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### ENERO

## Multi-ancestry genome-wide association meta-analysis of Parkinson's disease

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**Revista:** Nature Genetics
**DOI:** https://doi.org/10.1038/s41588-023-01584-8
**Tipo de articulo/ estudio:** Articulo original/ Metaanálisis

**Resumen:** Although over 90 independent risk variants have been identified for Parkinson's disease using genome-wide association studies, most studies have been performed in just one population at a time. Here we performed a large-scale multi-ancestry meta-analysis of Parkinson's disease with 49,049 cases, 18,785 proxy cases and 2,458,063 controls including individuals of European, East Asian, Latin American and African ancestry. In a meta-analysis, we identified 78 independent genome-wide significant loci, including 12 potentially novel loci (MTF2, PIK3CA, ADD1, SYBU, IRS2, USP8, PIGL, FASN, MYLK2, USP25, EP300 and PPP6R2) and fine-mapped 6 putative causal variants at 6 known PD loci. By combining our results with publicly available eQTL data, we identified 25 putative risk genes in these novel loci whose expression is associated with PD risk. This work lays the groundwork for future efforts aimed at identifying PD loci in non-European populations.

## Understanding the pathogenic mechanisms and therapeutic effects in neurocysticercosis

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**Revista:** Brain Pathology
**DOI:** https://doi.org/10.1111/bpa.13237
**Tipo de articulo/ estudio:** Articulo original/ Estudio observacional

**Resumen:** Despite being a leading cause of acquired seizures in endemic regions, the pathological mechanisms of neurocysticercosis are still poorly understood. This study aims to investigate the impact of anthelmintic treatment on neuropathological features in a rat model of neurocysticercosis. Rats were intracranially infected with Taenia solium oncospheres and treated with albendazole + praziquantel (ABZ), oxfendazole + praziquantel (OXF), or untreated placebo (UT) for 7 days. Following the last dose of treatment, brain tissues were evaluated at 24 h and 2 months. We performed neuropathological assessment for cyst damage, perilesional brain inflammation, presence of axonal spheroids, and spongy changes. Both treatments showed comparable efficacy in cyst damage and inflammation. The presence of spongy change correlated with spheroids counts and were not affected by anthelmintic treatment. Compared to white matter, gray matter showed greater spongy change (91.7% vs. 21.4%, $p < 0.0001$), higher spheroids count (45.2 vs. 0.2, $p = 0.0001$), and increased inflammation (72.0% vs. 21.4%, $p = 0.003$). In this rat model, anthelmintic treatment destroyed brain parasitic cysts at the cost of local inflammation similar to what is described in human neurocysticercosis. Axonal spheroids and spongy changes as markers of damage were topographically correlated, and not affected by anthelmintic treatment.

## Mental health impact of the COVID-19 pandemic on patients with neurodegenerative diseases and perceived family caregiver burden in Lima, Peru

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**Revista:** Brain and Behavior
**DOI:** https://doi.org/10.1002/brb3.3361
**Tipo de articulo/ estudio:** Articulo original/ Estudio experimental

**Resumen:** *Introduction.* Neurodegenerative diseases lead to difficulties with functional activities. In Peru, most caregivers are family members. Little is known about the COVID-19 pandemic's effect on caregivers in Peru. *Methods.* This was a cross-sectional, prospective study of family caregivers of dependent patients with dementia or Parkinson's Disease in Lima, Peru. A caregiver burden and mental health questionnaire was administered to the caregiver. *Results*. We enrolled 48 caregivers (65% females, mean ± SD age 49.0 ± 12.3 years); 70% of patients had dementia. Nearly 40% of caregivers reported having full-time jobs, and 82% felt overwhelmed with almost 75% dedicating more time to caregiving during the pandemic. Caregivers perceived patients felt lonelier (52%), had an increase in hallucinations (50%), or forgetfulness (71%) compared to pre-pandemic. *Conclusions.* Our study highlights that perceived caregiver burden and patient behavioral symptoms may have been exacerbated during the pandemic. In countries such as Peru, more caregiving resources and interventions are needed.

