ADVANCED MEDICINE

INTERNATIONAL CONGRESS OF INTEGRATIVE MEDICINE

5>6 DEC, 2025

OPORTO, PORTUGAL

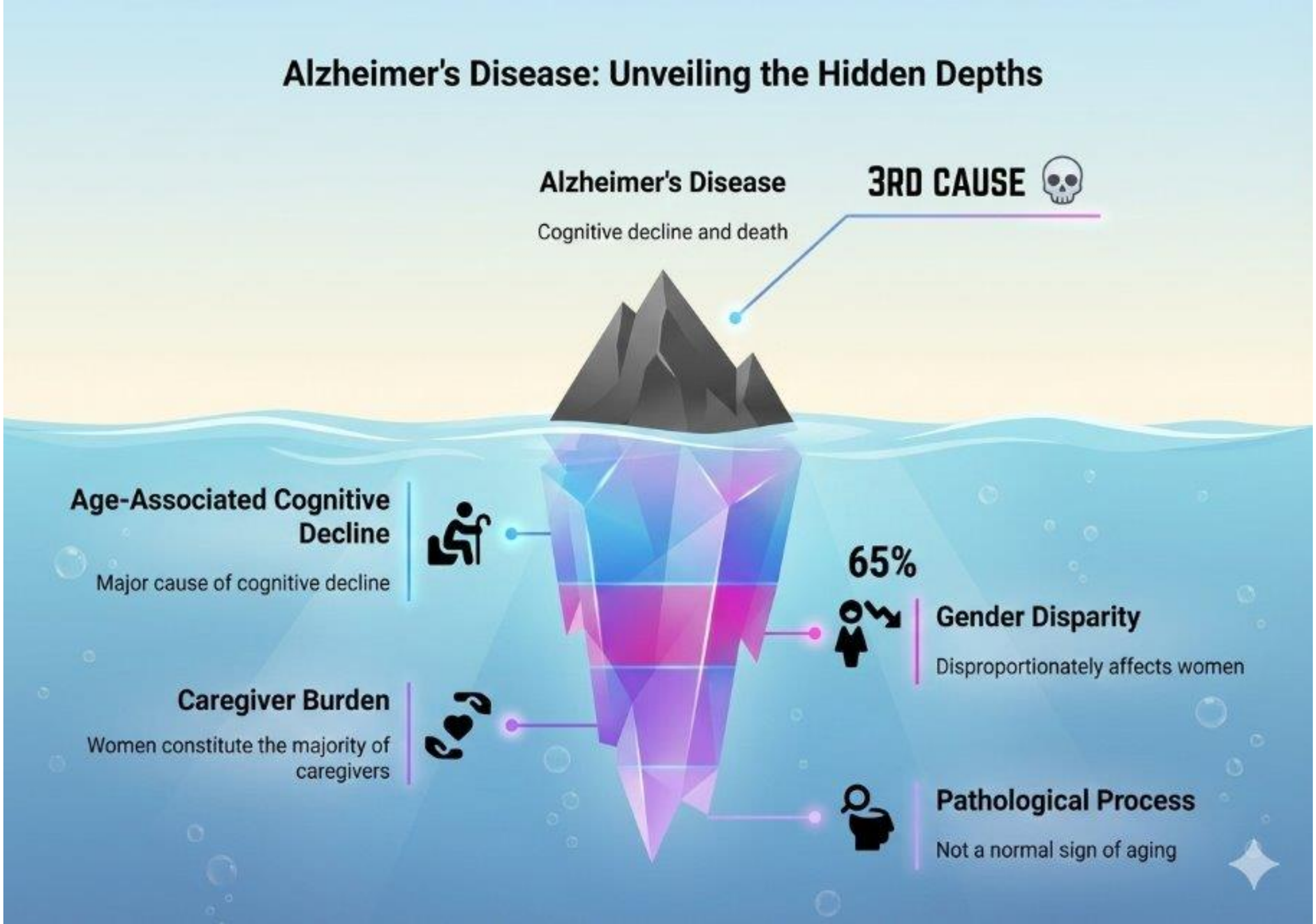
Reversing Cognitive Decline: A Precision Medicine Approach to Alzheimer's Prevention and Treatment

Alain Dutra

Dec 6, 2025


152M
by 2050

Alzheimer's Disease: Unveiling the Hidden Depths



Monotherapy failure necessitates a multi-faceted approach to Alzheimer's treatment.



Monotherapy Failure

Ineffective treatments leave patients without options.

Multi-Factorial Approach

Personalized interventions improve patient outcomes.

The Single-Target Failure and the Need for a Paradigm Shift in Alzheimer's

The 'Single-Target' Trap
(Past Decade)



Billions of Dollars Spent

Hundreds of Clinical Trials



NO significant success in cognitive improvement (merely slowing of decline).



"Amyloids sucked up all the air in the room."
– Dr. Lon Schneider
(Preventing comprehensive exploration).

URGENT PARADIGM SHIFT

The Multifaceted Approach
(The Way Forward)



Success in complex illnesses (HIV, Cardiovascular) via **COMBINATION THERAPIES.**



Transform patient outcomes (Real Cognitive Improvement).

Action: Reconceptualize, Diagnose, and Treat the disease's complex nature.

