

National Institutes of Health (NIH) CADASIL Disease Discovery Studies

Manfred Boehm, M.D.

Laboratory of Cardiovascular Regenerative Medicine
Translational Vascular Medicine Branch
National Heart, Lung, and Blood Institute

ULF / CureCADASIL Family Symposium 2026
Oak Brook IL
June 27th, 2026



"Our Promise to You" *"Our team is dedicated to understanding CADASIL from every angle. We partner with patients like you to turn today's research into tomorrow's hope."*

NIH Clinical Center -There's No Other Hospital Like It

Our team is dedicated to understanding CADASIL from every angle. We partner with patients like you to turn today's research into tomorrow's hope."

- “Protocol-centric care” at no cost to patient
- Patients from US and internationally
- Primary mission is science to advance human health
- The Clinical Center has been a leader in “bench-to-bedside” medicine



The CADASIL Research Team

Dr. E. Ferrante, NHLBI
Principal Investigator

Dr. A. Brofferio, NHLBI
Cardiovascular Studies

Dr. M. Boehm, NHLBI
Translational Research Studies

Dr. B. Kozel, NHLBI
Functional Vascular Studies
Functional Genetics

Dr. L. Iruela-Arispe,
Northwestern University
Basic Research Studies

NIH
CADASIL
Patients

Dr. C. Toro, NHGRI;
Neurological Studies

Dr. J. Snow, NIMH
Psychometric Studies

Dr. R. Leigh, NINDS
MRI Studies

Dr. E. Fitzgibbon, NEI
Eye Studies

Vascular Diagnostic Center,
NHLBI

Dr. Y. Kanthi, and J. Abraham, MHS/RVT
Small vessel Imaging Studies

Dr. G. Nair, NINDS
MRI Imaging and Quantification

Dr. R. Gottesman, NINDS
Stroke and Neurological Studies

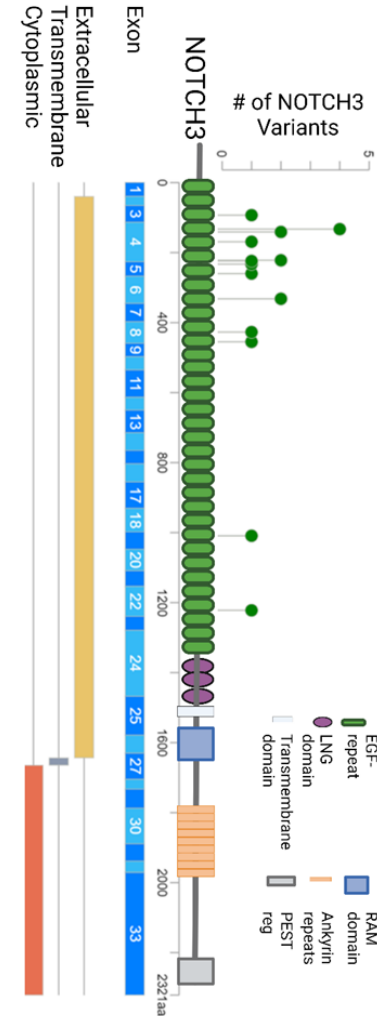
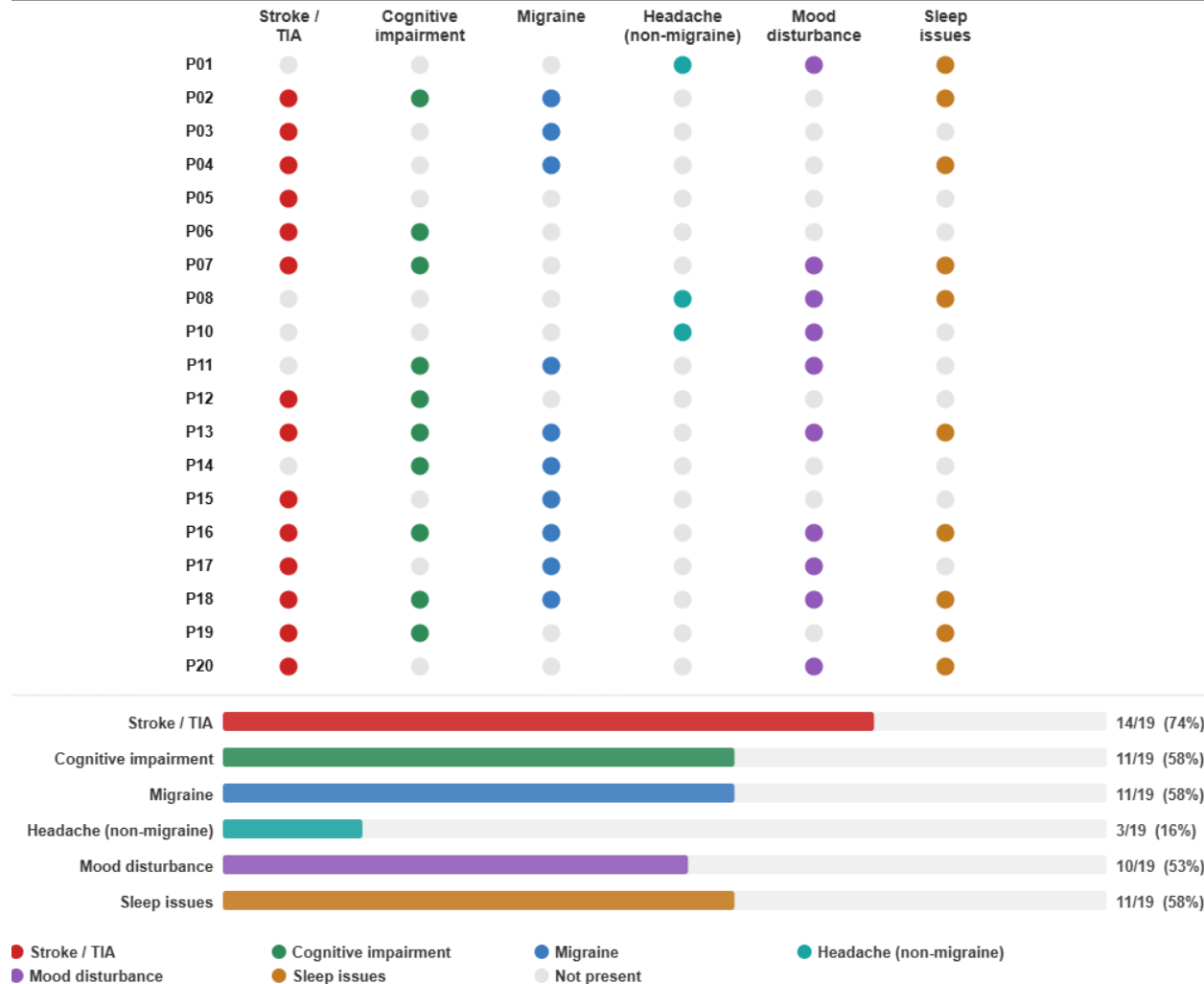
Study Snapshot

- **Natural History Protocol 2 (Ongoing)**
 - Goal- 100 patients and 40 healthy volunteers
 - 57 patients currently enrolled
 - Visits every 3 years for 9 years
- **Primary Objective:** Understand cellular causes of CADASIL and how the disease progresses
- **Secondary Objective:** Investigate variability of genotype and clinical phenotype
- **Comprehensive evaluations:** History and physical, clinical and research labs with biospecimen collection, genetics, neurology and ophthalmology consults, brain MRI, vascular studies, cognitive testing