## Genetic Testing for Parkinson's Disease and Movement Disorders in Less Privileged Areas: Barriers and Opportunities

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**Revista:** Movement Disorders Clinical Practice
**DOI:** https://doi.org/10.1002/mdc3.13903
**Tipo de articulo/ estudio:** Articulo original

## Antibody Banding Patterns on the Enzyme-Linked Immunoelectrotransfer Blot (EITB) Assay Clearly Discriminate Viable Cysticercosis in Naturally Infected Pigs

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**Revista:** Pathogens
**DOI:** https://doi.org/10.3390/pathogens13010015
**Tipo de articulo/ estudio:** Articulo original/ Estudio observacional

**Resumen:** Enzyme-linked immunoelectrotransfer blot (EITB) detects antibodies against seven *Taenia solium* larvae antigens in three protein families (GP50, T24/42, and 8-kDa) with different structures and functions. EITB banding patterns against these antigens in pigs provide information about the course of infection and may discriminate viable cysticercosis. We analyzed the banding patterns and infection outcomes (presence of viable cysts, degenerated cysts, and any cysts) of 512 rural pigs. Banding patterns were grouped into homogenous classes using latent class analysis, and relationships with infection outcomes were assessed. Four classes were identified: 1 (n = 308, EITB-negative or positive for the GP50 family), 2 (n = 127, positive for GP50 (GP50 family), GP42-39 and GP24 (T24/42 family), but negative for 8-kDa antigens), 3 (n = 22, positive for GP50 and T24/42 antigens (GP42-39 and GP24), as well as to 8-kDa bands GP13, GP14, and GP18, but negative for GP21), and 4 (n = 55, positive for GP50 and T24/42 antigens, as well as to 8-kDa antigens GP21 and GP18 in combination). Pigs in classes 3 and 4 were more likely to have viable cysts (72.6% and 96.4%, respectively) than pigs in classes 1 and 2 (0.7% and 27.6%, respectively; $p < 0.001$). The number of infections with any cysts was higher in classes 3 and 4 (77.3% and 98.2%, respectively) and lower in classes 2 and 1 (34.7% and 4.9%, respectively; $p < 0.001$). Pigs with viable cysts represented >90% of pigs with any cysts in classes 3 and 4 (94.1% and 98.2%, respectively), while degenerated cysts were frequent among pigs with any cysts in classes 1, 3, and 2 (86.7%, 47.1%, and 43.2%, respectively; $p < 0.001$). EITB banding patterns strongly correlate with cysticercosis infection status in rural pigs, with classes 3 and 4 being more predictive of viable infections.

## Frequency of Hereditary and GBA1-Related Parkinsonism in Latin America: A Systematic Review and Meta-Analysis

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**Revista:** Movement Disorders
**DOI:** https://doi.org/10.1002/mds.29614
**Tipo de articulo/ estudio:** Articulo original/ Metaanálisis

**Resumen:** *Introduction.* Identifying hereditary parkinsonism is valuable for diagnosis, genetic counseling, patient prioritization in trials, and studying the disease for personalized therapies. However, most studies were conducted in Europeans, and limited data exist on admixed populations like those from Latin America. *Objectives.* This study aims to assess the frequency and distribution of genetic parkinsonism in Latin America. *Methods.* We conducted a systematic review and meta-analysis of the frequency of parkinsonian syndromes associated with genetic pathogenic variants in Latin America. We defined hereditary parkinsonism as those caused by the genes outlined by the MDS Nomenclature of Genetic Movement Disorders and heterozygous carriers of GBA1 pathogenic variants. A systematic search was conducted in PubMed, Web of Science, Embase, and LILACS in August 2022. Researchers reviewed titles and abstracts, and disagreements were resolved by a third researcher. After this screening, five researchers reanalyzed the selection criteria and extracted information based on the full paper. The frequency for each parkinsonism-related gene was determined by the presence of pathogenic/likely pathogenic variants among screened patients. Cochran's Q and I2 tests were used to quantify heterogeneity. Meta-regression, publication bias tests, and sensitivity analysis regarding study quality were also used for LRRK2-, PRKN-, and GBA1-related papers. *Results.* We included 73 studies involving 3014 screened studies from 16 countries. Among 7668 Latin American patients, pathogenic variants were found in 19 different genes. The frequency of the pathogenic variants in LRRK2 was 1.38% (95% confidence interval [CI]: 0.52–2.57), PRKN was 1.16% (95% CI: 0.08–3.05), and GBA1 was 4.17% (95% CI: 2.57–6.08). For all meta-analysis, heterogeneity was high, and publication bias tests were negative, except for PRKN, which was contradictory. Information on the number of pathogenic variants in the other genes is further presented in the text. *Conclusions.* This study provides insights into hereditary and GBA1-related parkinsonism in Latin America. Lower GBA1 frequencies compared to European/North American cohorts may result from limited access to gene sequencing. Further research is vital for regional prevalence understanding, enabling personalized care and therapies. © 2023 The Authors. Movement Disorders published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