A New Paradigm: AD as a Multi-Factorial Network Dysfunction

The Old Model:
Single-Target, Single-Cause



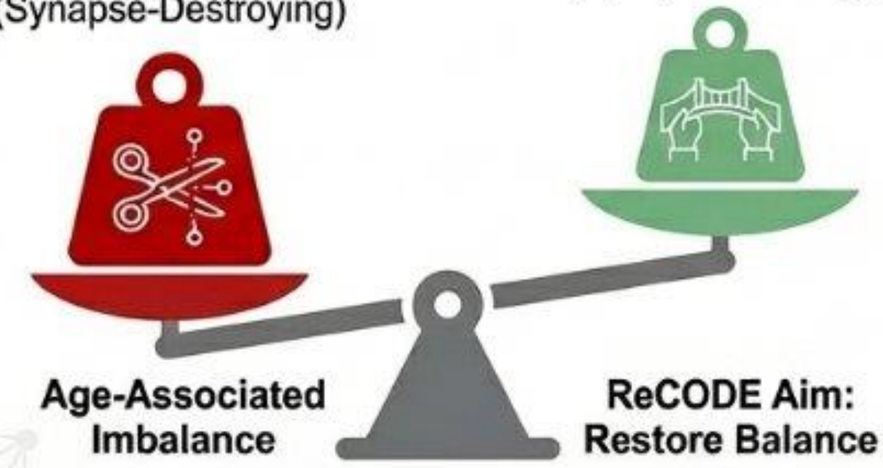
Cognitive decline viewed as a single disease with one primary cause (e.g., amyloid).



THE ReCODE SHIFT: SYSTEMS BIOLOGY

SYNAPTOCLASTIC
(Synapse-Destroying)

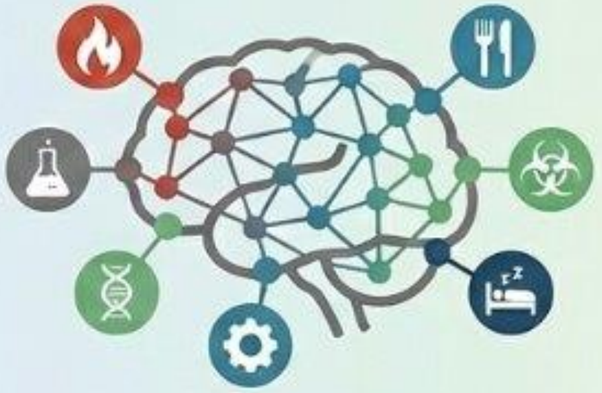
SYNAPTOBLASTIC
(Synapse-Building)



Age-Associated Imbalance

ReCODE Aim: Restore Balance

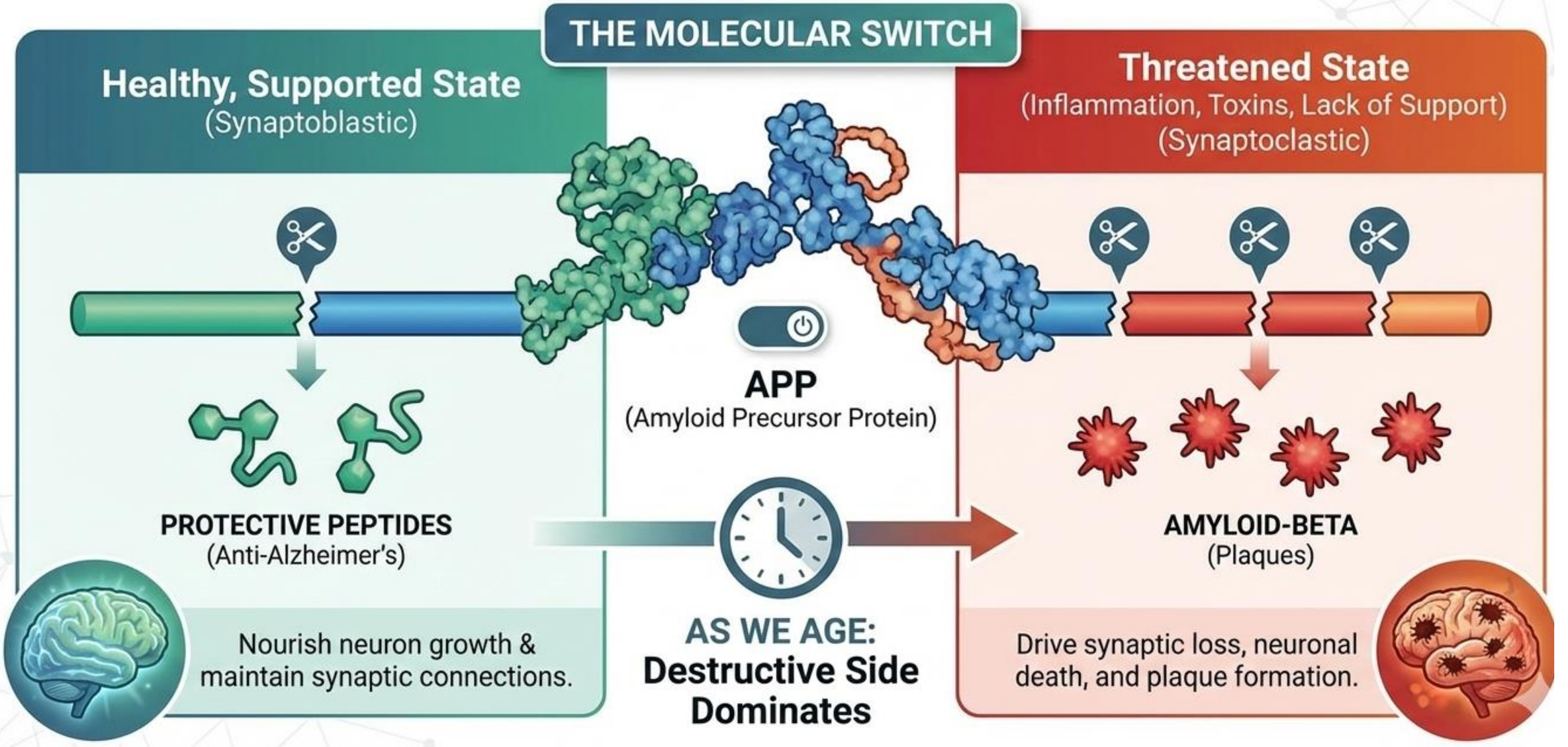
The New Paradigm:
Multi-Factorial Network Dysfunction



Cognitive decline is a protective response to multiple simultaneous systemic insults.



