



CENTER FOR NEUROSCIENCE AND CELL BIOLOGY

A RARE JOURNEY

A PROJECT FROM THE CENTER FOR NEUROSCIENCE AND CELL BIOLOGY OF THE UNIVERSITY OF COIMBRA, PORTUGAL

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SOME DISEASES ARE COMMON, SOME NOT AT ALL. THESE ARE CALLED **RARE**, OR **ORPHAN DISEASES**. AND HAVE A PREVALENCE OF LESS THAN 5 IN 10 000 PEOPLE.

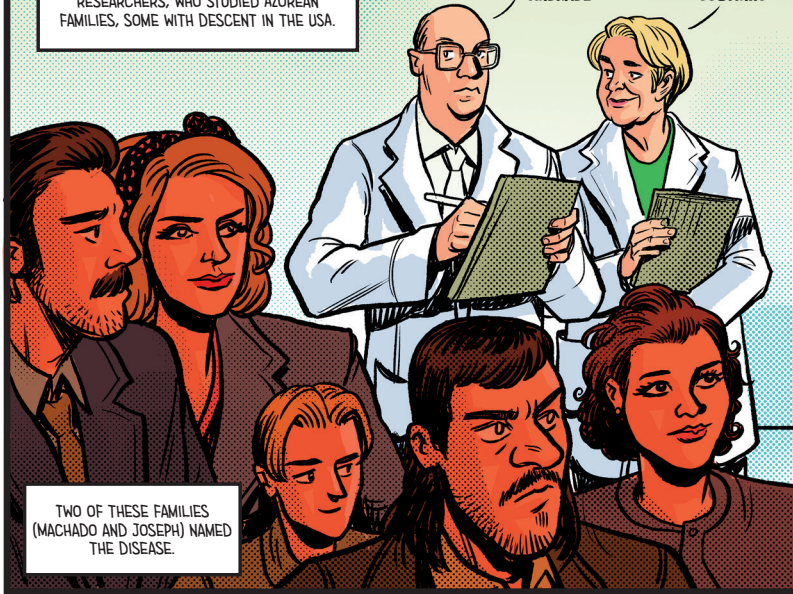


IT IS ESTIMATED THAT THERE ARE 5 TO 8 000 DIFFERENT RARE DISEASES, AFFECTING UP TO 6% OF THE POPULATION, WHICH MEANS THAT THERE ARE UP TO 600 000 PEOPLE WITH THESE DISEASES IN PORTUGAL.



MACHADO-JOSEPH DISEASE IS A RARE DISEASE THAT WAS CHARACTERIZED IN THE 1970S-80S BY TWO PORTUGUESE RESEARCHERS, WHO STUDIED AZOREAN FAMILIES, SOME WITH DESCENT IN THE USA.

CORINO DE ANDRADE
PAULA COUTINHO



TWO OF THESE FAMILIES (MACHADO AND JOSEPH) NAMED THE DISEASE.

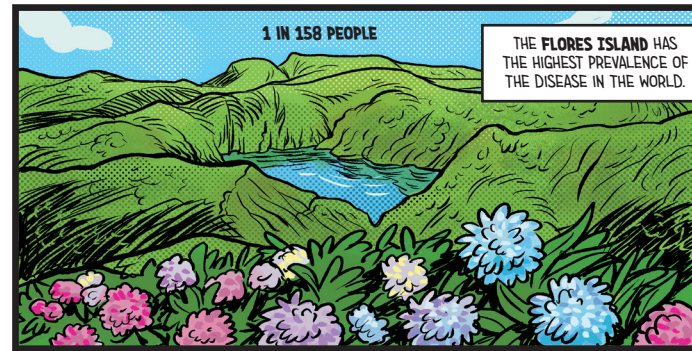
IN FACT, IN THE AZORES ARCHIPELAGO (AND ESPECIALLY IN THE FLORES ISLAND) THIS DISEASE IS NOT SO RARE.



