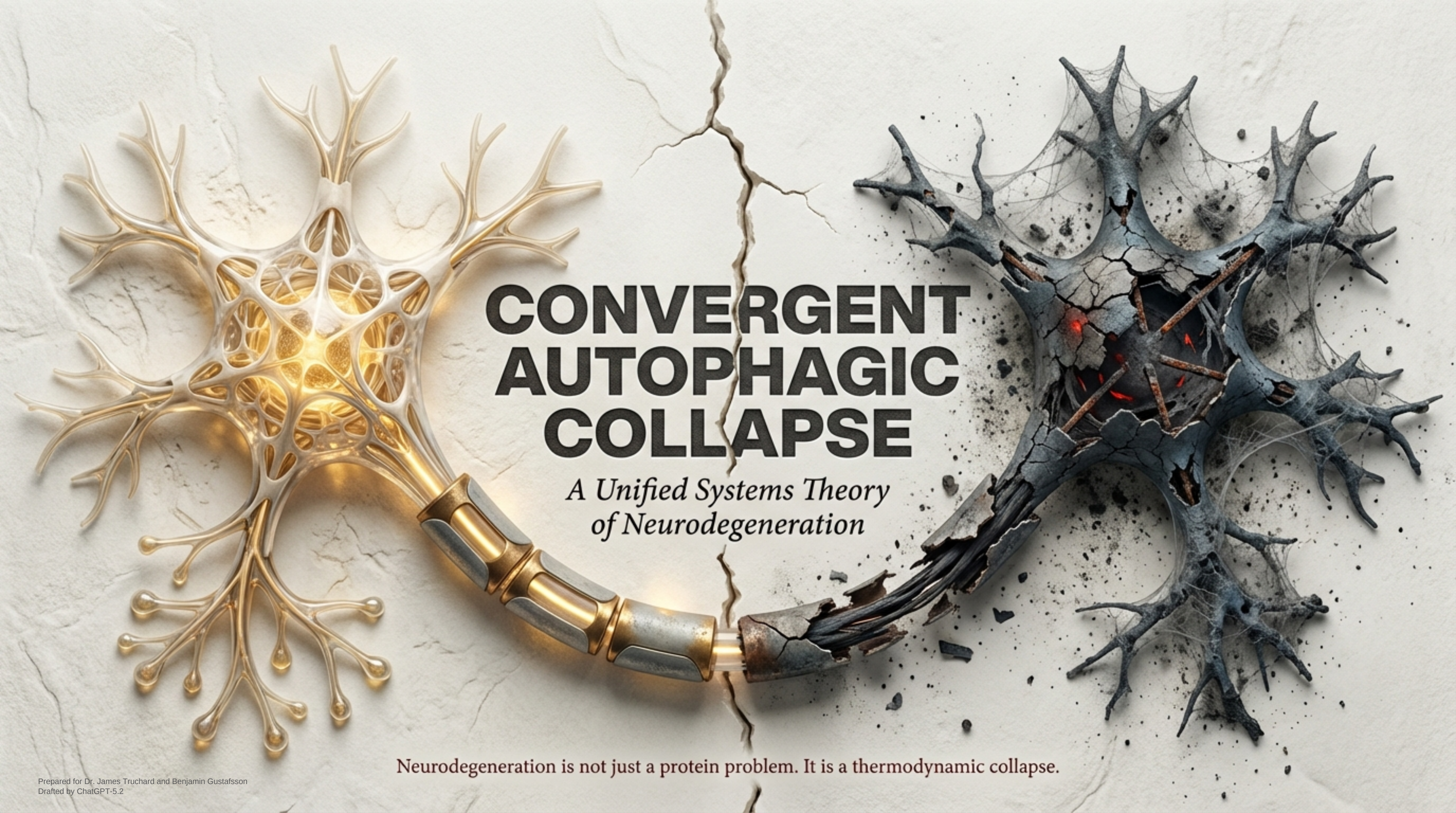




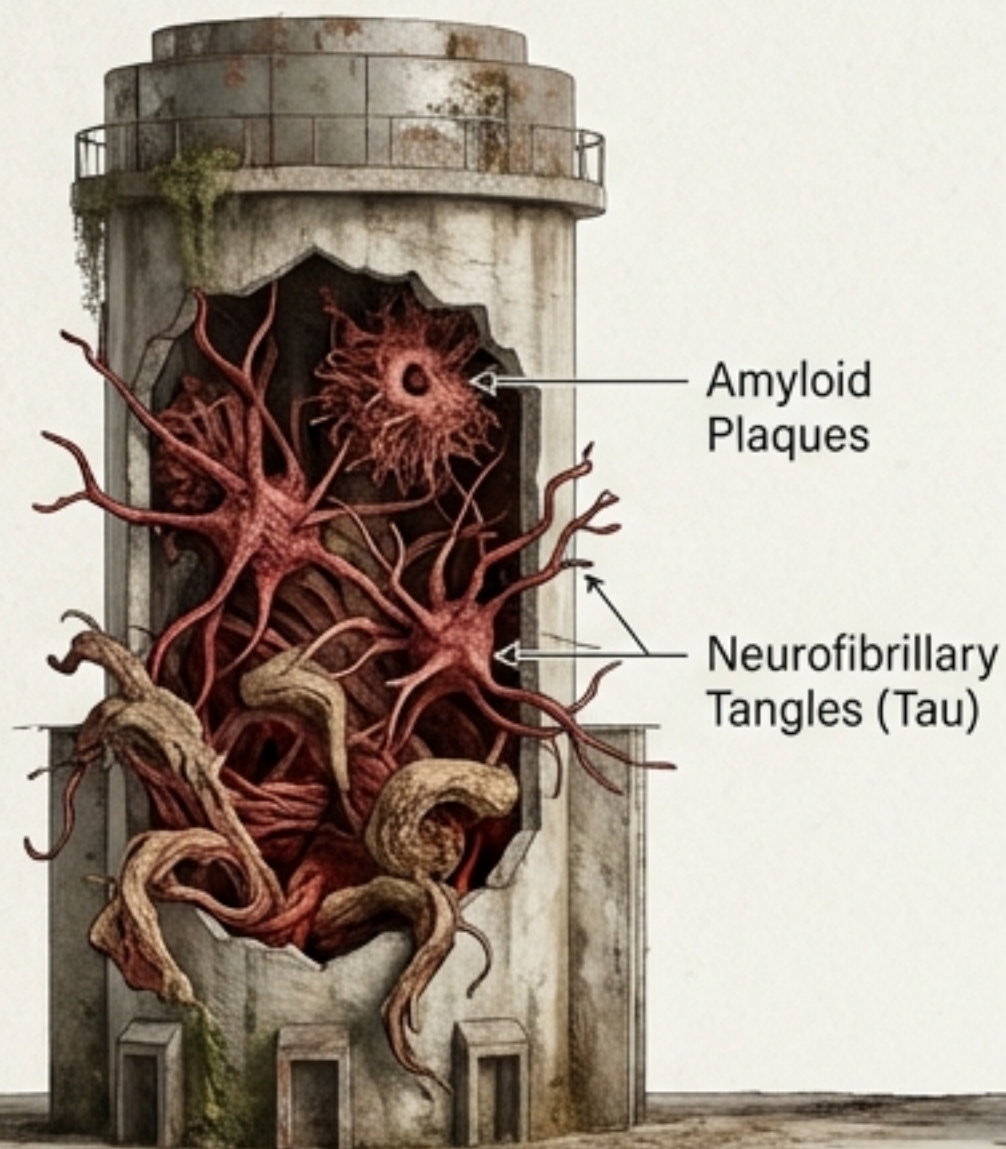
CONVERGENT AUTOPHAGIC COLLAPSE

*A Unified Systems Theory
