

## Parkinson's Disease and Movement Disorder

### Group leader

Kulisevsky Bojarski, Jaime (FGS)

### Researchers

Aracil Bolaños, Ignacio (FGS)

García Sánchez, Carmen (FGS)

Gironell Carrero, Alexandre (FGS)

Martínez Horta, Saul Indra (FGS)

Pagonabarraga Mora, Javier (FGS)

Pascual Sedano, Berta M (FGS)

Perez Perez, Jesus (FGS)

Ruiz Barrio, Iñigo (IR)

Sampedro Santalo, Frederic (FGS)

Vazquez Oliver, Anna (CIBER)

### Research Technicians

Alonso Del Olmo, Gloria (IR)

Berzosa Gonzalez, Irene (IR)

Campolongo Perillo, Antonia (FGS)

Carreras Vega, Mireia (IR)

Fernández Vizuete, Cristina (IR)

García Cornet, Julia (IR)

Horta Barba, Andrea (IR)

Olmedo Saura, Gonzalo (IR)

Perez Carasol, Laura (IR)

Pla Sánchez, Monica (IR)

Pons Pons, Gracia (IR)

Rivas Asensio, Elisa Maria (IR)

Rodríguez-Antigüedad Muñoz, Jon (IR)

Salvat I Rovira, Nil (IR)

Soler Almendros, Judit (IR)



### DESCRIPTION

Led by Jaime Kulisevsky MD, PhD, and based at the Movement Disorders Unit of Sant Pau Hospital and Sant Pau Biomedical Research Institute, the group focuses its interest on Parkinson's disease, Huntington's disease, atypical parkinsonisms, tremor, and other movement disorders research.

The priority lines include the study of neuronal mechanisms related to cognitive impairment development and neuropsychiatric symptoms in movement disorders, the development of specific instruments for these symptoms' diagnosis and the study of different pharmacological agents' responses.

To meet the challenge of deepening our knowledge of the mechanisms involved in these symptoms' development, the group works with neuroimaging techniques, neuropsychology, clinical assessment, brain stimulation, genetics, and biomarkers, among others.

### MAIN LINES OF RESEARCH

- Cognitive Impairment, Behavioural Dysfunctions and other non-motor symptoms in Parkinson Disease (PD):
  - Study of the neural correlates of cognitive performance, mild cognitive impairment, dementia, and behavioral alterations (apathy, visual hallucinations and impulse control disorders) in PD using neurophysiological techniques (event related brain potentials), structural, functional, and molecular neuroimaging.
  - Characterization of the neurodegenerative process underlying cognitive impairment in PD through the study of cortical atrophy patterns related to genetic and biomarker indicators.



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- Development and validation of PD-specific tools for cognitive and functional assessment to detect subtle changes in cognitive performance and treatment response.
- Prospective follow-up study of cognition and mood in PD patients with deep-brain stimulation of the subthalamic nucleus.
- Identification of blood-based, cognitive, and neurophysiological biomarkers of cognitive deterioration in PD.
- Identification of genetic and neurophysiological biomarkers of apathy and impulse control disorders in PD.
- Data science applied to large PD databases such as PPMI.
- Surgery and treatments of continuous infusion of intraduodenal levodopa.
- Study of the effects of continuous infusion of intraduodenal levodopa on cognition and mood.
- Follow-up and etiologic study of weight loss in patients treated with continuous infusion of intraduodenal levodopa.
- Huntington's disease (HD):
  - Characterization of the natural course HD in large and international cohort and studies (Enroll-HD).
  - Study of the neural correlates of clinical progression, cognitive performance, mild cognitive impairment, dementia and behavioral alterations in HD using neurophysiological techniques (event-related brain potentials), structural, functional and molecular neuroimaging.
  - Identification of potential neuroimaging, blood-based, muscular tissue, CSF, and clinical biomarkers of disease progression in premanifest and manifest HD.
  - Study of the prevalence and neural substrates of behavioral alterations in premanifest and manifest HD.
  - Development and validation of HD-specific tools for cognitive and functional assessment to detect subtle changes in cognitive performance and treatment response.
- Study of the effect of intermediate alleles and homozygous on the clinical presentation of HD.
- Data science applied to large HD databases such as Enroll-HD and Registry.
- Identification of different cognitive phenotypes in HD.
- Study of the role of TAU in the heterogeneity of cognitive deterioration and trajectory of neurodegeneration in HD.
- Progressive supranuclear palsy (PSP):
  - Development of a PSP-specific cognitive rating scale.
  - Development of a standardized eye movement evaluation.
  - Study of the neural correlates of clinical progression, cognitive performance and behavioral alterations in PSP using structural and functional neuroimaging.
- Essential tremor:
  - Molecular neuroimaging in essential tremor.
  - Clinical, neurophysiological and neuroimaging assessment of patients with FXTAS (fragile X-associated tremor/ataxia syndrome).

## SCIENTIFIC CHALLENGES

### Parkinson's Disease (PD)

- General
  - COPPADIS: Cohort of Patients with Parkinson's Disease in Spain (national collaborative study).
  - Intensification for Specialist Physicians of the "Strategic Research and Innovation Plan" (PERIS) Expedient Number: SLT008 / 18.
- Cognition
  - DuoCog: randomized, double blind and crossed study (immediate levodopa vs. intraduodenal in cognition and mood).
  - Neuropsychiatric disorders.
  - Prospective study: new method of music therapy in apathy and depression.
  - Choral singing in patients with PD. Study on its effects on apathy and depression.



