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Letter for Leonid Rubchinsky

I'm very pleased to write on behalf of Leonid Rubchinsky. I have known Leonid since 2001, when he became a Postdoctoral Research Fellow working with Dr. Karen Sigvardt of UC Davis. At that time, Karen was making a transition to working full time on scientific questions concerning Parkinson's disease (PD). She and I had been discussing this subject previously, and when Leonid joined her, the three of us began to work together on computational issues.

The problem we addressed was a difficult and open-ended one: to try to make sense of the variety of pathologies in PD from physiological properties of the substructures of the basal ganglia and their connections. Though PD is well studied in the medical community, the classic ways of thinking about the movement disorders associated with it were based on static conceptions of the activity in different pathways between the input structure (striatum) and output structure (globus pallidus) of the basal ganglia. It has been understood for some time that the classic approach is inadequate, and that dynamics are somehow needed. This is almost virgin territory: there is very little literature on this subject. The closest work is an interesting paper by Terman and collaborators, dealing with dynamics in an *in vitro* preparation of two interacting substructures of the basal ganglia; but that work does not address any functional issues.

The aim of the paper we did together was to explore how the dynamics and connectivity between the subthalamic nucleus (STN) and the two parts of the globus pallidus (Gpe, Gpi) could work together to discriminate between competing signals for motor program initiation. We found that dynamic properties of the basal ganglia subsets, such as rebound properties in the STN, were important in this discrimination. In our models, this rebound turned out to require long-lasting inhibition given by GABA_B. We also gave scenarios under which changes associated with PD in anatomical connections could give rise to the akinesias known to be primary symptoms of PD. In this collaboration, Leonid did the bulk of the work, with Karen and me acting mainly as consultants. The work is in press in PNAS.

The work I did with Leonid was all numerical, but in his previous incarnation as a physicist, he has written many papers on dynamical systems. Though I did not have the opportunity to see him in action working on analytical mathematics, I could see that he thinks very clearly and gets to the heart of questions. The simulations required a deep level of understanding of the dynamics, and I learned a lot from his heuristic analyses. I was very impressed by how fast he learned the relevant

biology, and how deeply he dug to find the relevant data. I also find it extremely impressive that he is now able himself to be the consulting physiologist for a PD operating team.

Personally, Leonid is soft-spoken but determined, and a pleasure to work with. I'm very happy to recommend him.

Sincerely,

Nancy Kopell

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