INSTITUTO CAJAL

SEMINARIO PRESENCIAL

Viernes, 20 de Septiembre de 2024
12:30 h. Instituto Cajal - CSIC

Dra. Ángeles García-Cazorla

Hospital Sant Joan de Déu

PEDIATRIC PARKINSONISM, ETIOLOGY AND PATHOPHYSIOLOGY

Abstract

Pediatric Parkinsonism (PP) is rare, and “Developmental Parkinsonism” is the most common and better described form of PP. It has been related to monoamine defects, a group of genetic diseases without nigrostriatal degeneration. However, clinical and biochemical patterns of neurodegenerative PP are poorly described.

In this work aetiology and pathophysiology of parkinsonism starting in the pediatric age is updated including the results of a personal series of 77 patients. We highlight clinical and genetic phenotypes, neurotransmitter metabolites and L-Dopa response.

Symptoms varied depending on the onset-age: i) 0-2 years: developmental encephalopathy, hypotonia, hypo/akinesia, oculogyric crisis, rigidity; ii) 2-10 years: subacute progressive gait instability, hypokinesia, distal rigidity and dystonia; iii) >10 years: bradykinesia, rigidity, dystonia and behavioural disorders. Twenty-two patients (65%) presented an abnormal NT profile. Mitochondrial disorders were the most common cause found followed by channelopathies, nucleotide metabolism and cell traffic defects. 43% of patients have some response to L-Dopa regardless of CSF homovanillic acid levels. Several genes were described as a cause of PP for the first time (GMF1, PTCD3, CHCHD6, KCNQ2, KIF1A, GNB1, AUTS2, ANKRD11, CSTB, DNAJC3). Additionally, we show experimental approaches to understand pathophysiology and response to treatments in some models of PP.

Affiliation and short bio

Dr Ángeles García-Cazorla is a Paediatric Neurologist at the Sant Joan de Déu Barcelona Children's Hospital, in Barcelona. She is an expert in rare neurometabolic and neurogenetic disorders.

Dr Cazorla obtained her degree in Medicine from the University of Barcelona. She then completed her clinical and scientific training in Inborn Errors of Metabolism and Neurometabolic Disorders at the Hospital Necker, in Paris, and at the University of Columbia in New York. She is an Associated Professor at the University of Barcelona since 2012 and the director of the International Master of Neurometabolism and Cell Biology for Clinicians.

She is currently the Head of the Neurometabolic Disorders Unit and the Director of Research and the “Brain Project” at Sant Joan de Déu Hospital. She is a member of the SSIEM Council, the coordinator of the subgroup of neurotransmitters and other small molecules affecting the brain at the MetabERN (European Reference Network of inherited metabolic disorders).

Her research interests include neurotransmission and the “metabolic environment of the synapse” in inborn metabolic diseases as well as the development of new therapies for these rare diseases. She is currently leading the synaptic metabolism and personalized therapies laboratory in Sant Joan de Déu Hospital. She works in the development of treatments based on brain metabolism modulation and has developed a formula, “Neuroprotect”, to improve neurodevelopment helping to achieve better cognitive and motor performance in children with neurological diseases.
She has published more than 250 peer-reviewed articles in the field of paediatric neurology and neurometabolism and is co-editor of the reference book “Inborn Errors of Metabolism: diagnosis and treatment” from Springer.

Related publications with the topic

Morales-Briceño H, Mohammad SS, Post B et al. Clinical and neuroimaging phenotypes of genetic Parkinsonism from infancy to adolescence. Brain. 2020;143(3):751–70.

Tetrahydrobiopterin (BH4) treatment stabilizes tyrosine hydroxylase: Rescue of tyrosine hydroxylase deficiency phenotypes in human neurons and in a knock-in mouse model.
Jung-Kc K, Tristán-Noguero A, Altankhuyag A, Piñol Belenguer D, Prestegård KS, Fernandez-Carasa I, Colini Baldeschi A, Sigatulina Bondarenko M, García-Cazorla A, Consiglio A, Martinez A.J Inherit Metab Dis. 2024 May;47(3):494-508.

iPSC-based modeling of THD recapitulates disease phenotypes and reveals neuronal malformation.
Tristán-Noguero A, Fernández-Carasa I, Calatayud C, Bermejo-Casadesús C, Pons-Espinal M, Colini Baldeschi A, Campa L, Artigas F, Bortolozzi A, Domingo-Jiménez R, Ibáñez S, Pineda M, Artuch R, Raya Á, García-Cazorla À, Consiglio A.EMBO Mol Med. 2023 Mar 8;15(3):e15847.

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