of Neurodegeneration*

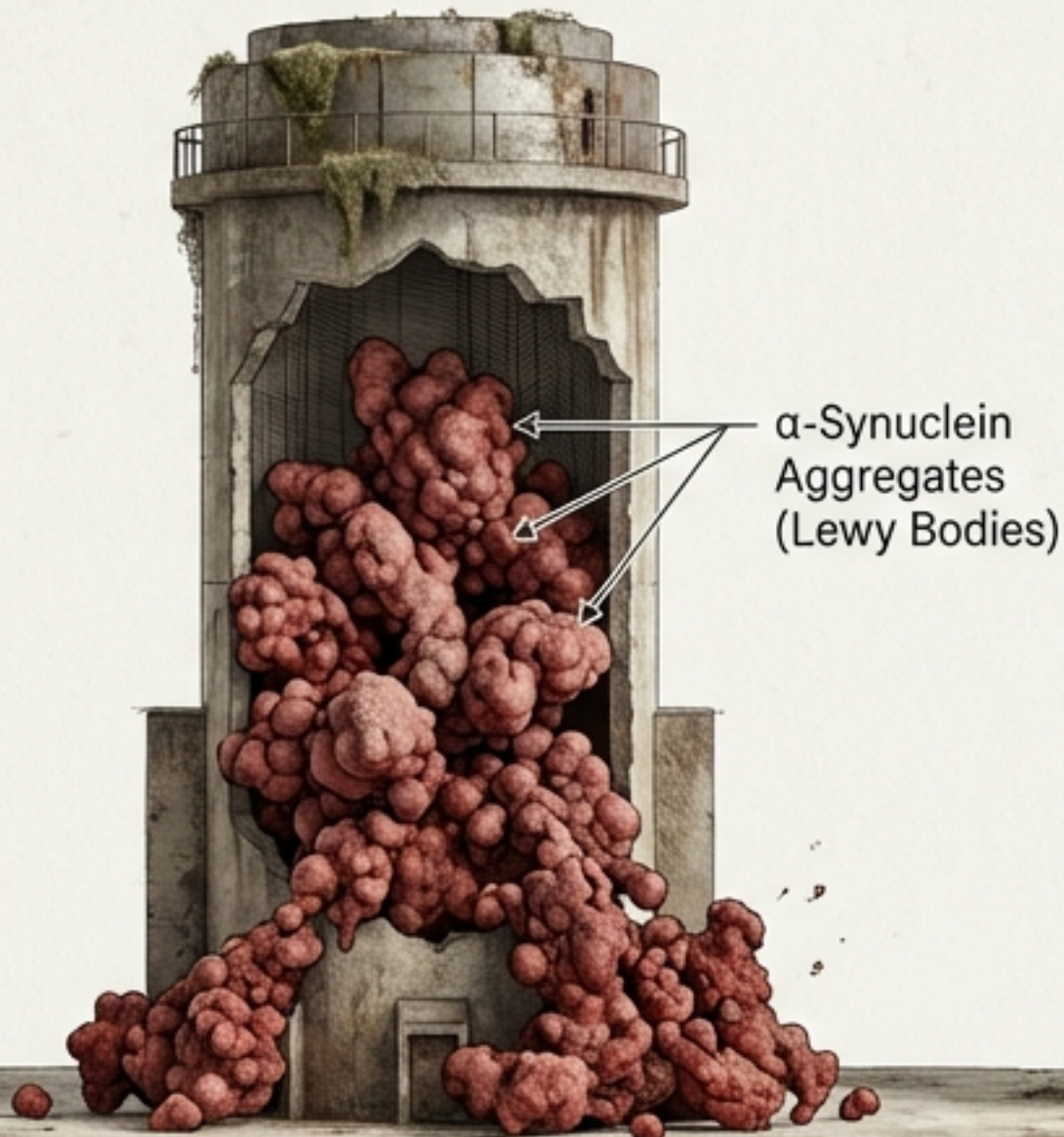
Neurodegeneration is not just a protein problem. It is a thermodynamic collapse.