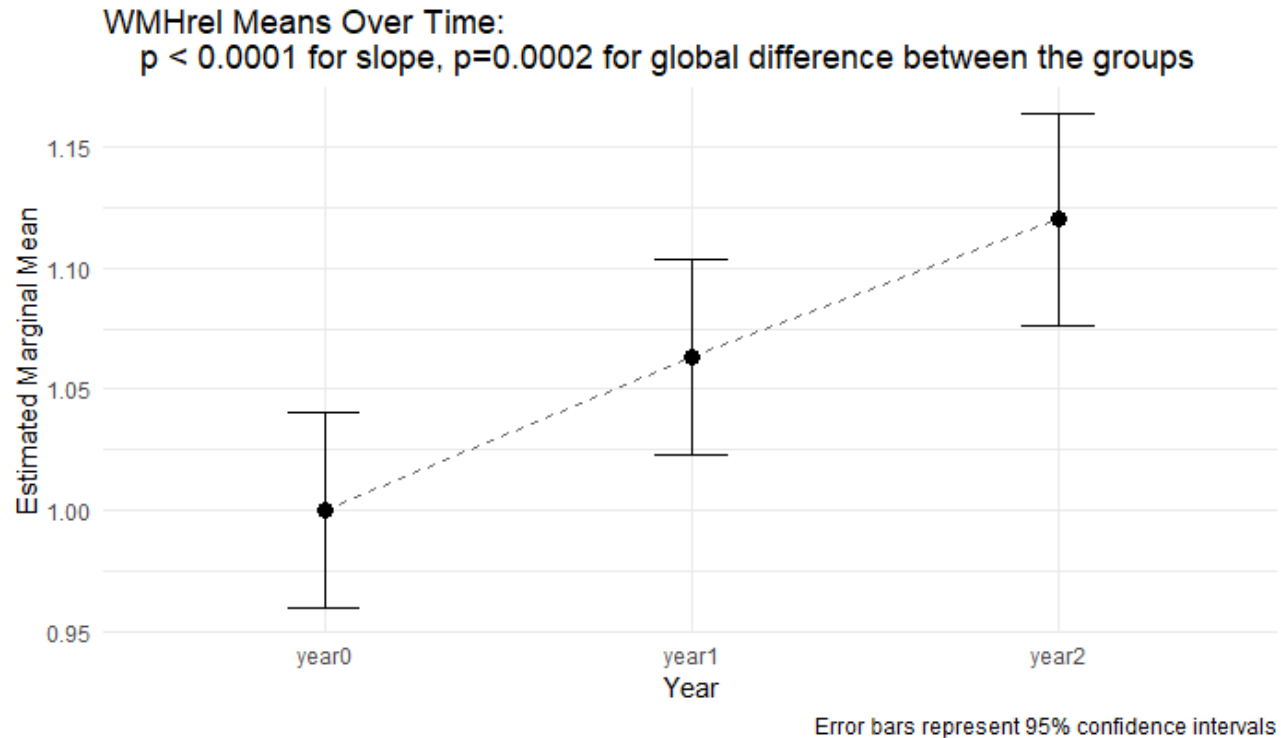
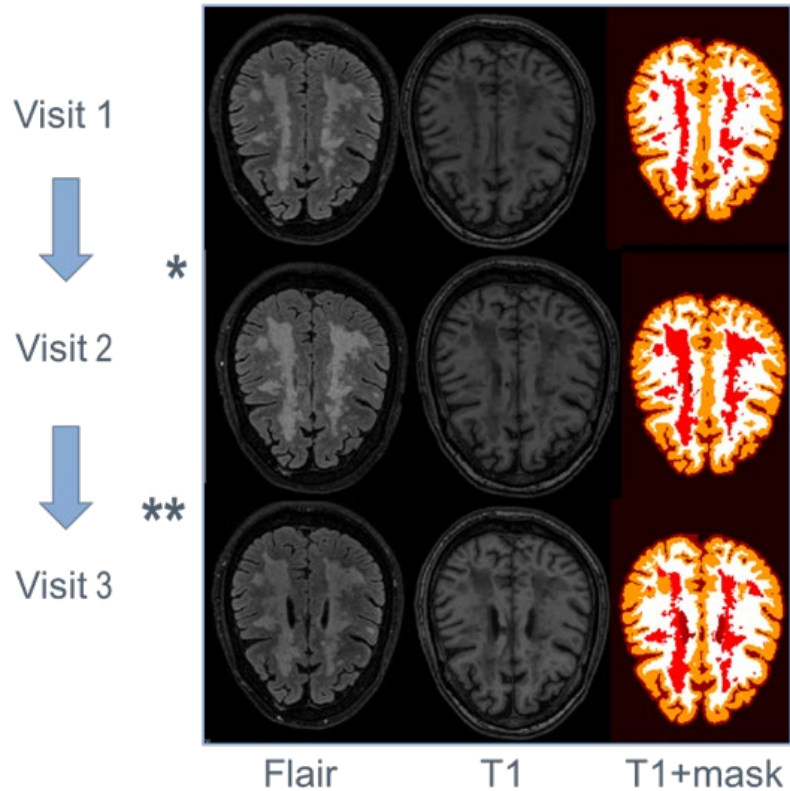
CADASIL is Different for Everyone

