



Presentation Abstract

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Presentation Title: Gap junctions as modulators of synchrony in Parkinson's disease

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Abstract: Parkinson's disease (PD) patients show abnormal levels of synchrony and low-frequency oscillations in the basal ganglia and the motor cortex. This altered neural activity is often associated with the motor symptoms of PD, but the mechanisms for the emergence of synchrony and oscillations remain debated. We suggest that neural gap junctions in cortex and basal ganglia contribute to this transition in activity. While gap junctions between interneurons of cortex and striatum are well described, we do not know whether they appear in GPe and internal globus pallidus (GPi). Using confocal microscopy, we were able to detect the gap junction protein Cx36 in the human GPe and GPi, which was up-regulated in PD patients. Also the corresponding rat tissue showed Cx36 expression. Dopamine has already been described to modulate the conductance of gap junctions [1], especially also in the rat striatum, where dye coupling was increased after dopamine depleting 6-OHDA lesions [2]. In a conductance-based network model of the basal ganglia, we investigate the effect of gap junctional coupling in GPe and GPi on synchrony. While chemical synapses normally desynchronize the network, gap junctional coupling of sufficient strength is able to synchronize the whole basal ganglia. Also synchronized input from cortex to subthalamic nucleus has impact on synchronization, in particular in the case of numerous gap junctions in GPe. To describe the effect of gap junctional coupling between cortical interneurons on synchronized oscillations in the cortex, we introduce a diffusion term in a mean-field model. For high gap junctional coupling, large-amplitude oscillations of low frequency occur which are absent for low gap junctional coupling. Via the hyperdirect pathway, these oscillations

could further synchronize the basal ganglia. We conclude that gap junctions can be a powerful trigger of synchrony in the basal ganglia. Their dependence on dopamine could explain the shifts of synchrony in PD. References 1. Li, H, Zhang, Z, Blackburn, MR, Wang, SW, Ribelayga, CP and O'Brien, J Adenosine and dopamine receptors coregulate photoreceptor coupling via gap junction phosphorylation in mouse retina. (2013) *The Journal of Neuroscience*, 33(7), 3135-3150. 2. Onn, SP and Grace, AA: Alterations in electrophysiological activity and dye coupling of striatal spiny and aspiny neurons in dopamine-denervated rat striatum recorded in vivo. (1999) *Synapse*, 33(1):1- 15.

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