THE FRAGMENTATION OF UNDERSTANDING

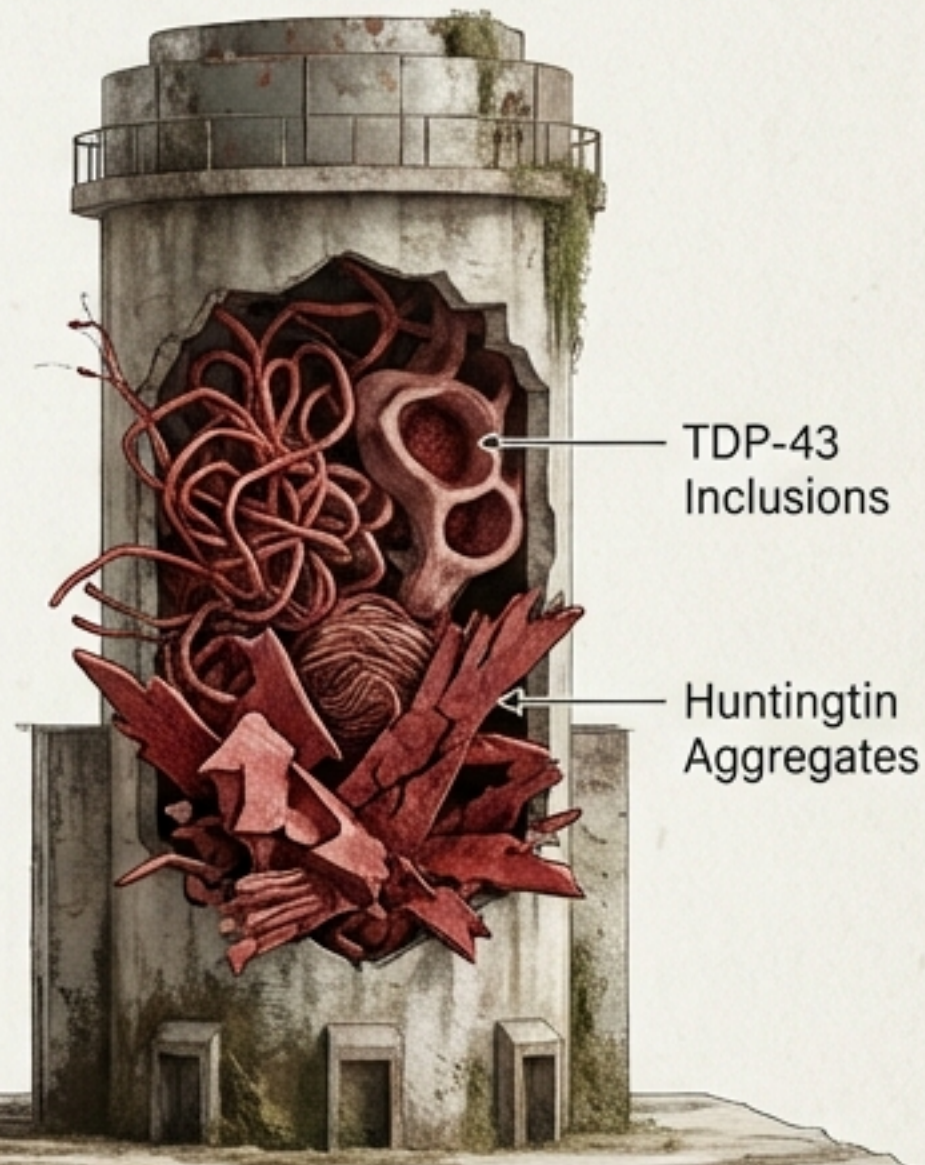
ALZHEIMER'S



PARKINSON'S

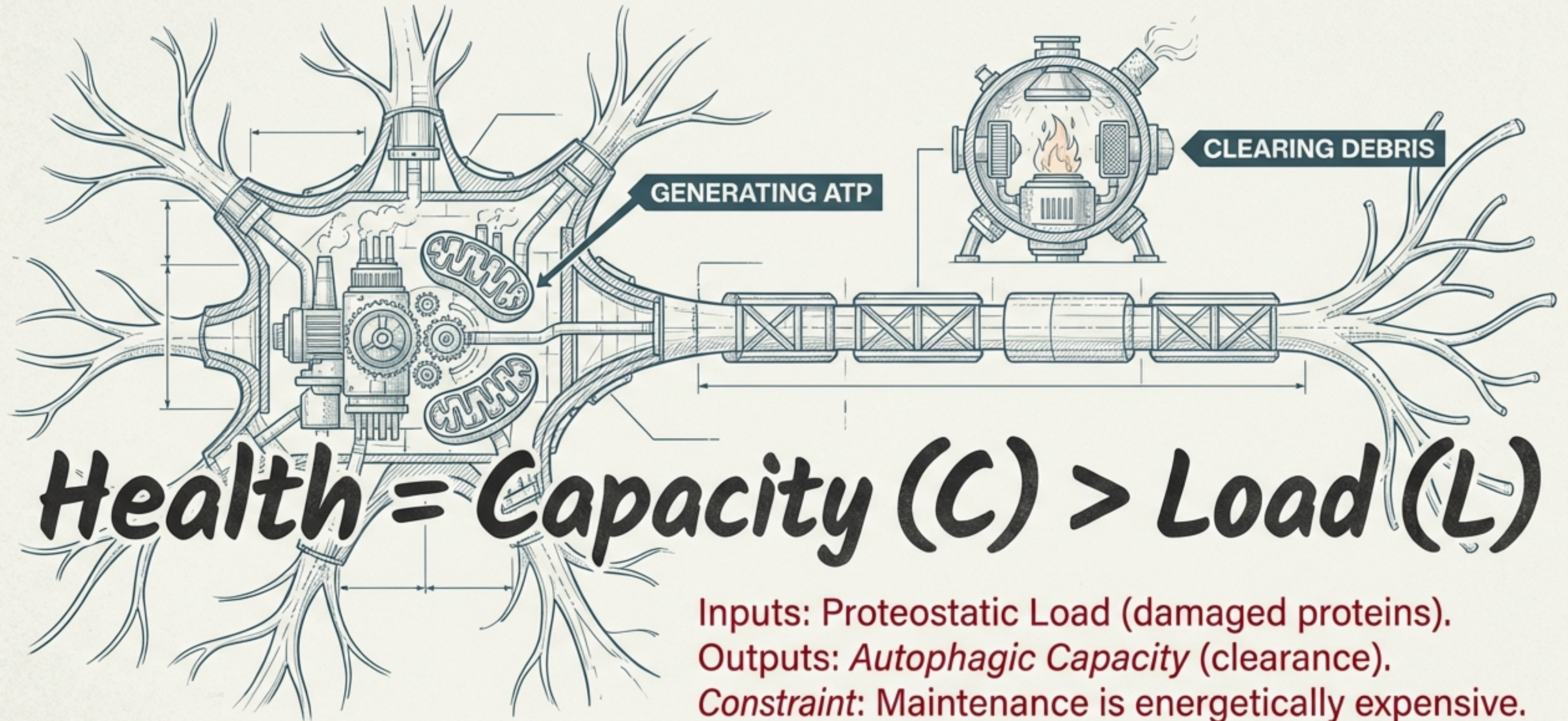


ALS / FTD / HD



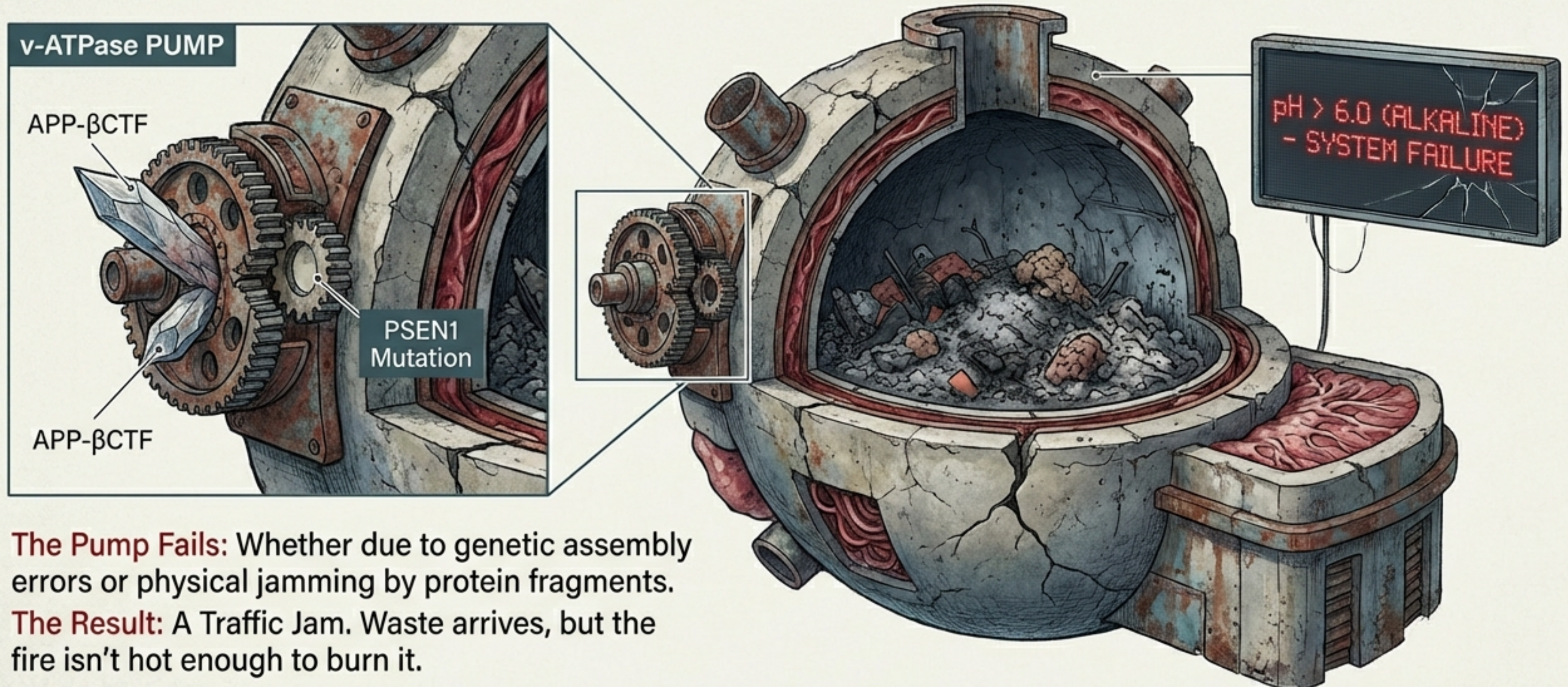
Decades of research have treated these as isolated "Proteinopathies" with unique suspects.
But the crime scene—the dying neuron—is identical: *Energy Failure & Waste Overload.*

THE ECONOMICS OF NEURONAL SURVIVAL