APP: The Molecular Switch in Brain Aging



The Necessity of a Multi-Pronged Approach: The Roof with 36 Holes Analogy

The Single-Drug ("One-Hole") Failure



Patching one hole does not stop the flood.

- Holes represent molecular mechanisms:
- Mitochondrial Function
- Neurotrophic Support
- Inflammation
- Detoxification
- Amyloid-Beta Breakdown



The Multi-Pronged ReCODE Protocol



Addressing ALL specific threats shifts APP signaling to Protective (Synaptoblastic) State.

THE BREDESEN SHIFT:
COMPREHENSIVE DIAGNOSTICS & TREATMENT



Practical Necessity: Identify every potential "hole" for each individual patient.

The Diagnostic Framework: The 'Cognoscopy' and Patient Subtyping

The Old Way: 'One-Size-Fits-All' Diagnosis



Alzheimer's Disease



Generic Treatment

Limited diagnosis, misses specific drivers.
Ineffective, broad treatments.

THE "COGNOSCOPY" SHIFT: PERSONALIZED ASSESSMENT

The New Paradigm: 'Cognoscopy' & Patient Subtyping



THE COGNOSCOPY: Comprehensive Evaluation

Type 1 (Inflammatory) - Chronic systemic inflammation (e.g., leaky gut, poor diet, infections).
Specific diet, anti-inflammatories.

Type 1.5 (Glycotoxic) Insulin resistance and chronic high blood glucose.
Low-carb diet, metformin.

Type 2 (Atrophic) - Suboptimal support from hormones, nutrients, and trophic factors.
HRT, nutrients, exercise.

Type 3 (Toxic) - Chronic exposure to toxins (heavy metals, mold mycotoxins).
Detox protocol, binders.

Type 4 (Vascular) - Impaired blood flow & oxygenation to the brain.
Cardio health, oxygen therapy.

Type 5 (Traumatic) - Head trauma, especially if repeated or severe.
Brain rest, targeted rehab.

Identifies unique drivers.
Allows for creation of targeted, effective treatment plan.

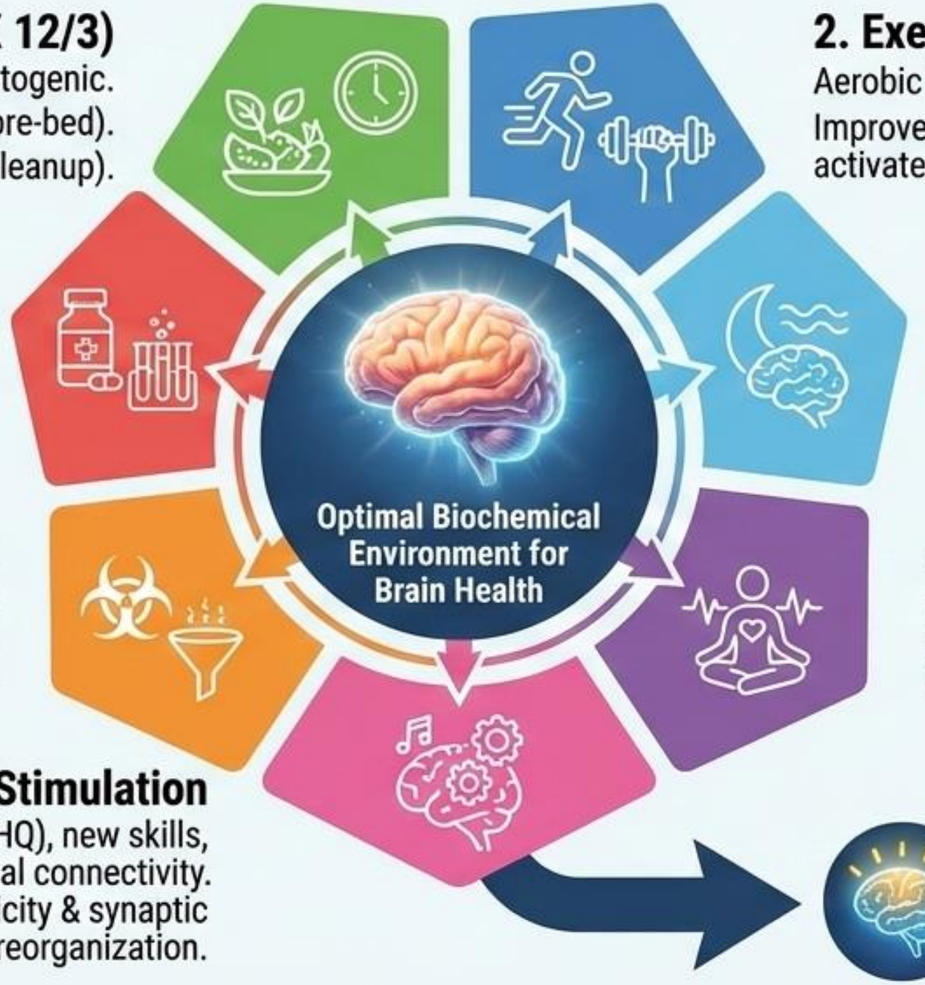
Goal: Create a targeted, effective treatment plan unique to each individual.

The ReCODE Intervention: A Personalized, Programmatic Approach & The Bredesen 7 (B7)

Not a single treatment, but a **personalized**, synergistic program to address specific contributors to cognitive decline.