## Calcified cerebral toxoplasmosis associated with recurrent perilesional edema causing neurological manifestations in an HIV-infected individual: case report with a decade-long follow-up

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**Revista:** Revista do Instituto de Medicina Tropical de Sao Paulo
**DOI:** https://doi.org/10.1590/S1678-9946202466015
**Tipo de articulo/ estudio:** Reporte de caso

**Resumen:** Four cases of people living with HIV/AIDS (PLWHA) with calcified cerebral toxoplasmosis associated with perilesional edema causing a single episode of neurological manifestations have recently been reported. Here, we describe the first detailed description of perilesional edema associated with calcified cerebral toxoplasmosis causing three episodes of neurological manifestations in a PLWHA, including seizures in two of them. These recurrences occurred over approximately a decade. Throughout this period, the patient showed immunological and virological control of the HIV infection, while using antiretroviral therapy regularly. This case broadens the spectrum of an emerging presentation of calcified cerebral toxoplasmosis, mimicking a well-described finding of neurocysticercosis in immunocompetent hosts.

## A Novel Variant in SQSTM1 Gene Causing Neurodegeneration with Ataxia, Dystonia, and Gaze Palsy in a Peruvian Family

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**Revista:** Movement Disorders Clinical Practice
**DOI:** https://doi.org/10.1002/mdc3.14025
**Tipo de articulo/ estudio:** Articulo Original

## Calcified Neurocysticercosis: Demographic, Clinical, and Radiological Characteristics of a Large Hospital-Based Patient Cohort

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**Revista:** Pathogens
**DOI:** https://doi.org/10.3390/pathogens13010026
**Tipo de articulo/ estudio:** Articulo original/ Estudio observacional

**Resumen:** Neurocysticercosis (NCC), the infection of the central nervous system caused by Taenia solium larvae (cysticerci), is a major cause of acquired epilepsy worldwide. Calcification in NCC is the most common neuroimaging finding among individuals with epilepsy in T. solium-endemic areas. We describe the demographic, clinical, and radiological profiles of a large hospital cohort of patients with calcified NCC in Peru (during the period 2012–2022) and compared profiles between patients with and without a previous known diagnosis of viable infection. A total of 524 patients were enrolled (mean age at enrollment: 40.2 ± 15.2 years, mean age at symptom onset: 29.1 ± 16.1 years, 56.3% women). Of those, 415 patients (79.2%) had previous seizures (median time with seizures: 5 years, interquartile range (IQR): 2–13 years; median number of seizures: 7 (IQR: 3–32)), of which 333 (80.2%) had predominantly focal to bilateral tonic-clonic seizures; and 358 (68.3%) used antiseizure medication). Patients had a median number of three calcifications (IQR: 1–7), mostly located in the frontal lobes (79%). In 282 patients (53.8%) there was a previous diagnosis of viable infection, while 242 only had evidence of calcified NCC since their initial neuroimaging. Most patients previously diagnosed with viable infection were male, had previous seizures, had seizures for a longer time, had more calcifications, and had a history of taeniasis more frequently than patients without previously diagnosed viable infection (all $p < 0.05$). Patients with calcified NCC were heterogeneous regarding burden of infection and clinical manifestations, and individuals who were diagnosed after parasites calcified presented with milder disease manifestations.