ALZHEIMER'S: THE BROKEN INCINERATOR

Choke Point: Lysosomal Acidification Failure



PARKINSON'S: THE POWER PLANT FAILURE

Choke Point: Mitophagy Arrest

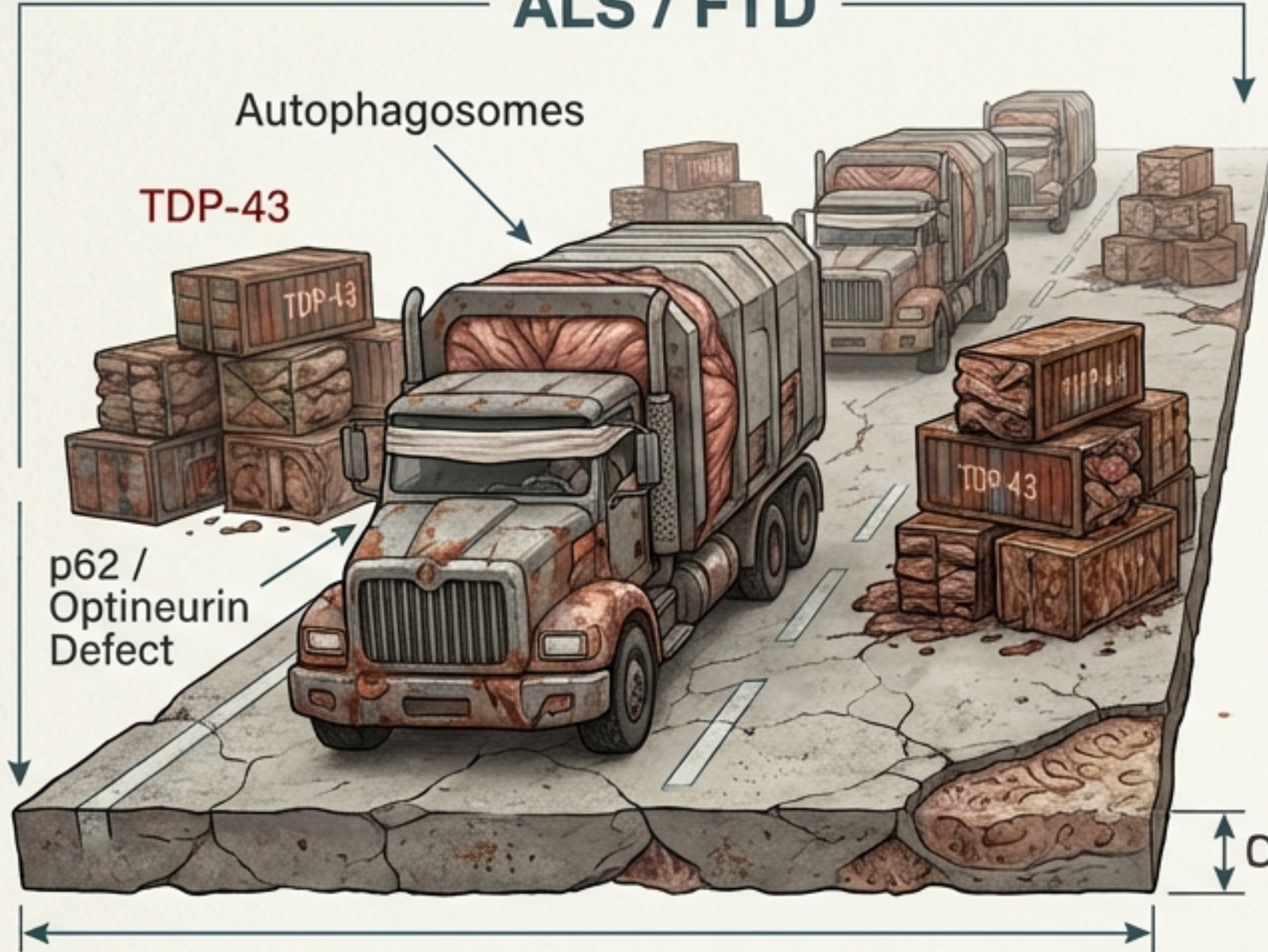


The Sensor Breaks: Quality control fails to flag damaged generators. The Result: Dirty Fuel.
Leaky mitochondria accumulate, spewing toxic exhaust (ROS) that poisons the rest of the system.