1. Diet (KetoFLEX 12/3)
Plant-rich, mildly ketogenic.
Nightly fast (12+ hrs, 3 hrs pre-bed).
Promotes ketogenesis & autophagy (cellular cleanup).

2. Exercise
Aerobic & strength training.
Improves cerebral blood flow, upregulates BDNF, activates glymphatic system for waste clearance.



7. Targeted Supplementation
Personalized regimen based on lab results.
Addresses deficiencies (vitamins, minerals, hormones, trophic factors) for synaptic health.

3. Sleep
7-8 hours quality, restorative sleep.
Facilitates "glymphatic cleanse" (20x clearance of beta-amyloid during deep sleep).

6. Detoxification
Identify & remove "dementogens": metals (mercury), organic chemicals, biotoxins (mold).

4. Stress Management
Meditation, yoga, mindfulness, biofeedback.
Reduces chronic stress, lowers neurotoxic cortisol levels.

5. Brain Stimulation
Brain training (BrainHQ), new skills, social connectivity.
Promotes neuroplasticity & synaptic reorganization.

Synergistic Application:
The combined, programmatic approach shifts the brain's biochemistry from neurodegeneration to **REGENERATION.**

ReCODE Protocol: The Comprehensive Diagnostic Workup

Comprehensive Lab Testing



- Systemic Inflammation (e.g., hs-CRP)
- Metabolic Health (e.g., HOMA-IR, fasting glucose)
- Hormonal Status
- Nutrient Levels (e.g., Vitamin D, B vitamins)
- Metals & Toxins (e.g., mycotoxins, heavy metals)

Genetic Analysis



- Evaluation of key genetic risk factors
- Primary focus on ApoE4 status
- Assesses susceptibility to late-onset AD

Cognitive Assessments



- Standardized Tools (e.g., MoCA)
- Computerized Battery (e.g., CNS Vital Signs)
- Establish cognitive baseline
- Track changes over time

Patient History



- Detailed medical questionnaires
- Past & current medical history
- Diet & lifestyle patterns
- Sleep habits & Stress levels
- Environmental exposures



Software-Based Algorithm

Identifies Potential Contributors to Cognitive Decline

ReCODE Protocol: Clinical Evidence & Patient Outcomes (Proof-of-Concept Trial)

Sep 2021

255-Participant Proof-of-Concept Trial

255

Goal: Evaluate efficacy of multi-factorial, personalized program.
Participants in earlier stages of decline.



Key Trial Outcomes (Compelling Initial Evidence)

Metabolic Risk Factors

Significantly Modulated (Improved)
Better metabolic health markers.

Cognitive Function

Stabilized or Improved
Better cognitive performance, particularly in early stages.

The Path Forward: Provides compelling initial evidence; large-scale, randomized, controlled trial is warranted for further validation.

Key Metabolic Outcomes

Sep 2021

The study documented statistically significant improvements across several key metabolic markers, validating the protocol's ability to address the underlying drivers of inflammation and insulin resistance.

Metabolic Marker	Sample Size (n)	Outcome	P-Value
hs-CRP (Inflammation) 🔥	177	↓ Significant Decline	$p < 0.001$
HOMA-IR (Insulin Resistance) 👉	176	↓ Significant Decline	$p < 0.002$
Fasting Glucose 🧊	208	↓ Significant Reduction	$p < 0.01$
Vitamin D ☀️	207	↑ Significant Increase	$p < 0.001$

Cognitive Outcomes: MoCA Performance

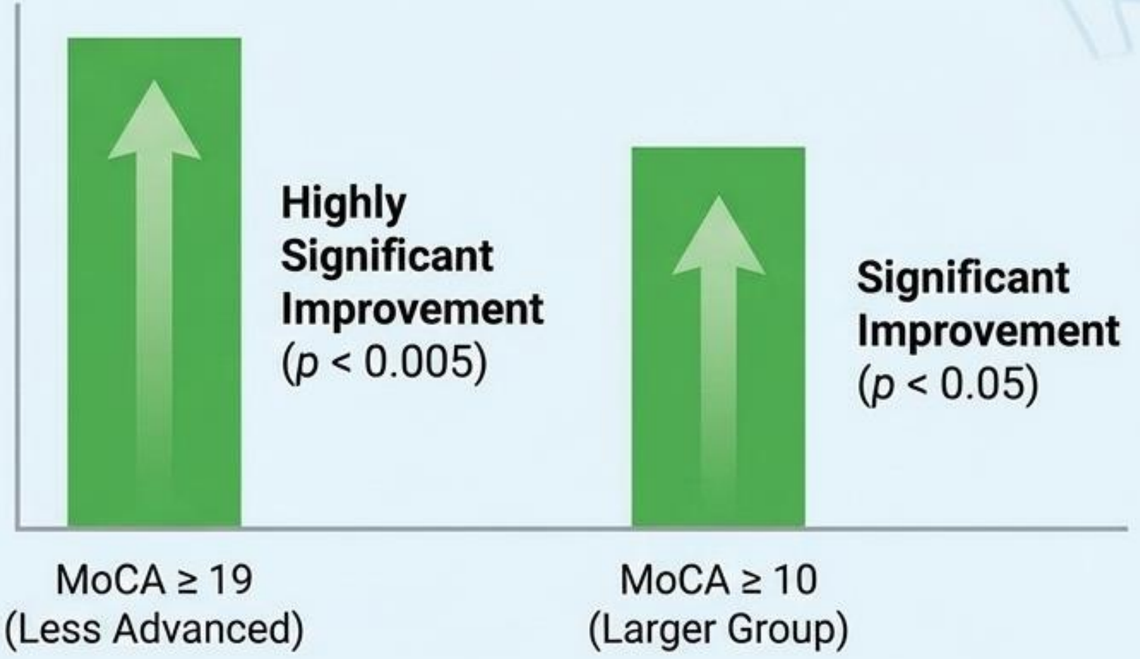
Sep 2021

Overall MoCA Trend



Stabilization or improvement across entire pool.