1 IN 100000



1 IN 158 PEOPLE



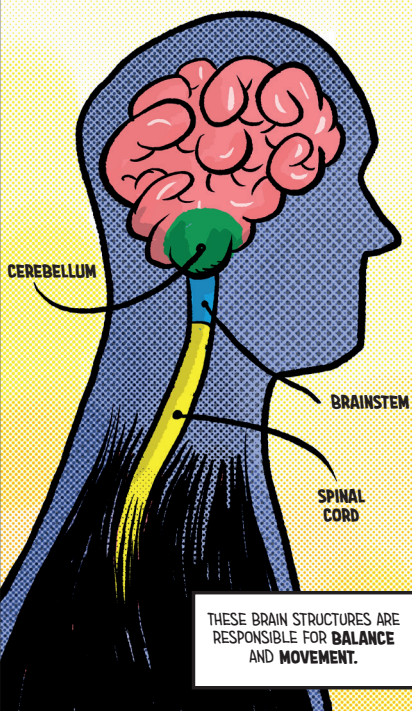
THE FLORES ISLAND HAS THE HIGHEST PREVALENCE OF THE DISEASE IN THE WORLD.

MACHADO-JOSEPH DISEASE IS A **NEURODEGENERATIVE, HEREDITARY, PROGRESSIVE AND DOMINANT** DISEASE.



A CHILD WITH ONE DISEASED PARENT IS 50% LIKELY TO HAVE IT, AND SYMPTOMS MANIFEST MOSTLY WHEN PATIENTS ARE BETWEEN 35 AND 50 YEARS OLD.

THE PROBLEM OF THIS PATHOLOGY LIES IN A CHANGE IN A SPECIFIC GENE, WHICH AFFECTS THE FUNCTION OF CERTAIN BRAIN AREAS: THE **CEREBELLUM**, THE **BRAINSTEM**, THE **BASAL GANGLIA** AND THE **UPPER PART OF THE SPINAL CORD**.

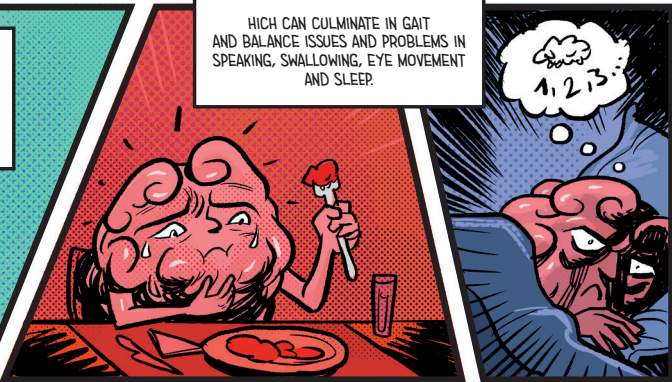


THESE BRAIN STRUCTURES ARE RESPONSIBLE FOR **BALANCE AND MOVEMENT**.

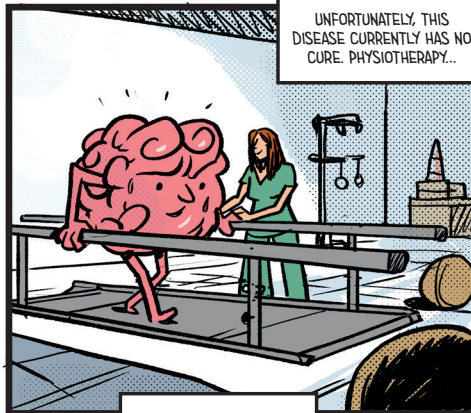
THEREFORE, MACHADO-JOSEPH PATIENTS HAVE PROGRESSIVELY IMPAIRED MOVEMENT COORDINATION, AND LOSS OF BALANCE (THE SO-CALLED **"ATAXIA"**).



HIGH CAN CULMINATE IN GAIT AND BALANCE ISSUES AND PROBLEMS IN SPEAKING, SWALLOWING, EYE MOVEMENT AND SLEEP.