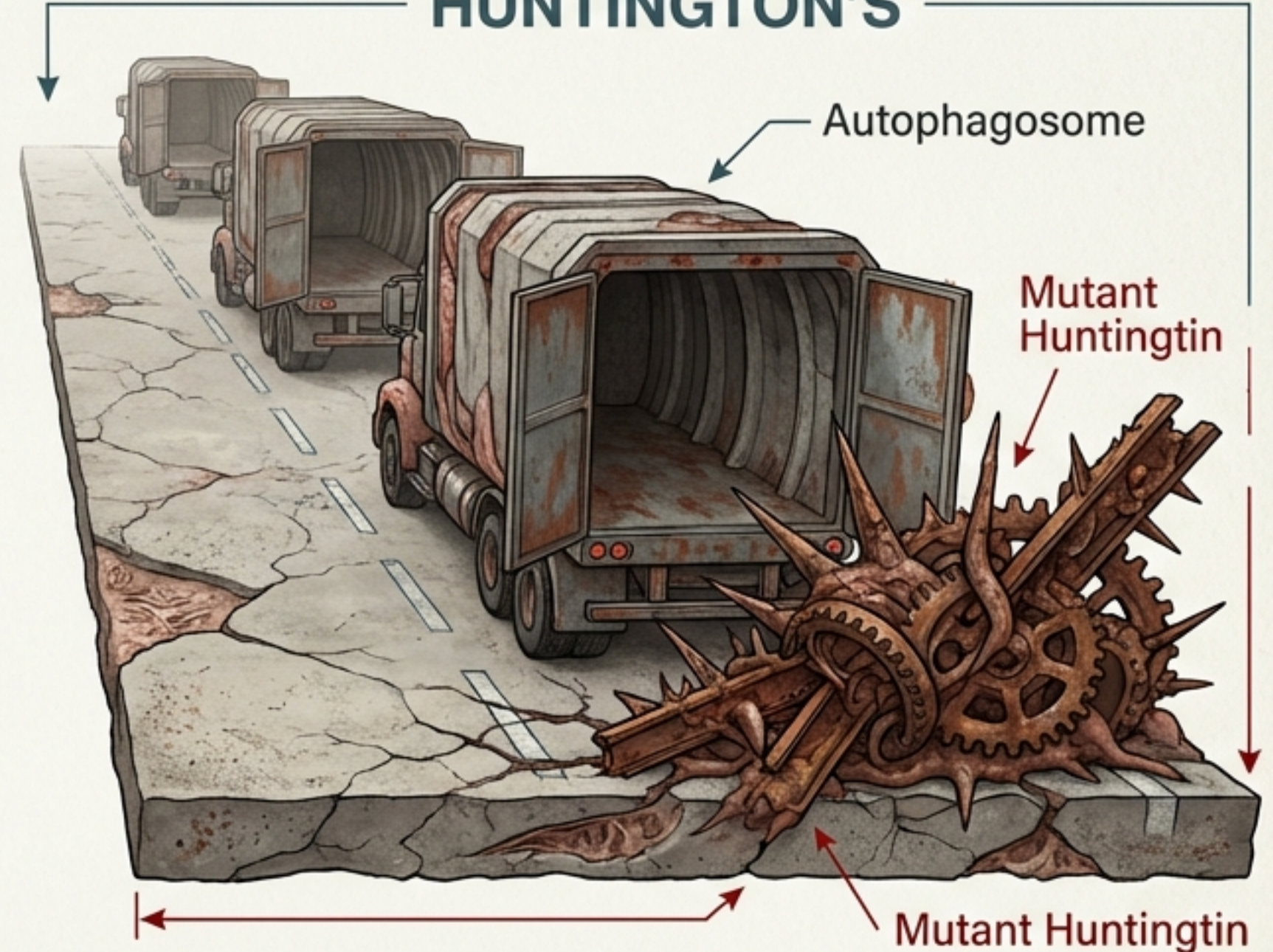
ALS, FTD, & HD: LOGISTICS & LOADING FAILURE

Choke Point: Cargo Recognition & Engulfment

ALS / FTD



HUNTINGTON'S



Futile Cycling: The neuron burns expensive fuel to drive empty or blind trucks.

Result: High energy cost, zero waste removal.

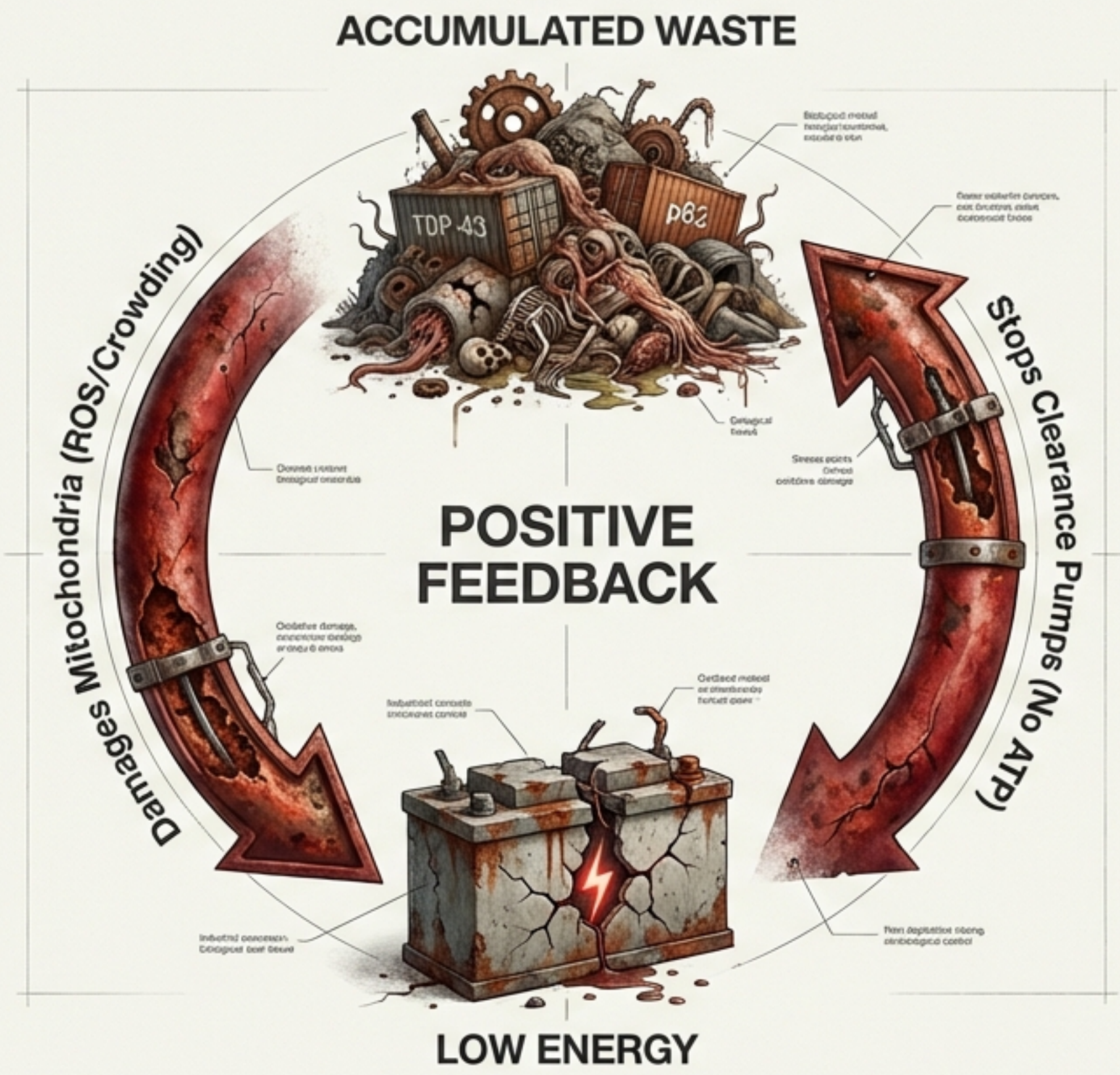
DISTINCT TRIGGERS, SHARED FATE

Convergent Autophagic Collapse



PROTEOSTATIC OVERLOAD (Trash Buried)
BIOENERGETIC INSOLVENCY (Bankrupt)