Cohort phenotype: broad symptom overlap — no two patients alike

NIH CADASIL Protocol 1 · n = 19 · 6 symptom domains



CADASIL 1 MRI Analysis – AI/Machine Learning Methods

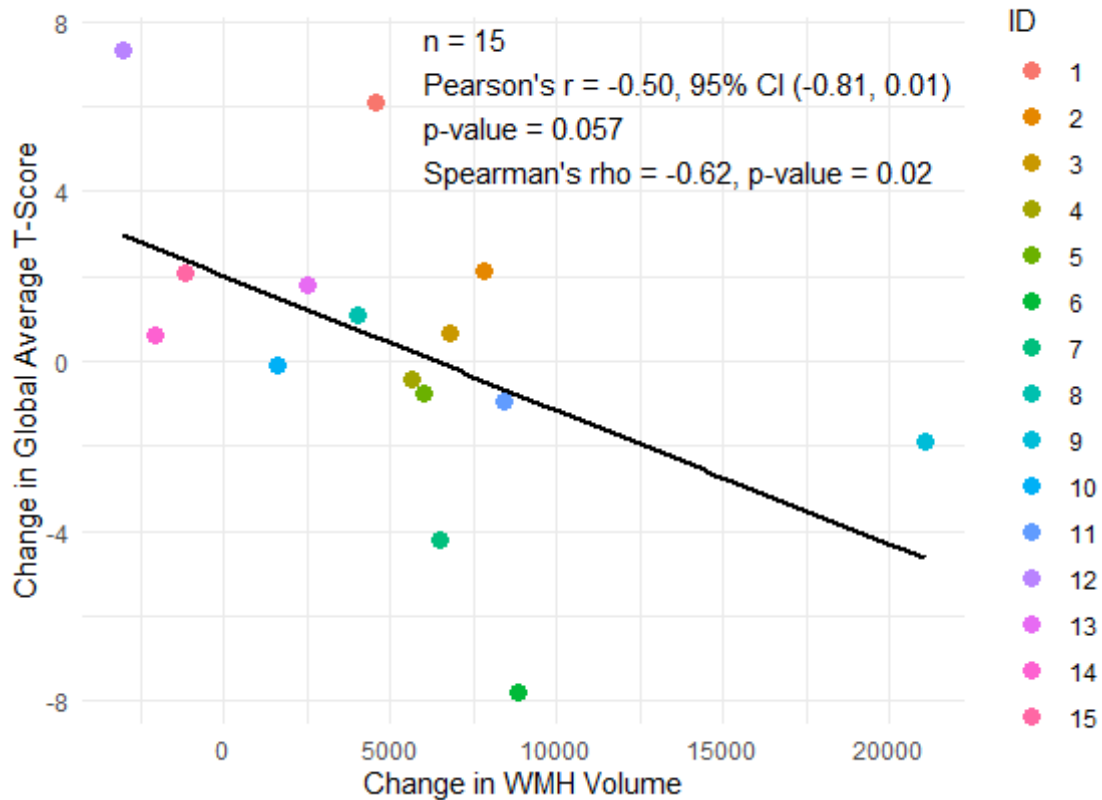


What This Means for You:

We can track progression of white matter changes in CADASIL by an automated computer program

