COBRE
Investigators

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Title off project: Co-Transmission of Glutamate with Dopamine in *C. elegans* Movement Based Behaviors.

Summary:
Parkinson's disease (PD) characterized by loss in control of skeletal muscle movement with its initial indicators of impaired balance, and subtle tremors, and pre-clinical models have suggested assessing habituation to balance perturbations for early detection of PD. Dopamine dysregulation and ultimately degeneration of dopaminergic neurons is clearly known to play a central role in PD, and recent observations also implicate another neurotransmitter glutamate which is based in part on the relative effectiveness of PD drugs targeting metabotropic glutamate receptors. Even though the mechanisms underlying the onset of PD remain unclear, there is increasing evidence indicating that glutamate and dopamine may play synergistic roles, and that dysregulation of glutamatergic transmission in PD may be directly linked to its potential co-transmission with dopamine. Our focus is on investigating co-transmission of glutamate with dopamine in *Caenorhabditis elegans* to understand the role of glutamate in movement control. Two alternate models of glutamate/dopamine co-transmission have been proposed: either glutamate is packaged along with dopamine in the same vesicles and therefore the two neurotransmitters are co-released at the same synaptic connections (a), or the two neurotransmitters are packaged into separate vesicles thereby allowing the neuron to release different neurotransmitters at different structures (b). Our working hypothesis is that the worm dopaminergic neurons co-transmit glutamate, and disruption of signaling in dopaminergic neurons directly influences glutamatergic transmission that results in aberrant movement related behaviors. Our approach with the *C. elegans* model uses data-mining, genetic, molecular, behavioral and imaging techniques to study individual dopaminergic neurons and their synaptic targets *in vivo* in ways that are technically difficult if not impossible, in mammals. The specific aims listed in the next section bridge them with our previous work on the molecular interactions of a worm D2-like receptor and its role in anterior touch habituation with the reported role of glutamate receptors in tap habituation by our collaborators (CH) lab.