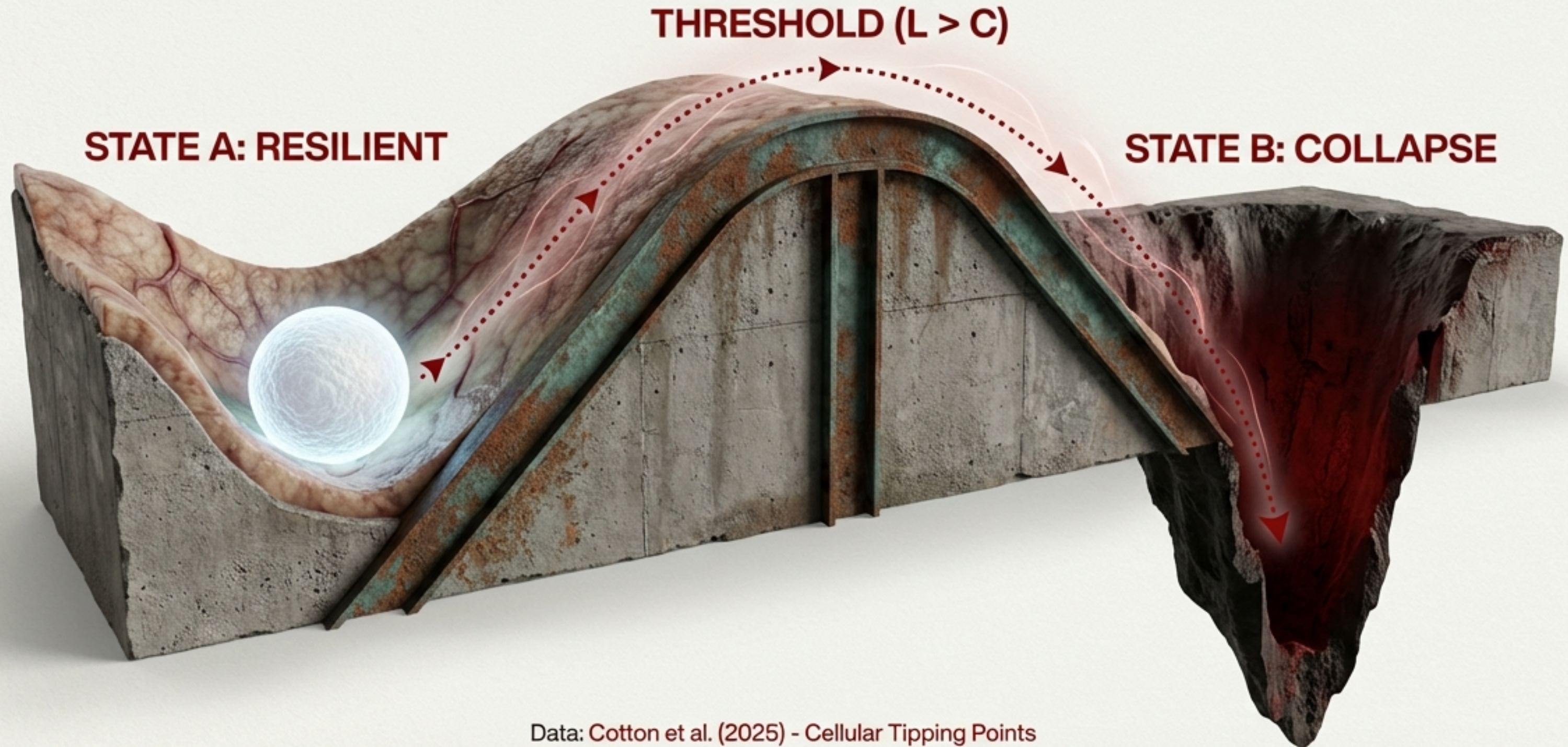
THE THERMODYNAMIC DEATH SPIRAL



Waste kills energy. Low energy prevents waste removal. Once the cycle starts, entropy wins.

