing the receptor will be carried out, distinguishing between cholinergic and non-cholinergic neurons. The potential coexpression of markers will also be determined using dual immunofluorescence labeling and subsequent analysis at the confocal microscope.

References

Gut and Winn (2015) Deep brain stimulation of different pedunculopontine targets in a novel rodent model of parkinsonism. J Neurosci. 35 (12):4792-803. doi: 10.1523/JNEUROSCI.3646-14.2015.

Wang and Morales (2009) Pedunculopontine and laterodorsal tegmental nuclei contain distinct populations of cholinergic, glutamatergic and GABAergic neurons in the rat. Eur J Neurosci 29: 340-358.

Mena-Segovia et al (2004) Pedunculopontine nucleus and basal ganglia: distant relatives or part of the same family? Trends Neurosci. 27(10):585-8.

POSSIBILITY OF PhD

YES*

* (PhD grant required)