Efficacy by Impairment Level



Conclusion: Protocol is **MOST EFFECTIVE** when implemented **before** severe impairment **(Early Intervention).**

Illustrative Case Study: Protocol Impact - Patient Outcome (Case 1)

Patient Profile & Baseline (Before ReCODE)



ApoE4+
66-Year-Old Man



Senior Moments

Multiple Metabolic Abnormalities

Initial Clinical Data

Fasting Insulin: 32 (High)

hs-CRP (Inflammation): 9.9 (High)

Hippocampal Vol.: 17th %ile (Low)



Low Volume

After 10 Months on ReCODE Protocol

Patient Outcome (After 10 Months)

Outcome Clinical Data

Fasting Insulin: 8 (Optimal)

hs-CRP (Inflammation): 3 (Improved)

Hippocampal Vol.: 75th %ile (Dramatic Improvement)



Significant Improvement in Metabolic Markers & Brain Structure



Improved Volume

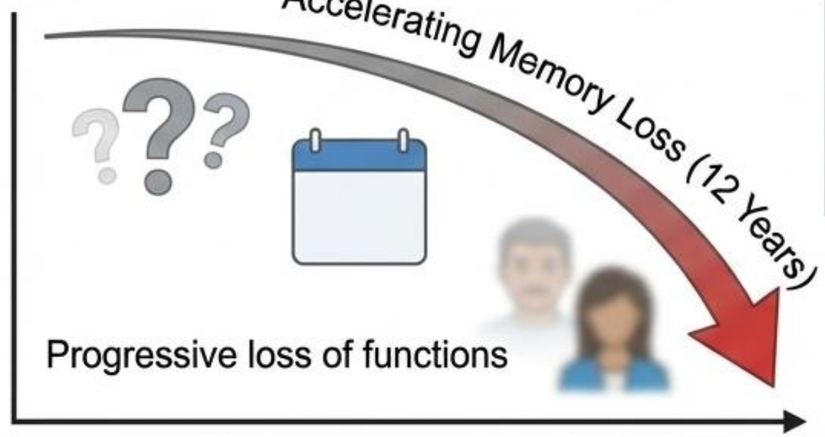
Real-World Impact: ReCODE protocol reversed metabolic dysfunction and led to measurable structural brain improvement.

Illustrative Case Study: Protocol Impact - Patient Outcome (Case 2)

Patient Profile & 12-Year History (Before ReCODE)



70-Year-Old Man



Start of ReCODE Protocol After 6 Months

Patient Outcome (After 6 Months)

Subjective & Objective Improvements



Wife noted decline "completely stopped."





Remembering Faces (Improved)



Remembering Schedules (Improved)



Remembering Numbers at Work (Improved)

Accelerating Decline

Objective Improvements & Decline Halted

Real-World Impact: ReCODE protocol halted a 12-year history of accelerating cognitive decline and restored specific functional abilities within 6 months.

Primary Criticisms of the Protocol: Lack of Rigorous Evidence

Current Evidence: Descriptive Case Series



Relies on anecdotal, observational data from individual cases. Lacks control groups.

Scientific Rigor

Existing evidence lacks the methodological rigor needed.



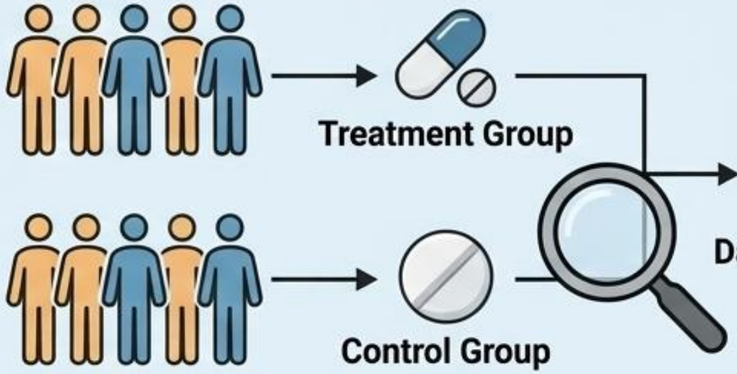
Dr. Joanna Hellmuth



No Placebo Control

?

The Gold Standard: Randomized Clinical Trials (RCTs)



Methodologically rigorous, placebo-controlled, randomized. Proves effectiveness beyond placebo effect.

Scientific Rigor

RCTs remain the gold standard for proving a treatment's effectiveness.



Double-Blind, Placebo-Controlled

Conclusion: Critics argue the protocol's effectiveness is unproven without large-scale, rigorous RCTs.

Primary Criticisms of the Protocol: High Financial Burden

Program Enrollment Fees



$1,399 (e.g., Apollo Health).
Initial cost to join the program.

Practitioner Consultations



Up to $450/hour
Significant fees for ongoing expert guidance.



Extensive & Repeated Lab Work



Initial Panels **> $850.**
Frequent re-testing adds up quickly.

Wide Array of Supplements



Significant ongoing expense for numerous recommended supplements.



Generally Not Covered by Insurance.





Conclusion: The protocol's exceptional cost places it far beyond the financial reach of a vast portion of the population.

Primary Criticisms of the Protocol: Commercialization and Conflicts of Interest

The Commercial Enterprise (Apollo Health)



- Program Marketing & Promotion
- Fee-Based Practitioner Training
- Associated Supplement Lines

Concerns & Potential Conflicts

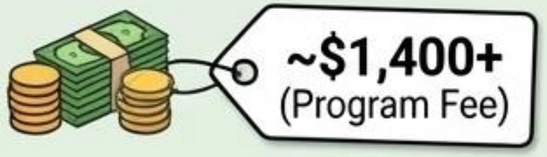


- Potential for Conflicts of Interest
- Financial Incentives vs. Clinical Needs
- Influence on Clinical Recommendations

Core Criticism: Monetization raises ethical questions about whether financial gain could override patient well-being in clinical decisions.