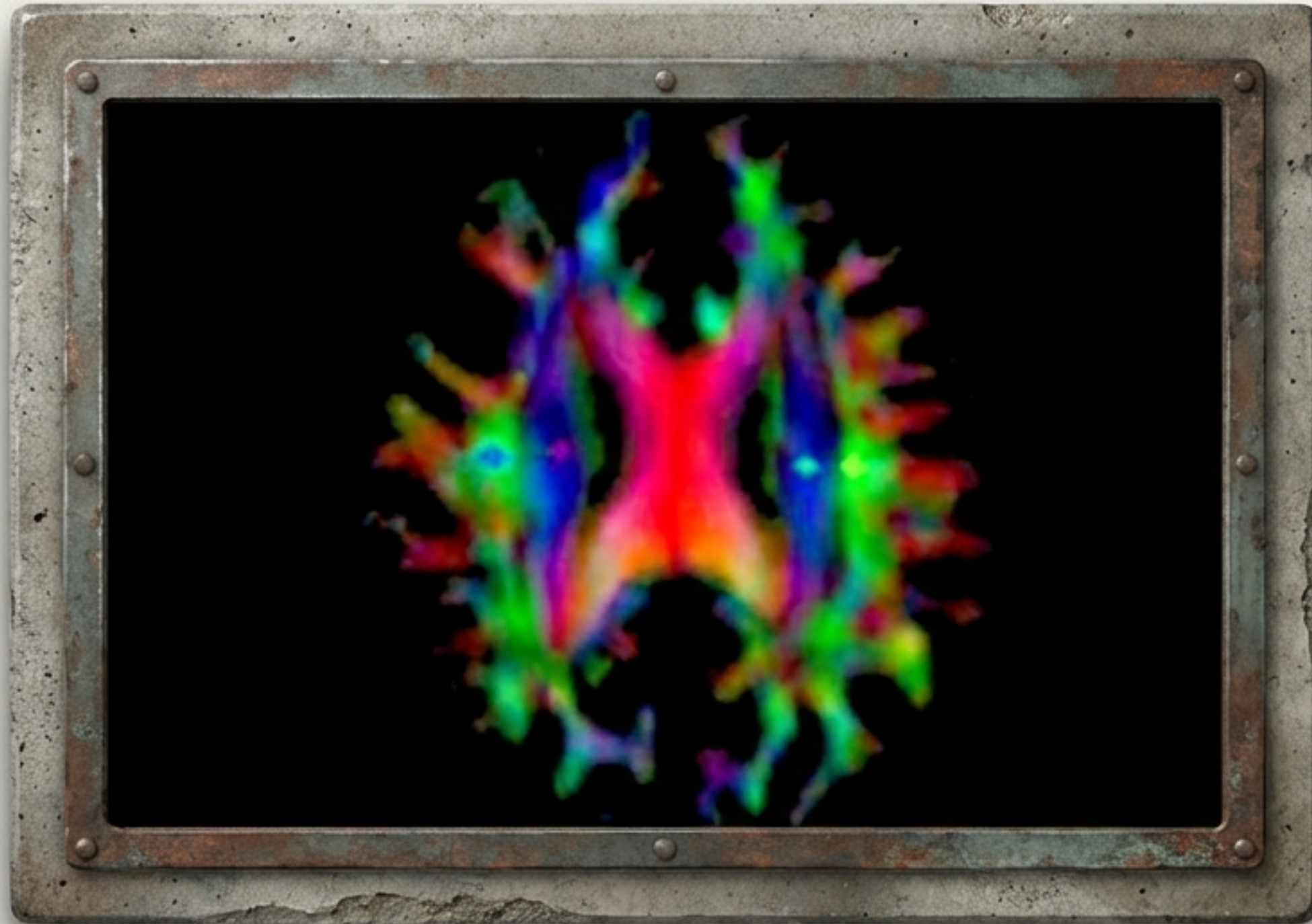
THE CELLULAR PHASE TRANSITION

Neurodegeneration is Bistable, not Linear.



Data: Cotton et al. (2025) - Cellular Tipping Points

TREATING THE SYMPTOM, IGNORING THE SYSTEM



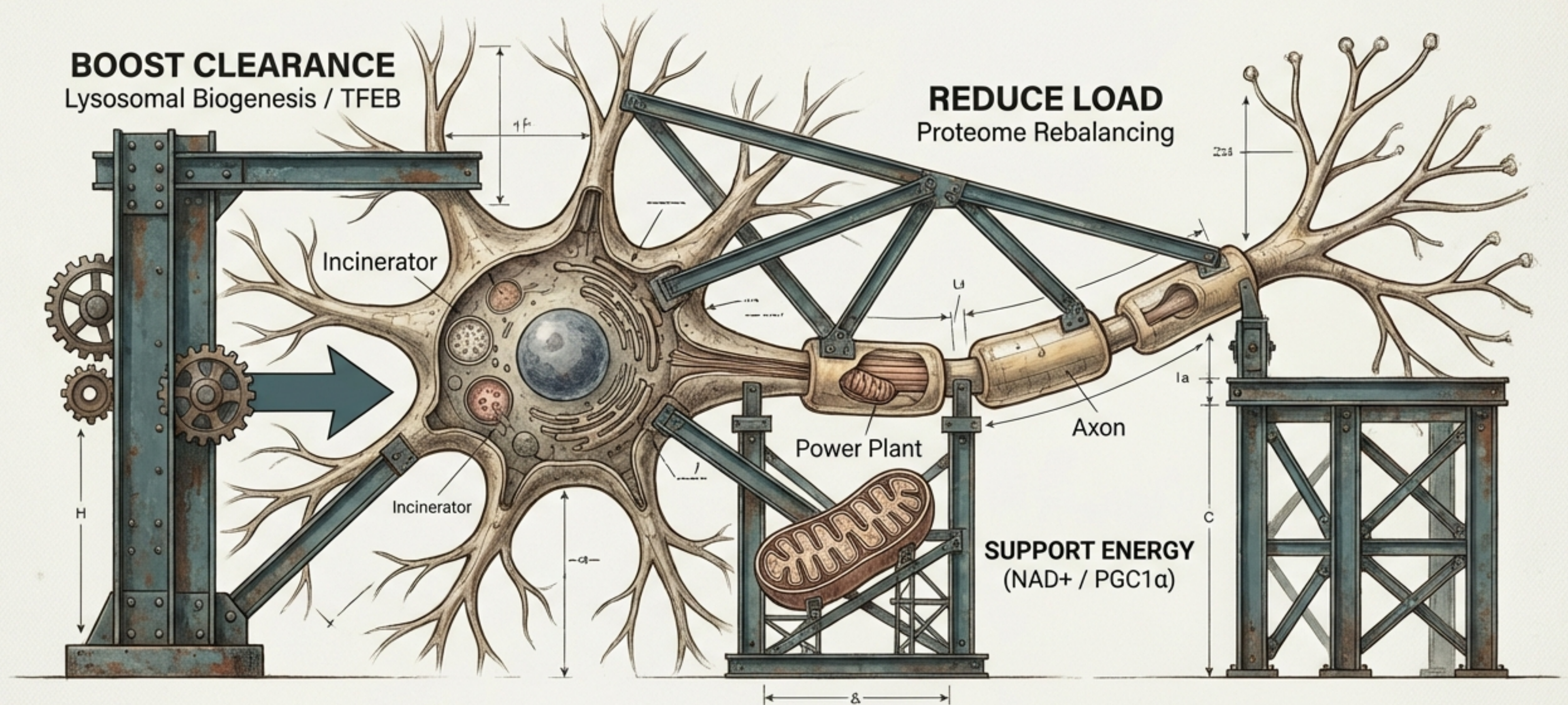
Evidence: Osaka Metropolitan University Study (Lecanemab).

Finding: Even after Amyloid- β plaques were cleared, the brain's waste clearance function (Glymphatic system) did not improve.

