

Electrophysiological properties of dopaminergic neurons in physiological and pathological conditions

N. Berretta¹, A. Ledonne¹, D. Mango¹, E. Guatteo¹, M. Federici¹, P. Krashia¹, R. Nisticò¹, N.B. Mercuri^{1,2}

¹IRCCS Fondazione Santa Lucia, 00143 Rome, Italy

²Dipartimento di Medicina dei Sistemi, University of Rome Tor Vergata, 00133 Rome Italy

The dopaminergic neurons of the ventral mesencephalon are able to fire spontaneously *in vitro* because of an intrinsic pacemaker currents. This activity is under the influence of released neurotransmitters that transform the pacemaker firing in irregular- or burst-like in *in vivo* condition. In this presentation, several physiological and pharmacological features of ventral tegmental area (VTA) and substantia nigra pars compacta neurons (SNpc) will be examined. Of paramount importance for the modality of firing and thus, the release of dopamine in the terminal fields, is the tone of dopamine itself that activates D2 autoreceptors at the somato-dendritic and terminal level of the dopaminergic cells. Therefore, different drugs by acting on the metabolism, release and uptake of this catecholamine affect the firing properties of the DAergic neurons. Moreover, the specific conductances and intracellular pathways activated by ionotropic and metabotropic receptors in these cells will be delineated in normal condition and in *in vitro* models of Parkinson disease. In particular, we will establish if a treatment with the DA precursor levodopa exerts acute toxic effects on the functioning of the dopaminergic neurons. Moreover, preliminary data regarding a rat model of synucleinopathic disturbance will be presented. A particular attention will be paid to the modalities of DA release in the striatum and the influence of abused drugs on catecholamine overflow .

To accomplish this we will use *in vitro* extracellular, intracellular and patch-clamp electrophysiological recordings plus amperometric detection of DA release in mesencephalic and striatal slices obtained from wild and affected rodents.