Addressing the "Commercialization" Critique: A Comparative Economic Perspective on Alzheimer's Care

ReCODE Protocol
(Precision Medicine & Lifestyle)





Emphasizes groceries, supplements, lifestyle changes. Cost covers complex software for analyzing 36+ variables & trained practitioner guidance

Legitimate costs of precision medicine.

LEAST COMMERCIAL OPTION

Anti-Amyloid Drug
(e.g., Lecanemab)





$26,500 drug cost + infusion fees + frequent MRI monitoring for bleeds.

Marginally effective drugs at exorbitant prices.

HIGH PHARMA COST & MONITORING

Standard Nursing Home Care
(Advanced Dementia)





Full-time residential care for advanced cognitive decline.

The massive monetization of "hopelessness".

HIGHEST COST OF CARE

The Reality of "Monetization"

ReCODE's "Legitimate Costs"
Necessary tools for complex, personalized analysis.

Pharma's "Monetization of Hopelessness"
Profiting from marginally effective, high-cost interventions.

Accusations of "profiteering" against ReCODE ignore the vastly higher costs of standard pharmaceutical and institutional care.

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

TRIAL DESIGN & PARTICIPANTS

- 6 US Sites
- N=72 Participants, Aged 45-76
- MCI or Early Dementia
- Completed Oct 31, 2025

Multicenter Randomized Controlled Trial (RCT). Enrolling individuals with Mild Cognitive Impairment (MCI) or early dementia.

INTERVENTION (9 Months, 2:1 Randomization)

PERSONALIZED PRECISION MEDICINE (ReCODE Approach)

Addressing Root Causes

- Inflammation
- Insulin Resistance
- Hormones
- Toxins
- Vascular
- Nutrients

- Diet (KetoFLEX 12/3)
- Exercise
- Sleep Optimization
- Stress Reduction
- Stress Reduction
- Targeted Supplementation

VS

STANDARD CARE

Current medical standards.

KEY OUTCOMES MEASURED

- **MoCA** (Montreal Cognitive Assessment)
- **CNS Vital Signs** (Neurocognitive Index)
- **Caregiver Reports** (AQ-21, AQ-C)
- **Brain MRI Volumetrics**
- **Biomarkers** (p-tau 217, GFAP, NfL)

PRELIMINARY RESULTS & SIGNIFICANCE (Dr. Dale Bredesen)

UNPRECEDENTED COGNITIVE IMPROVEMENT

Improvement in cognition greater than seen in any other trial. Large, clinically significant, and statistically significant differences vs. control.

- **REDUCED DEPRESSION SCORES** (PHQ-9)
- **NORMALIZED BRAIN FUNCTION** Normalization of Arterial Spin Labeling MRI (in documented cases).

FIRST RCT VALIDATING PRECISION MEDICINE'S SUPERIORITY OVER STANDARD CARE.

Based on pilot data showing 84% improvement. Complete data analysis expected Early 2026.

STUDY POPULATION: Inclusion & Exclusion Criteria

INCLUSION CRITERIA
(Eligible to Participate)

- **Age:** 45-76 years
- **Diagnosis:** Mild Cognitive Impairment or Early-Stage Dementia
- **MoCA Score:** ≥ 19
- **Study Partner Presence:** For protocol adherence
- **Residence:** Within 1 hour of participating center

EXCLUSION CRITERIA
(Not Eligible)

- **MoCA Score:** < 19
- **Uncontrolled Serious Medical Illnesses**
- **Major Psychiatric Diagnoses**
- **Psychoactive Meds:** Impacting cognition
- **Use of Statins, Anticoagulants**
- **MRI Findings:** Hydrocephalus, infarctions, extensive white matter disease
- **Symptomatic Traumatic Brain Injury**
- **Other Neurodegenerative Diseases:** (Non-Alzheimer's)
- **Prior ReCODE Treatment:** Or similar methodology
- **Inability to Remedy Toxicity:** Identified sources

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

INTERVENTION - PRECISION MEDICINE GROUP:
Core Program



KetoFLEX 12/3 Diet
Plant-rich, mildly ketogenic diet with 12-hour daily fast.



Aerobic Exercise
Minimum 45 minutes per day, 6 days a week.



Strength Training
2 times per week.



Mental Exercise & Cognitive Training
Engage in brain training, learning new skills.



Sleep Optimization
7-8 hours per night.



Stress Reduction
Meditation, yoga, mindfulness practices.

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

Comprehensive Diagnostic Panels: Tests Performed

Chronic Inflammation & Infections



Assess systemic inflammatory markers & pathogen exposure.

Intestinal Dysbiosis



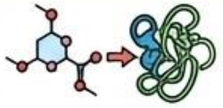
Evaluate gut microbiome balance and gut barrier integrity.

Insulin Resistance



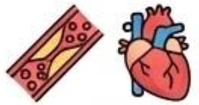
Measure glucose metabolism and insulin sensitivity.

Protein Glycation



Assess advanced glycation end-products (AGEs).

Vascular Disease



Evaluate cardiovascular health, blood flow, and endothelial function.

Nocturnal Hypoxemia



Monitor oxygen levels during sleep for desaturation.

Hormonal Insufficiency/Dysregulation



Test levels of key hormones (thyroid, sex, adrenal).

Nutritional Deficiencies



Screen for vitamins, minerals, and essential nutrient levels.