*“You cannot save a collapsing city just by sweeping the streets.
The infrastructure remains broken.”*

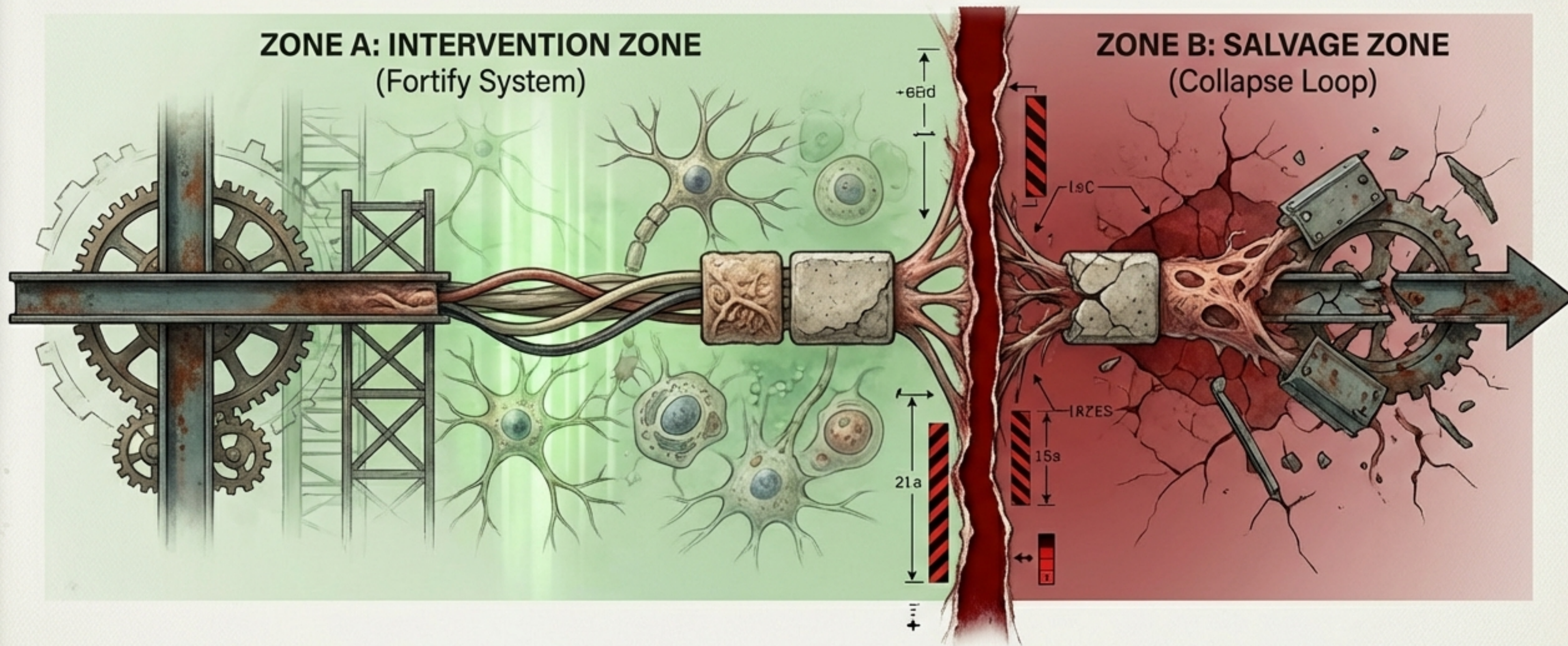
A NEW BLUEPRINT: RESTORING SYSTEMIC CAPACITY

From Target-Specific Hunting to Capacity-Building.

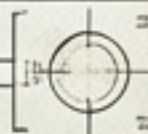


INTERVENTION MUST PRECEDE COLLAPSE

THE TIPPING POINT



Future Requirement: Biomarkers for System Stress (Flux/Metabolism), not just atrophy.



UNIFYING THE FIGHT

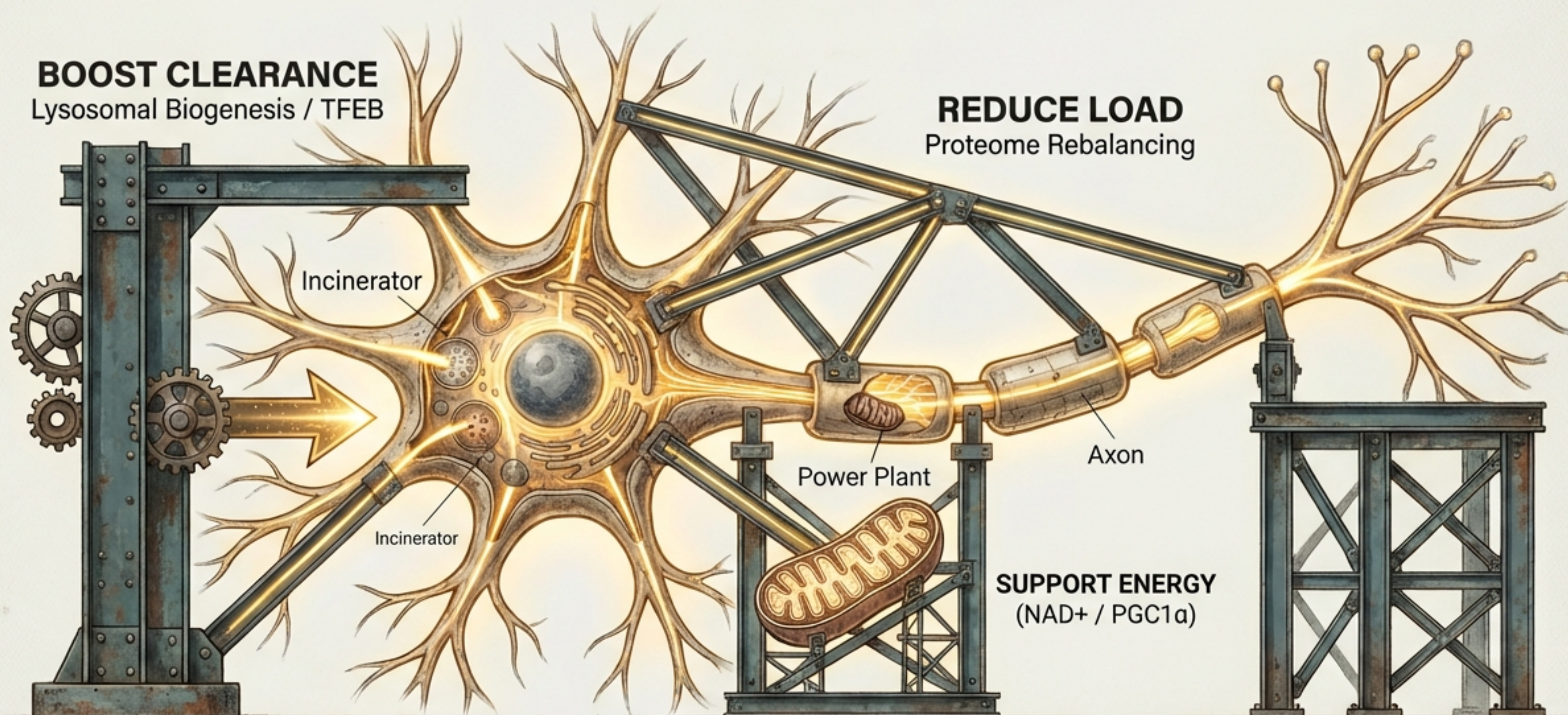
By fixing the engine rather than just wiping the windshield, we can prevent the crash.

BOOST CLEARANCE

Lysosomal Biogenesis / TFEB

REDUCE LOAD

Proteome Rebalancing



SUPPORT ENERGY
(NAD⁺ / PGC1α)

Distinct Triggers. Shared Collapse. Unified Solution: Restore Thermodynamic Capacity.