How Changes in the Brain Affect Thinking

Change in WMH Volume vs Change in Global Average T-Score
Visit 1 to Visit 3



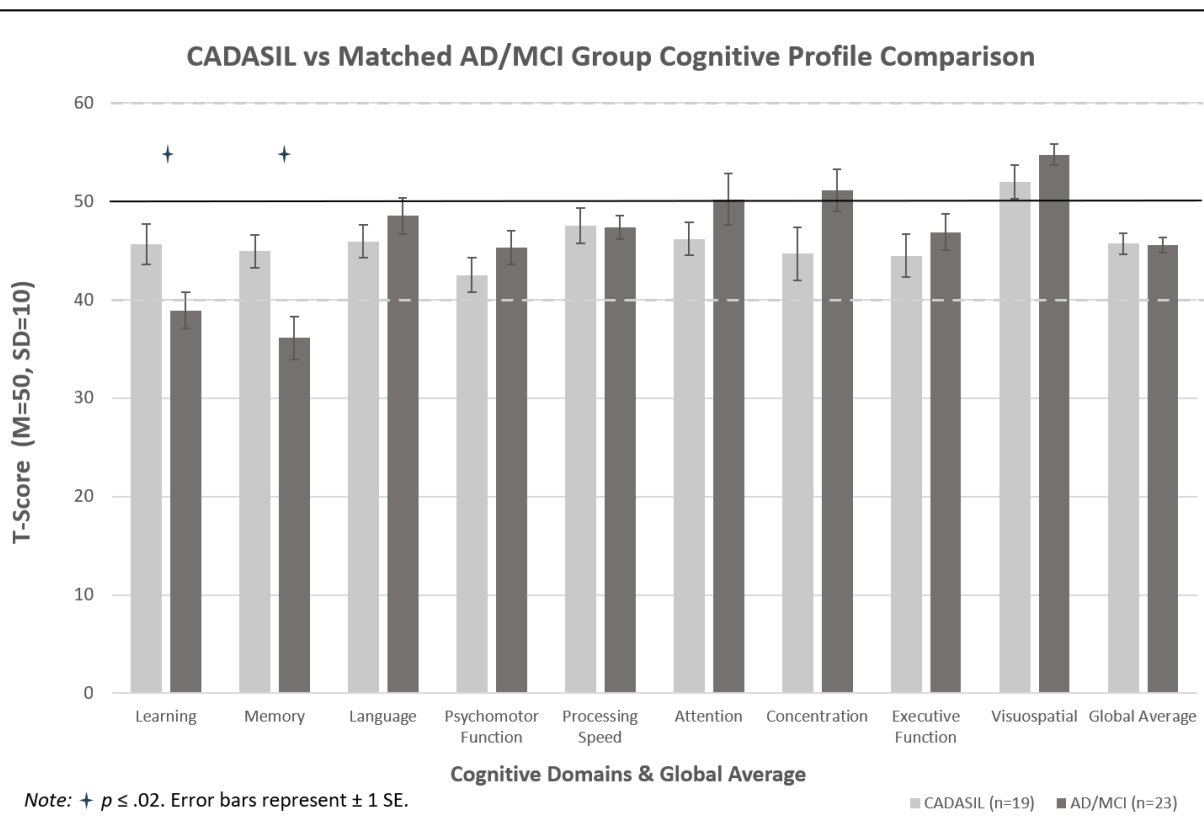
■ What This Means for You:

This research confirms the link between the white matter changes we see on an MRI and the thinking or memory challenges you may be experiencing. It helps us track the disease in a meaningful way

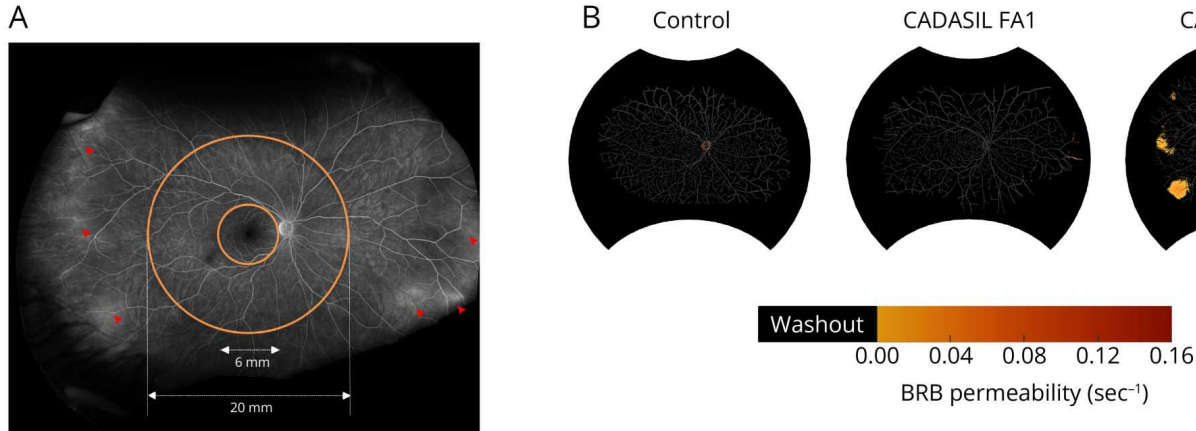
How Thinking in CADASIL Differs from Alzheimer's Disease