Exposure to Toxins & Heavy Metals



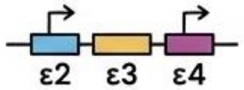
Test for environmental toxins, heavy metals, and biotoxins.

Genetic Predisposition to Cognitive Decline



Analyze genetic markers linked to cognitive risk.

ApoE Genotyping



Determine ApoE status (e.g., ApoE4) for Alzheimer's risk.

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

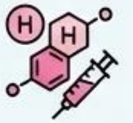
STUDY GROUPS & INTERVENTIONS

PERSONALIZED INTERVENTIONS
(Active Treatment Group)



Individualized Nutritional Supplementation

Custom regimen based on metabolic needs.



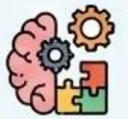
Hormone Replacement Therapy (HRT)

Prescribed when clinically indicated.



Stress Management Support Devices

Tools for biofeedback and relaxation.



Brain Exercises

Cognitive training and stimulation programs.

CONTROL GROUP
(Standard Care)



Received Standard Care

Routine medical management for 9 months.

Future Option

Eligible for up to 6 months of Precision Medicine treatment after completing control period.

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

PRIMARY OUTCOMES

COGNITIVE ASSESSMENTS



- **Montreal Cognitive Assessment** (MoCA)
- **CNS Vital Signs Neurocognitive Index**: Computerized battery (memory, executive function, reaction time, cognitive flexibility, etc.)
- **Brain HQ**: Computerized brain training & assessment
- **AQ-21**: Alzheimer's Caregiver Assessment Questionnaire (Subjective partner scale)
- **AQ-C**: Alzheimer's **Questionnaire Change Scale** (Subjective improvement/decline scale)

NEUROIMAGING



- Brain MRI with Volumetry: At baseline & conclusion of study
- Arterial Spin Labeling (ASL): Highly sensitive MRI technique for Alzheimer's pathophysiology

BIOMARKERS



- p-tau 217
- GFAP (Glial Fibrillary Acidic Protein)
- NfL (Neurofilament Light Chain)

ADDITIONAL ASSESSMENTS



- PHQ-9: Depression measure
- Data Epigenetics
- Biochemical parameters
- Genomic data
- Wearable device data

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

PRELIMINARY RESULTS (ANNOUNCED OCTOBER-NOVEMBER 2025)

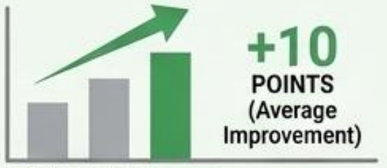
COGNITIVE EFFICACY

"Greater improvement in cognition than seen in any other trial."
– Dr. Dale Bredesen



COMPARISON WITH PREVIOUS PILOT STUDY (2021)



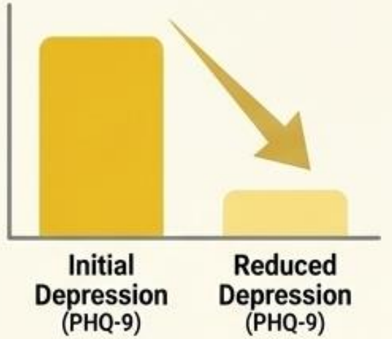


CNS Vital Signs (Standard Score)

Statistically significant improvement in MoCA scores & AQ-C.

Brain MRI demonstrated that typical brain atrophy was prevented.

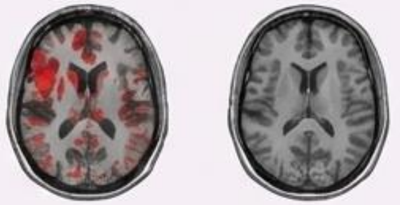
REDUCTION IN DEPRESSION



Data from PHQ-9 demonstrated depression was also reduced.

Work published by Dr. Ram Rao and colleagues.

NORMALIZATION OF IMAGING BIOMARKERS



BEFORE (Initial ASL)
Classic Alzheimer's Changes

AFTER (Follow-up ASL)
Completely Normal

Documented case of an ApoE 4/4 patient after 1 year of ReCODE treatment.

Evaluated by Dr. Cyrus Raji, Professor of Radiology, Washington University School of Medicine.

The Evanthea Trial (NCT05894954): First RCT Validating Precision Medicine for MCI & Early Dementia

TECHNOLOGICAL INNOVATIONS AT THE REZILIR CENTER

As the only center in the Evanthea study with access to:

Hyperbaric Oxygenation Chamber



Pressurized chamber for enhanced oxygen delivery to tissues.

19-Channel Neurofeedback



Real-time brainwave monitoring for self-regulation training.

High-Intensity Light Therapy



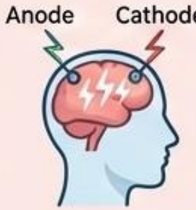
Bright light exposure to regulate circadian rhythms and mood.

REZILIR CENTER

Low-Intensity Photobiomodulation



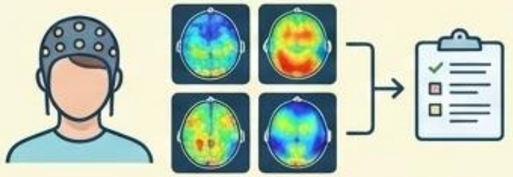
Low-level light therapy to stimulate cellular repair and reduce inflammation.



Direct Electrical Stimulation Therapies

Non-invasive brain stimulation to modulate neuronal activity.

