Miniscope-Based Neural Circuit Profiling in Freely Behaving Animals for Preclinical Therapeutic Assessment

Shan Huang[1], David Cheng[1], Amelie Simonnet[2], Emilie Noe[2], Gregory Porras[2], Erwan Bezard[2], Jonathan Zapata[1] and Jonathan Nassi[1]

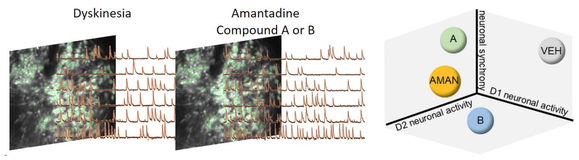
[1]Inscopix, Mountain View, California, United States; [2]Motac neuroscience, Bordeaux, France

Background

- Existing preclinical assays for Parkinson's disease (PD) that rely on behavioral and histological endpoints are largely unable to differentiate between distinct mechanisms and have a poor track record of predicting clinical performance.
- Progress on new PD therapies will be strongly aided by more sensitive, information-rich, and predictive preclinical models.
- The miniscope imaging platform developed by Inscopix allows for cellular resolution activity measurements from hundreds of genetically defined neurons at once in freely moving animals.
- Simultaneous large-scale neural activity and behavior recordings reveal detailed relationships between neural circuit activity and behavioral symptoms and allow the construction of predictive preclinical assays based on the treatment-induced response of large populations of neurons.

Traditional behavior-based assay

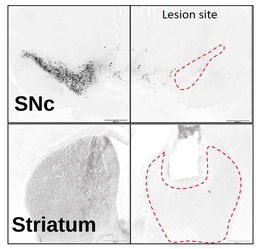
Inscopix integrated neural activity & behavior-based assay

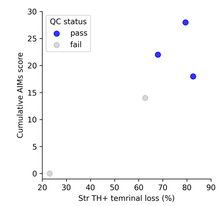


D1 MSN profile of PD, levodopa-induced dyskinesia (LID), and approved PD medications

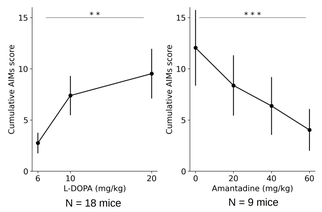
Model Validation

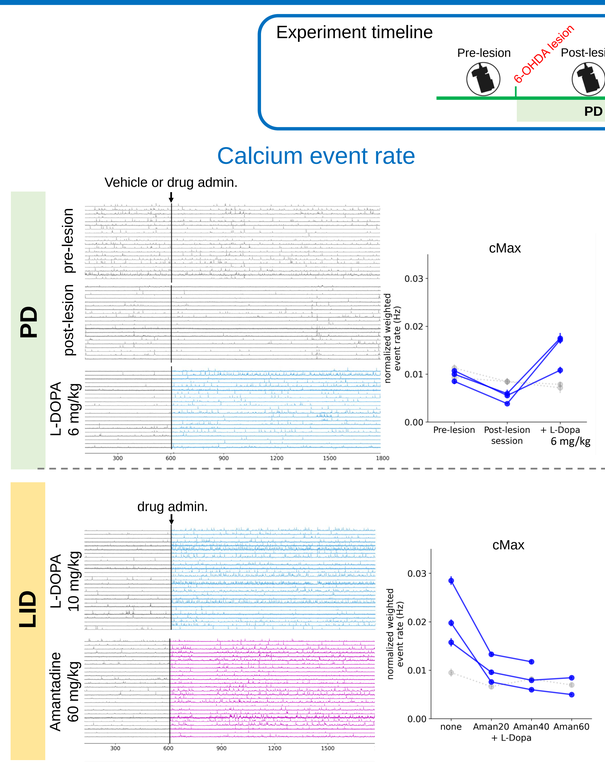
TH⁺ cell loss



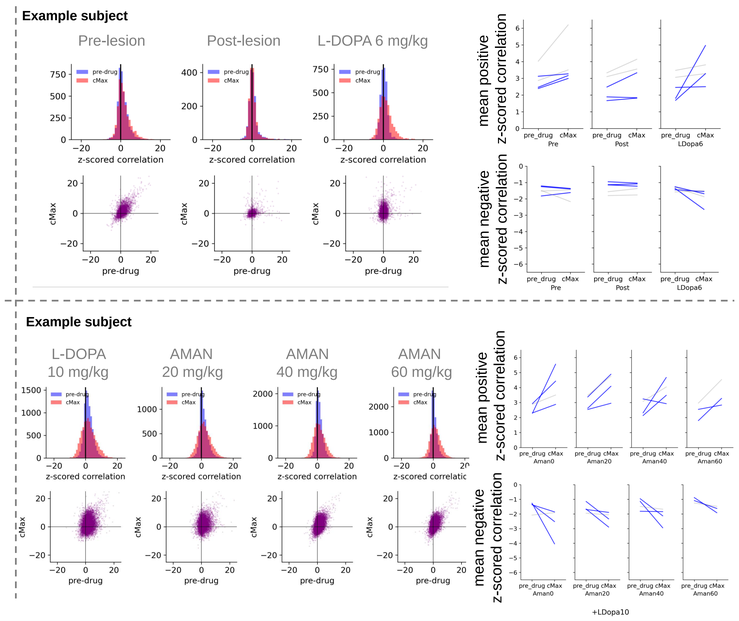


Behavioral Pharmacology



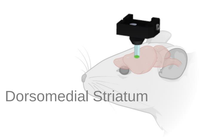


Pairwise neural correlation

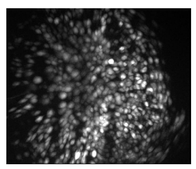


Data processing workflow

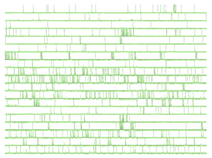
Single-cell resolution calcium imaging



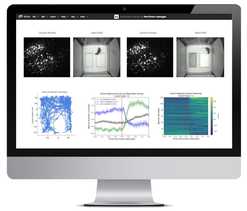
Cell identification



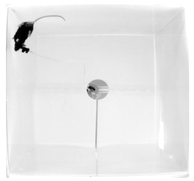
Deconvolved Ca²⁺ spikes



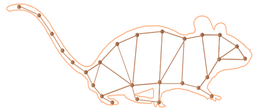
Integrated neural-behavior analysis



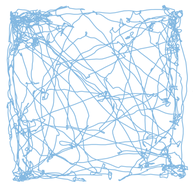
Simultaneous free-behavior recording



DeepLabCut pose estimation



Behavior tracking



*High throughput data processing and analysis pipeline powered by the **IDEAS** platform*

α-synuclein Pre-Formed Fibrils (PFF) model development

- In addition to the traditional neurotoxin models in rodents and primates, which are valuable for studying symptom pathophysiology and treatment, neurodegeneration models offer the potential to show, at a physiological level, how a disease-modifying strategy can normalize abnormal basal ganglia activity.
- The α-synuclein preformed fibril (PFF) mouse model highlights such consequences.