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- Effects of mindfulness on the presence and development of TCI.
- Natural history and neural correlates of psychotic symptoms in PD patients.
- Advanced PD
  - Nutritional analysis in patients with intraduodenal levodopa.
  - Prospective study of cognitive, behavioral, sleep and quality of life in patients with deep brain stimulation (DBS) and intraduodenal levodopa.
  - Prospective study of patient satisfaction after DBS.
  - Subthalamic DBS study in PD: functional reorganization of brain networks and repercussions on postsurgical complications.
  - Monitoring the mobility using a sensor in fluctuating PD for therapeutic purposes. Multicenter Clinical Trial (INV-PROC-A118).

#### Huntington Disease (HD)

- Coordination of the "Cognitive Phenotype Working Group" (European Huntington's Disease Network).
- Spanish Coordination of Enroll-HD: A Prospective Registry Study in a Global Huntington's Disease Cohort (PI in Spain: J. Kulisevsky)
- Validation of cognitive (HD-CRS) and functionality (HD-CFRS) scales.
- Development and validation of new tools for cognitive and functional assessment of cognitive impairment in HD.

#### Tremor

- Development of a tremor diagnostic system using a mobile app and software. Joint project with Mediktor company
- Perampanel in essential tremor. "Real life" study.

#### Other neurodegenerative diseases

- Neural correlates of hypofrontality in different subtypes of progressive supranuclear palsy (PSP).
- Neuropsychiatric and behavioral symptoms in PSP subtypes.
- FXTAS: collaborative research with Genetics

from Hospital Clínic (Barcelona) and Associació Catalana X Fràgil (ACXF).

- Collaboration with GEMT-CAT (Movement Disorders Group Catalan Neurology Society) in the Consensus Document on Genetics in Movement Disorders.

#### Neuroimaging and data engineering

- Dynamic connectivity models in cognitive impairment in PD. In collaboration with the Center for Brain and Cognition, Pompeu Fabra University, Barcelona.
- Neuroimaging and neurophysiology of hallucinations in PD: Project: "Unraveling dysfunctional brain networks in patients with Parkinson's disease suffering from hallucinations", in collaboration with Prof. Blanke, Ecole Polytechnique Fédérale de Lausanne (EPFL), Switzerland.
- Effects of dopaminergic treatment of PD on neurocognitive networks. Collaborative study with Hospital del Mar, Barcelona.
- Functional and structural brain correlates in HD: cognition, apathy, depression, irritability, biomarkers, oxytocin levels. Collaborative study with Hospital de Burgos (HUBU).
- Analysis of collaborative databases ("big-data"): ENROLL (EH), PPMI (EP), COPPADIS (EP).
- Analysis of local databases: PSP, EH, EP.

#### Parkinson's disease and other movement disorders' laboratory

- Processing, biobanking and biomarker analyses of human liquid biological samples (plasma, serum, CSF, and urine) from different movement disorders.
- Development and optimization of methods for extracellular vesicle isolation from different biofluids in movement disorders.
- Identification of molecular signatures in brain, plasma, CSF, and urine extracellular vesicles in Huntington's disease to improve disease prognosis and stratification of patients in clinical trials.
- To explore the clinical utility of the determination of tau and phosphorylated alpha-synuclein in skin tissue, for the early and di-



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Differential diagnosis of Atypical Parkinsonian Syndromes.

#### ACTIVE GRANTS

- Aracil Bolanos, Ignacio. Contratos Juan Rodés 2022. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2026. 180.000,00 €.
- Kulisevsky Bojarski, Jaime. Historia natural y correlatos neuronales de los síntomas psicóticos en pacientes con enfermedad de Parkinson. PI18/01717. Instituto de Salud Carlos III (ISCIII). Duration: 2019-2023. 93.170,00 €.
- Kulisevsky Bojarski, Jaime. Desarrollo y validación de instrumentos específicos de evaluación cognitiva basados en la biología de la enfermedad de Huntington. PI21/01758. Instituto de Salud Carlos III (ISCIII). Duration: 2022-2024. 244.420,00 €.
- Kulisevsky Bojarski, Jaime. ParkinsonAID. ParkinsonAID. Unión Europea. Duration: 2022-2023. 30.000,00 €.
- Kulisevsky Bojarski, Jaime. MALALTIA DE PARKINSON I TRANSTORNOS DEL MOVIMENT. 2022 INV-1 00048. Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR). Duration: 2022-2024. 66.217,84 €.
- Kulisevsky Bojarski, Jaime. Ensayo clínico multicéntrico, aleatorizado, doble ciego y controlado por placebo, de evaluación de la eficacia y la seguridad del donepezilo versus placebo en el deterioro cognitivo leve asociado a la Enfermedad de Parkinson. ICI22/00082. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2026. 575.328,45 €.
- Ruiz Barrio, Iñigo. Contratos Rio Hortega 2022. CM22/00072. Instituto de Salud Carlos III (ISCIII). Duration: 2023-2024. 65.000,00 €.

#### GRANTS AWARDED

- Kulisevsky Bojarski, Jaime. Investigación y desarrollo de una nueva terapia para el tratamiento de la enfermedad de Huntington. CPP2022-009575. Ministerio de Ciencia e Innovación (MICIIN). Duration: 2023-2026. 312.446,20 €.

#### SCIENTIFIC PRODUCTION

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