Multiple QEEGs to Assist Neuromodulatory Interventions

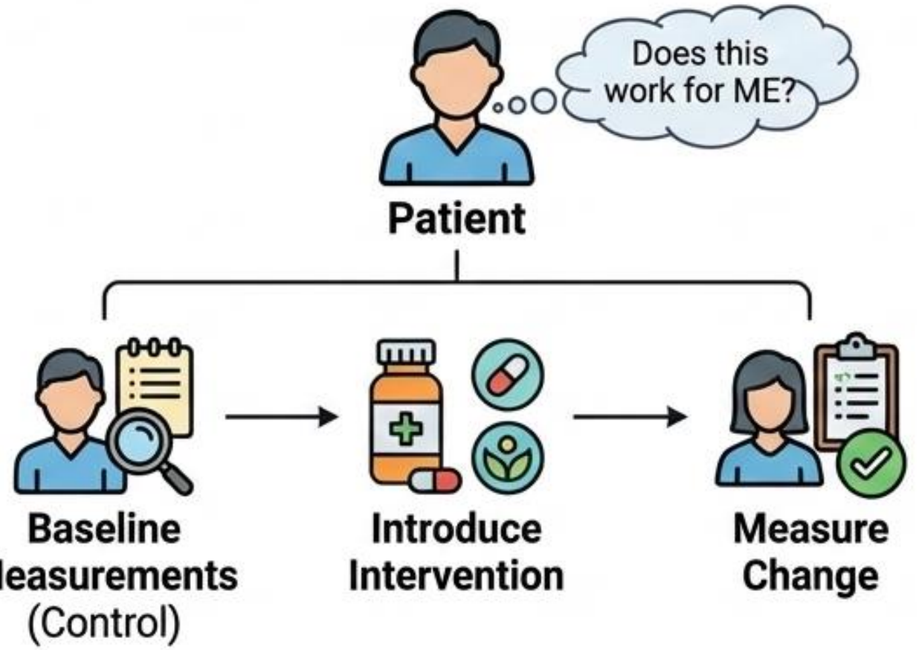


Quantitative EEG for brain mapping to guide personalized interventions.

All technologies are part of the Evanthea study protocol at the Rezilir Center.

The N-of-1 Trial: The Future of Clinical Practice

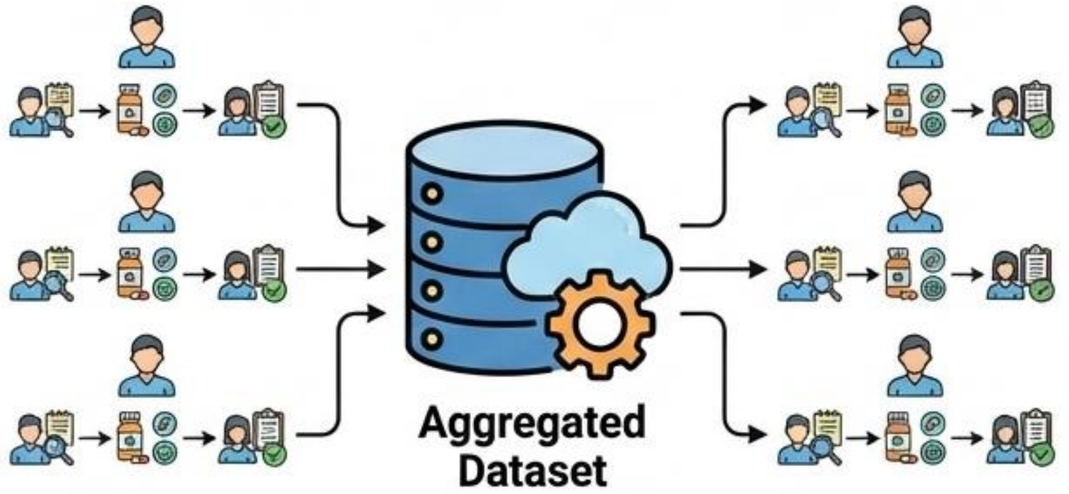
Understanding the N-of-1 Trial Design



Statistical Power: Higher power to detect effects by eliminating between-subject variability.

Relevance: Answers the question the patient cares about: "Does this work for me?"

Aggregating N-of-1 Trials
(e.g., Bredesen's Case Series)



Proven Efficacy Across Diverse Biological Subtypes

Conclusion: When you have 100 consecutive N-of-1 trials showing benefit, you have a dataset arguably **MORE** robust than an RCT.

ROBUST DATASET

5.2 Dense Dynamic Data Clouds: The P4 Medicine Approach

The P4 Medicine Approach & Dense Dynamic Data Clouds (Dr. Leroy Hood)

PREDICTIVE (Identify future risks)

PREVENTIVE (Proactive intervention)

PERSONALIZED (Tailored to the individual)

PARTICIPATORY (Patient engagement)



DENSE DYNAMIC DATA CLOUDS
(Billions of data points: Genome, Proteome, Microbiome)

Understanding health and disease through deep, multi-omic data.

Systems Medicine vs. Traditional Trials: Resolution & Signal-to-Noise

SYSTEMS MEDICINE
(Resolution)



Measure MANY variables in FEW people.
High Resolution.

TRADITIONAL TRIALS
(Randomization)



Measure FEW variables in MANY people.
Low Resolution.

Signal-to-Noise

High Signal
(Deep Phenotypic Data)



Network Dynamics Clearly Visible.
Noise disappears.

High Noise
(Limited Data)



Individual Noise Obscures Network.
Difficult to see dynamics.

Bredesen's Alignment & Mechanistic Validation



Create Patient "Data Cloud" (Detailed Markers)

Successful Manipulation (e.g., Lower Homocysteine, Raise Vitamin D)

MECHANISTIC VALIDATION of Therapy (Proven Network Effect)

Bredesen's protocol aligns by using deep data to understand and treat the individual's unique network dysfunction.



The future of brain health: a pill or a lifestyle overhaul



ADVANCED MEDICINE

INTERNATIONAL CONGRESS OF INTEGRATIVE MEDICINE

5>6 DEC, 2025

OPORTO, PORTUGAL

THANK YOU!

@DRALAINDUTRA