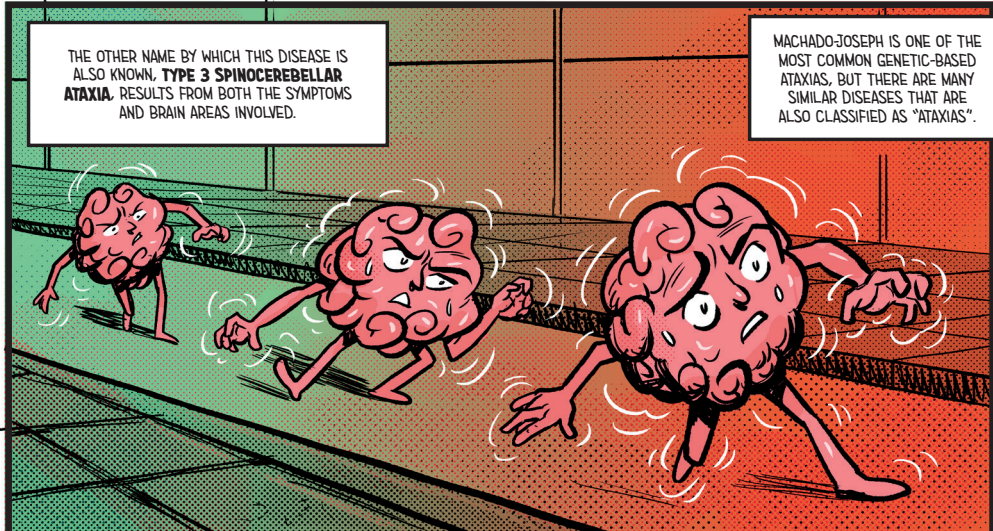
UNFORTUNATELY, THIS DISEASE CURRENTLY HAS NO CURE. PHYSIOTHERAPY...



...AND SOME MEDICATION HELPS REDUCE SYMPTOMS.



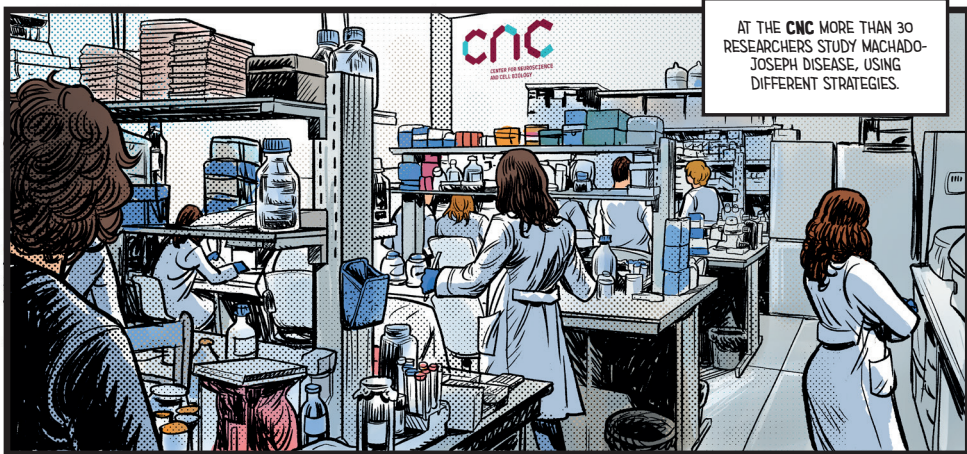
THE OTHER NAME BY WHICH THIS DISEASE IS ALSO KNOWN, **TYPE 3 SPINOCEREBELLAR ATAXIA**, RESULTS FROM BOTH THE SYMPTOMS AND BRAIN AREAS INVOLVED.



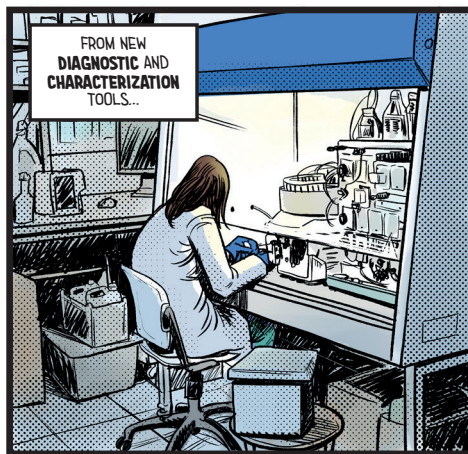
MACHADO-JOSEPH IS ONE OF THE MOST COMMON GENETIC-BASED ATAXIAS, BUT THERE ARE MANY SIMILAR DISEASES THAT ARE ALSO CLASSIFIED AS "ATAXIAS".

BUT THERE IS HOPE, BOTH IN RESEARCH AND IN ONGOING CLINICAL TRIALS.

