INSTITUTO CAJAL

SEMINARIO PRESENCIAL

Viernes, 8 de Marzo de 2024
12:30 h. Instituto Cajal (CSIC) Madrid

DRA. CRISTINA ALCACER
Alcalá University

BEHAVIORAL FEATURES AND STRIATAL PATHWAYS IN A MOUSE MODEL OF L-DOPA-INDUCED DYSKINESIA

Abstract

L-DOPA is the standard treatment for Parkinson's disease (PD), yet its long-term use leads to L-DOPA-induced dyskinesia (LID), characterized by disabling abnormal involuntary movements. Recent studies in mice show that LID is associated with the hyperactivity of striatal projection neurons of the “direct pathway” (dSPNs) and the hypoactivity of the “indirect pathway” neurons (iSPNs), but detailed measurement of dyskinetic behavior is lacking. In this project, we introduce a novel, automated method to quantify dyskinetic movements with unprecedented time-scale precision, combined with calcium imaging in freely-moving mice to study striatal activity. We found distinct behavioral clusters in dyskinetic mice, with specific subsets of dSPNs and iSPNs positively modulated for each dyskinesia type. This semi-supervised method allows precise behavioral measurement, revealing that dyskinesia is not explained solely by changes in average SPN activity but by specific hyperactive subsets. This research provides insight into the neural mechanisms underlying different forms of dyskinesia in PD.

Affiliation and short bio

Cristina Alcacer obtained her PhD in neuroscience from the University of “Pierre et Marie Curie” in the lab of Dr. Girault at the Institut du Fer-à-Moulin (CNRS) in Paris, where she studied the intracellular signaling responses involved in L-DOPA-induced dyskinesia (LID) in a mouse model of Parkinson’s disease (PD). After her PhD, she joined the group of Prof. Cenci, the Basal Ganglia Pathophysiology Unit, at Lund University (Sweden), where she set up and implemented chemogenetics to study the contribution of striatal neurons in PD and LID mouse models. This project resulted in relevant findings disclosing a previously undescribed role of the indirect pathway in dyskinesia pathophysiology. After her post-doc in Sweden, she joined Dr. Rui Costa’s lab (Neurobiology of Action lab) at the Champalimaud Foundation in Lisbon (Portugal). There, she focused on identifying patterns of striatal activity coding for dyskinesia in freely-moving mice, using calcium imaging. She also developed automated tools to detect dyskinesia, using motion sensors and machine learning algorithms, to correlate specific dyskinetic movements with striatal activity. She is now a Maria Zambrano postdoctoral researcher affiliated to the University of Alcalá (Motor and Visual System Neurophysiology lab) and working in collaboration with Prof. Moratalla at the Cajal Institute, developing a project on the effects of dopamine depletion in the retinal cells involved in movement perception.

GOBIERNO DE ESPAÑA MINISTERIO DE CIENCIA E INNOVACIÓN

CSIC
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

Instituto Cajal. CSIC
Avda. Doctor Arce, 37. 28002. Madrid. Tel. 91 585 4750
www.cajal.csic.es

Related publications with the topic:

Alcacer C, Klaus A, Mendonça M, Abalde S, Cenci MA and Costa R. A new automated tool to cluster dyskinesia reveals highly specific striatal patterns associated with distinct dyskinetic movements. In prep

Alcacer C*, Andreoli L, Sebastianutto I, Jakobsson J, Fieblinger T, Cenci MA. 2017. Chemogenetic stimulation of striatal projection neurons modulates responses to Parkinson's disease therapy. J Clin Invest. Vol 127(2): 720-734. (* corresponding author). DOI: 10.1172/JCI90132

Fieblinger T, Graves SM, Sebel LE, Alcacer C, Plotkin JL, Gertler TS, Chan CS, Heiman M, Greengard P, Cenci MA, Surmeier DJ. 2014. Cell type-specific plasticity of striatal projection neurons in parkinsonism and L-DOPA-induced dyskinesia. Nat Commun. Vol 5:1-15. DOI: 10.1038/ncomms6316

Alcacer C, Santini E, Valjent E, Gaven F, Girault JA, Hervé D. 2012. Gα(olf) mutation allows parsing the role of cAMP-dependent and extracellular signal-regulated kinase-dependent signaling in L-3,4-dihydroxyphenylalanine-induced dyskinesia. J Neurosci. Vol 32(17): 5900-10. DOI: 10.1523/jneurosci.0837-12.2012

Instituto Cajal. CSIC

Avda. Doctor Arce, 37. 28002. Madrid. Tel. 91 585 4750

www.cajal.csic.es