What it means to you:

- Distinct changes from Alzheimer's disease and other mild cognitive impairments
- Better performance in learning and memory
- Attenuated performance in concentration and attention

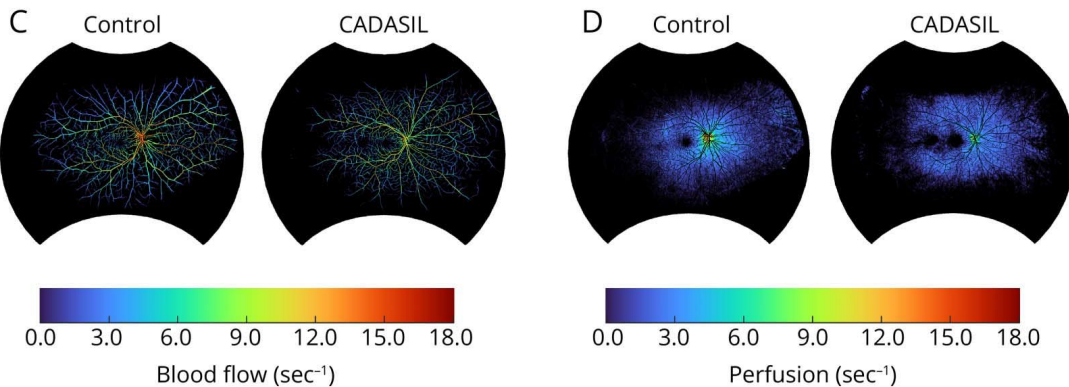


The Eye: A Window to the Brain



The eye is filled with tiny blood vessels, we study it to learn more about how blood flow is affected in CADASIL.

We can measure blood flow and how "leaky" the blood vessels are in the eyes of CADASIL patients compared to healthy individuals.



What This Means for You: This research could lead to a new, less invasive way to track the severity of CADASIL and provide important clues about how the disease affects blood vessels throughout the body.



CADASIL Summary so far



Variable genetics/clinical symptom presentation (no symptoms vs. significant) – interest in identifying modifiers (genetic or lifestyle)



Slow progression over the study period (2 years)



Typical White Matter changes in all patients (quantifiable)



Eye findings may be reflective of brain pathology



Cognitive domain signature compared to AD and MCI patients



Acknowledgments



TVMB Clinical Team, NHLBI

Manfred Boehm
Alessandra Brofferio
Sherrell Apugo
Rebecca Huffstutler
Cornelia Cudrici
Elisa Ferrante
Doug Rosing
Wil Whalen
Ingrid Velasquez
Marta Cardenas
Mahmood Rashidi

Extramural Collaborators

Luisa Iruela-Arispe
Milagros Romay
Rich Leigh
Fanny Elahi
James Meschia
Jane Paulsen

All CADASIL patients and their families CureCADASIL Foundation

Intramural Research Programs of the NIH



Laboratory of Cardiovascular Regenerative Medicine, NHLBI

Manfred Boehm
Elisa Ferrante
Cornelia Cudrici
Robin Schwartzbeck
Natalia Dmitrieva
Dan Yang
Kevin Emmerich

NIH Collaborators

Camilo Toro
Yonatan Serlin
Joseph Snow
Chantal Cosineau-Krieger
Daniel Reich
Govind Nair
Rebecca Gottesman
Amreen Mughal

Questions?



NIH Researchers are studying genetic and physical characteristics of the small vessel disease called CADASIL

(cerebral autosomal dominant arteriopathy with subcortical infarct and leukoencephalopathy)

Volunteers are needed to serve as study participants with CADASIL or as healthy controls


National Heart, Lung, and Blood Institute

Looking to Participate in NIH Research?
NHLBI Researchers are Looking for You!



Project goal: identify molecular mechanism underlying CADASIL by applying complex models/modern techniques