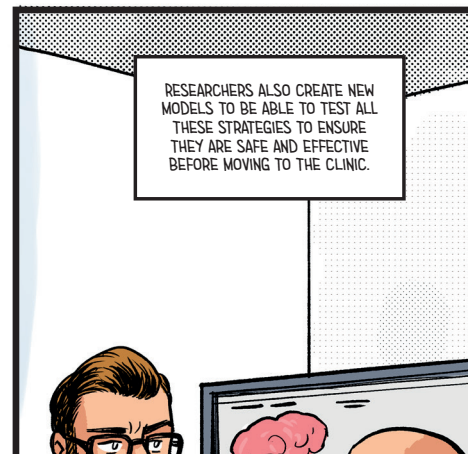




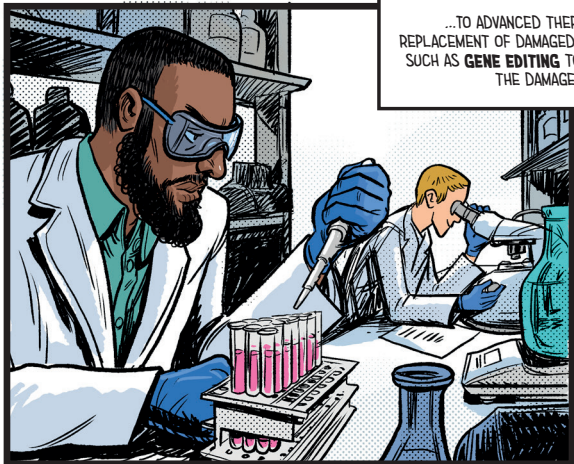
AT THE **CNC** MORE THAN 30 RESEARCHERS STUDY MACHADO-JOSEPH DISEASE, USING DIFFERENT STRATEGIES.



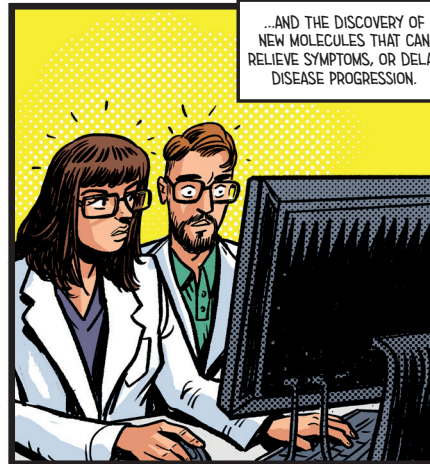
FROM NEW **DIAGNOSTIC AND CHARACTERIZATION TOOLS...**



RESEARCHERS ALSO CREATE NEW MODELS TO BE ABLE TO TEST ALL THESE STRATEGIES TO ENSURE THEY ARE SAFE AND EFFECTIVE BEFORE MOVING TO THE CLINIC.



...TO ADVANCED THERAPIES INCLUDING REPLACEMENT OF DAMAGED CELLS, **GENE THERAPY** SUCH AS **GENE EDITING** TO SILENCE OR CORRECT THE DAMAGED GENE...



...AND THE DISCOVERY OF NEW MOLECULES THAT CAN RELIEVE SYMPTOMS, OR DELAY DISEASE PROGRESSION.



SOMETIMES THE POSSIBILITY THAT WE SHOULD FOCUS MORE ON THE STUDY OF COMMON DISEASES IS DISCUSSED.

THAT IS NOT THE BEST APPROACH, FOR TWO REASONS.



FIRSTLY, BECAUSE WE HAVE TO ADDRESS PATIENTS NEED FOR A THERAPY.

SECONDLY, BECAUSE THESE DISCOVERIES MAY HAVE SEVERAL ADDITIONAL APPLICATIONS IN MEDICINE AND BIOTECHNOLOGY, AND NOT ONLY ON ATAXIAS.....



...BUT ALSO IN OTHER NEURODEGENERATIVE DISEASES SUCH AS ALZHEIMER'S OR PARKINSON'S.

WITH THE SUPPORT OF EVERYONE (PATIENTS, FAMILIES, RESEARCHERS, CLINICIANS, AND THE GENERAL PUBLIC), THE ULTIMATE GOAL IS TO MAKE THE EFFECTS OF DISEASES SUCH AS MACHADO-JOSEPH'S RARER AND RARER!

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