

Is there a prophylactic medication in REM sleep disturbances, which hint at synucleinopathias?

Werner, F.-M.^{1,2}; Coveñas, R.²

1 Euro-Schulen Pößneck, Pößneck, Germany

2 Institute of Neurosciences of Castilla and León (INCYL), Laboratory 14, University of Salamanca, Spain

Introduction: In the DGSM congress 2014, REM sleep behavioral disorders were reported: the SPECT examination showed an asymmetric description of the dopamine transporter system. These sleep disturbances predict synucleinopathias such as Parkinson's disease. The question, whether there is a prophylactic mediation for these neurodegenerative diseases, will be answered by means of a neural network in the extrapyramidal system.

Material/methods: The neural network can be described as follows: **D1** and **D2** dopaminergic neurons in the substantia nigra activate dopaminergic neurons in the caudate nucleus. **D1** dopaminergic neurons weakly activate dynorphin neurons, which weakly inhibit via kappa receptors substance P neurons. The latter neurons activate weakly, via **NK1** receptors, GABAergic neurons located in the globus pallidus internus. In the caudate nucleus, **D2** dopaminergic neurons weakly activate GABAergic neurons in the globus pallidus externus, which inhibit glutaminergic neurons in the subthalamic nucleus. The latter neurons strongly inhibit, via **NMDA** receptors, **D2** dopaminergic neurons located in the substantia nigra and GABAergic neurons in the globus pallidus internus. In the latter nucleus, GABAergic neurons weakly inhibit thalamic glutaminergic neurons, which activate other cortical glutaminergic neurons. These neurons can activate **D1** and **D2** dopaminergic neurons in the caudate nucleus. In the globus pallidus internus, GABAergic neurons weakly inhibit **M4** muscarinic cholinergic, **5-HT2A** serotonergic and **NTS1** neurotensin neurons located in the putamen. The latter neurons transmit a strong postsynaptic excitatory impulse to glutaminergic neurons, which inhibit via **NMDA** receptors **D2** dopaminergic neurons located in the putamen. The **D2** dopaminergic neurons in the putamen are connected to other dopaminergic neurons located in the caudate nucleus.

Results: Since in Parkinson's disease, apart from dopamine and acetylcholine alterations, a GABA deficiency and a glutamate surplus can be found, it might be possible to weaken the neurotransmitter imbalance by a drug, which exerts simultaneously a **GABAA** agonistic and a **NMDA** antagonistic effect. Through the **GABAA** agonistic effect the acetylcholine, serotonin and neurotensin surplus could be reduced. The **NMDA** antagonistic effect could increase dopamine levels through a reduced presynaptic inhibition.

Conclusion: It is very important to observe patients with REM sleep behavioral disorders and to minimize the risk for synucleinopathias by using an appropriate medication.

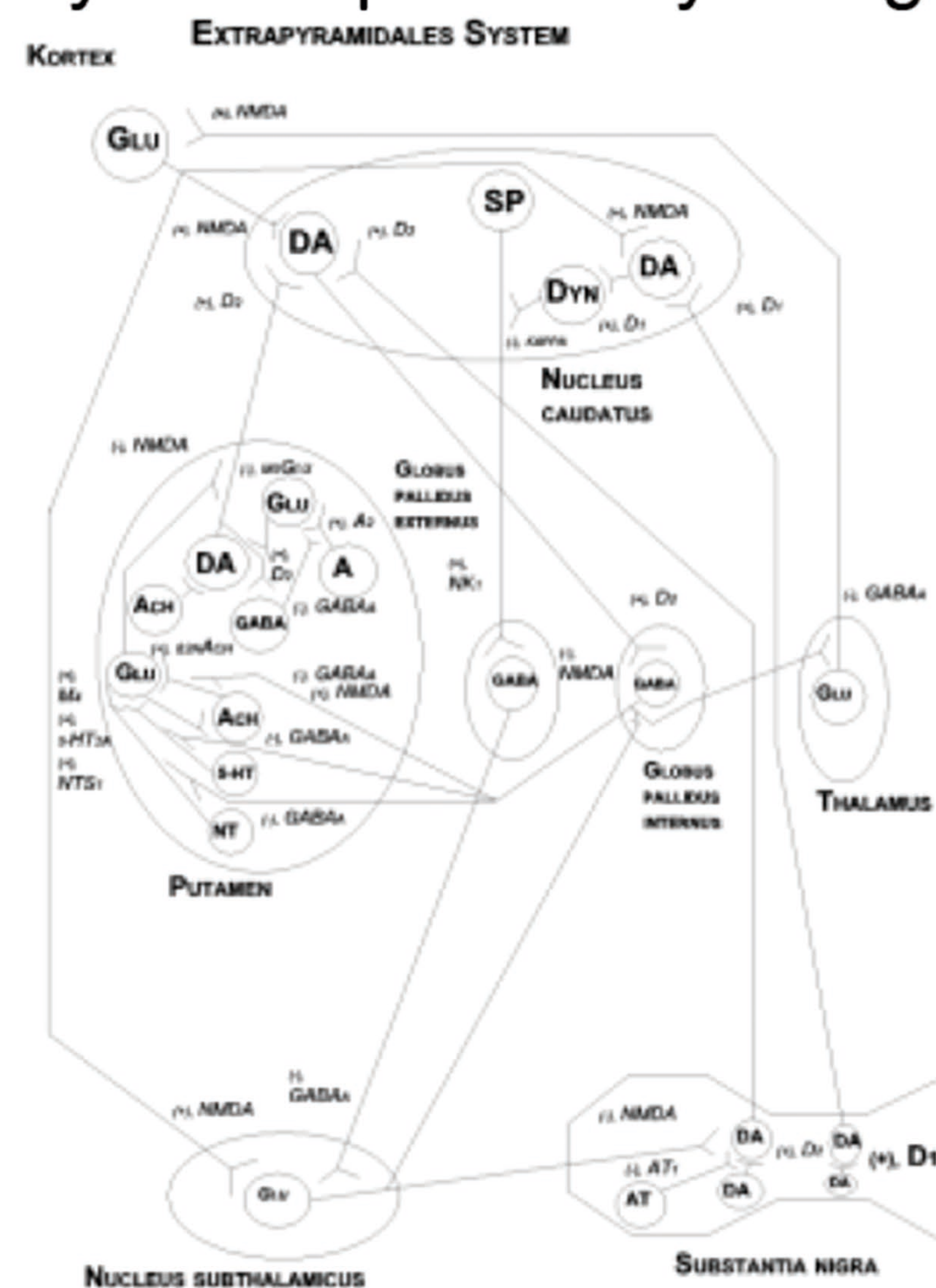


Fig.1: Neural networks in the extrapyramidal system.