**MARZO**

## Spinocerebellar ataxia type 2 has multiple ancestral origins

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**Revista:** Parkinsonism & Related Disorders
**DOI:** https://doi.org/10.1016/j.parkreldis.2023.105985
**Tipo de articulo/ estudio:** Articulo original/ Estudio observacional

**Resumen:** *Introduction.* Spinocerebellar ataxia type 2 (SCA2) is a dominant neurodegenerative disorder due to expansions of a CAG repeat tract (CAGexp) at the ATXN2 gene. Previous studies found only one ancestral haplotype worldwide, with a C allele at rs695871. This homogeneity was unexpected, given the severe anticipations related to SCA2. We aimed to describe informative ancestral haplotypes found in South American SCA2 families. *Methods*. Seventy-seven SCA2 index cases were recruited from Brazil, Peru, and Uruguay; 263 normal chromosomes were used as controls. The SNPs rs9300319, rs3809274, rs695871, rs1236900 and rs593226, and the STRs D12S1329, D12S1333, D12S1672 and D12S1332, were used to reconstruct haplotypes. *Results.* Eleven ancestral haplotypes were found in SCA2 families. The most frequent ones were A-G-C-C-C (46.7 % of families), G-C-C-C-C (24.6 %) and A-C-C-C-C (10.3 %) and their mean (sd) CAGexp were 41.68 (3.55), 40.42 (4.11) and 45.67 (9.70) ($p = 0.055$), respectively. In contrast, the mean (sd) CAG lengths at normal alleles grouped per haplotypes G-C-G-A-T, A-G-C-C-C and G-C-C-C-C were 22.97 (3.93), 23.85 (3.59), and 30.81 (4.27) ($p < 0.001$), respectively. The other SCA2 haplotypes were rare: among them, a G-C-G-A-T lineage was found, evidencing a G allele in rs695871. *Conclusion.* We identified several distinct ancestral haplotypes in SCA2 families, including an unexpected lineage with a G allele at rs695871, a variation never found in hundreds of SCA2 patients studied worldwide. SCA2 has multiple origins in South America, and more studies should be done in other regions of the world.

# Postsurgical Outcomes of Mesial Temporal Lobe Epilepsy due to Hippocampal Sclerosis Associated with Calcified Neurocysticercosis

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**Revista:** American Journal of Tropical Medicine and Hygiene
**DOI :** https://doi.org/10.4269/ajtmh.23-0506
**Tipo de articulo/ estudio:** Articulo original/ Estudio observacional

**Resumen:** The aim of this study was to analyze postsurgical outcomes for individuals with mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) who underwent anterior temporal lobectomy, based on the presence of calcified neurocysticercosis (cNCC). A retrospective cross-sectional study was conducted on 89 patients with MTLE-HS who underwent anterior temporal lobectomy between January 2012 and December 2020 at a basic epilepsy surgery center located in Lima, Peru. We collected sociodemographic, clinical, and diagnostic information. The postsurgical results were analyzed using bivariate analysis according to the Engel classification. We included 89 individuals with a median age of 28 years (interquartile range [IQR]: 24–37), and more than half (55.1%) were male. Seventeen (19.1%) were diagnosed with cNCC. A greater number of patients with cNCC had lived in rural areas of Peru during their early life compared with those without cNCC (12 [70.6%] versus 26 [36.1%]; P = 0.010). Patients with cNCC exhibited a greater median frequency of focal to bilateral tonic-clonic seizures per month (1 [IQR: 0–2] versus 0 [0–0.5]; P = 0.009). Conversely, a lower proportion of patients with cNCC reported a history of an initial precipitating injury in comparison to the group without cNCC (4 [23.5%] versus 42 [58.3%]; P = 0.014). At the 1-year follow-up, most patients (82.4%) with cNCC were categorized as Engel IA. Similarly, at the 2-year follow-up, nine (75.0%) were classified as Engel IA. Our findings suggest that most patients diagnosed with cNCC exhibit favorable postsurgical outcomes, comparable to those without cNCC. Additionally, it can be postulated that cNCC may play a role as an initial precipitating injury.