Parkinson’s Disease and Why Development Matters

Parkinson’s Disease (PD) is defined clinically by motor symptoms that usually arise late in life and are the result of the loss of dopaminergic neurons, but a variety of nonmotor symptoms including depression can precede these symptoms by many years, and genes causing PD are normally expressed throughout the lifespan, including development. It is with this in mind, that we have been examining the effect of PD-causing gene mutations on brain development. Our data show that a knockin mutation of the most prevalent genetic cause of PD, LRRK2-G2019S, alters the structure and function of corticostriatal circuits, and suggest that LRRK2-G2019S coopts synaptic circuits early in life, biasing the actions of cellular pathways in ways that have enduring consequences for learning and stress-related responses in young adulthood. The changes we observe serve to outline novel pathways that can be used to understand, detect, or treat PD.