Dr. Gurpreet Singh Padda, MD discusses Alzheimer's Research, Not Just Plaque

On World Alzheimer's Day, Dr. Gurpreet Singh Padda, MD, of The Starved Brain, suggests cognitive decline is a fuel-inflammation problem, not just plaque



The Starved Brain Logo

ST. LOUIS, MO, UNITED STATES, September 21, 2026 / EINPresswire.com/ -- Dr. Gurpreet Singh Padda, MD, MBA, MHP, a board-certified physician and author of The Starved Brain, is using World Alzheimer's Day to make an argument the field has circled for a decade without adopting: the difficulty in Alzheimer's disease may be diagnostic rather than pharmacological. For three decades the dominant model has centered on amyloid plaques, and for three decades therapies aimed at clearing them have produced results modest relative to the investment.

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>
> *Dr. Gurpreet Singh Padda, MD, MBA, MHP*

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The energy argument

The adult brain is roughly two percent of body weight and consumes close to twenty percent of resting energy expenditure. It is the least metabolically forgiving organ in the body, with almost no capacity to store its own fuel. Whatever it needs has to arrive continuously.

Reduced cerebral glucose metabolism appears remarkably early. Reiman and colleagues documented FDG-PET reductions in asymptomatic APOE4 carriers in their twenties and thirties, decades before the age at which Alzheimer's pathology is expected and before measurable amyloid deposition. Later work found that apolipoprotein E, not fibrillar amyloid, accounted for reduced glucose metabolism in normal aging (Journal of Neuroscience, 2012;32(50):18227). The metabolic signal is not a late consequence of the disease. It arrives first, by a margin measured

in decades.

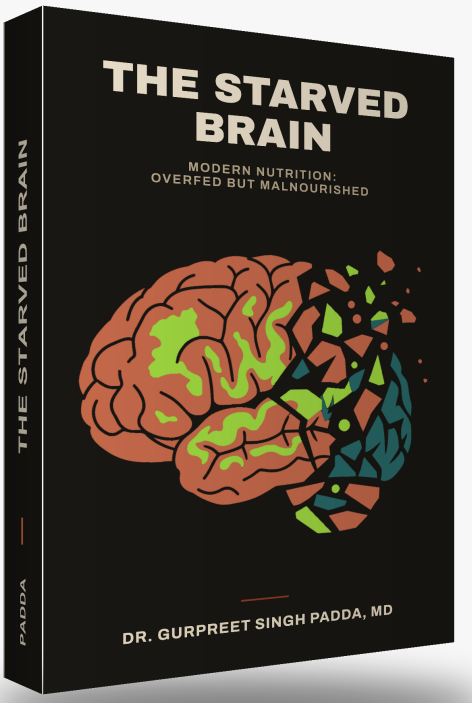
The decisive observation comes from the Sherbrooke group led by Stephen Cunnane. Using PET tracers for both fuels, they showed that while brain glucose uptake is roughly 20 to 25 percent lower in Alzheimer's disease, brain ketone uptake is essentially preserved. The neurons in hypometabolic regions are not dead. They are starving, and they retain the machinery to burn an alternative substrate.

A parallel finding sharpens the point. Thiamine diphosphate reduction correlates strongly with brain glucose hypometabolism in Alzheimer's disease, whereas amyloid deposition does not. The cofactor required to metabolize glucose tracks the metabolic failure better than the protein the field has spent thirty years targeting.

"Glucose uptake collapses, and ketone uptake does not," Padda said. "That is not a dead neuron. That is a neuron cut off from the fuel it was using, waiting for another one."

The insulin argument

There is a mechanistic bridge between the metabolic and amyloid stories that is rarely reported, and it is elegant. Insulin-degrading enzyme clears insulin, and it also clears amyloid-beta. The two are competing substrates for the same enzyme.



Starved Brain Book

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In chronic hyperinsulinemia, the enzyme is occupied. Amyloid clearance slows, not because the

brain has begun producing more of it, but because the machinery that removes it is saturated by a metabolic signal originating in the periphery. On that reading, the plaque is a downstream consequence of systemic metabolic dysfunction rather than a primary event, which would explain why removing plaque late has helped less than the model predicted.



Padda Institute

Dr. Padda is careful about how far that argument reaches. The enzymatic competition is well established at the bench; its clinical weight remains debated, and the book presents it as hypothesis-generating rather than settled. What is not in dispute is the direction of the arrow: peripheral metabolic state reaches the brain, and it reaches it early.

The nutrient argument

The Oxford VITACOG trial randomized 271 people over 70 with mild cognitive impairment to high-dose folic acid, B6 and B12 or placebo for two years. Among the 168 who completed serial MRI, whole-brain atrophy was 0.76 percent per year on treatment versus 1.08 percent on placebo, a 29.6 percent reduction ($p = 0.001$). In participants whose baseline homocysteine exceeded 13 micromoles per liter, atrophy was 53 percent lower on treatment (Smith AD et al., PLOS ONE 2010;5(9):e12244).

Follow-up found cognitive and clinical benefit as well, and found that the effect depended on omega-3 status. B vitamins helped those with adequate long-chain omega-3 levels and not those without (de Jager et al., 2012). Two modifiable inputs, interacting, neither sufficient alone. That interaction itself argues for measuring rather than supplementing unthinkingly.

B12 deficiency is prevalent in older adults and in long-term users of metformin and proton pump inhibitors, two of the most widely prescribed drug classes in the population most at risk. Unlike most Alzheimer's risk factors, it shows up on a standard panel and can be corrected.

"A 53 percent reduction in brain atrophy came from three vitamins and a blood test nobody ordered," Padda said. "We are not short of interventions. We are short of the will to measure."

What this changes

The framing does not promise reversal, and the book does not claim it. Nothing in The Starved

Brain asserts that any intervention prevents, treats,s or reverses Alzheimer's disease, and Dr. Padda is explicit that the honest version of this argument stops well short of that.

Instead, it argues a question of sequence. Glycemic control, insulin sensitivity, B-vitamin status, inflammatory load, and sleep deserve to be treated as first-line clinical variables rather than as lifestyle advice appended to a pharmacological plan. Each is measurable on tests already available in any primary care office. Each is modifiable. And each, on the evidence above, is moving years or decades before a diagnosis is available to be made.

The Starved Brain runs ten chapters on that argument and is published in Kindle and paperback editions. Each chapter ends with a code that opens a free technical supplement for readers to hand to their own physician, published at thestarvedbrain.com one chapter at a time.

ABOUT THE STARVED BRAIN AND ITS AUTHOR

The Starved Brain examines cognitive decline through brain energy metabolism, nutrient status, and systemic inflammation. Its author, Dr. Gurpreet Singh Padda, MD, MBA, MHP, is a board-certified physician and founder of Regen.MD in St. Louis, board-certified in anesthesiology, pain medicine, interventional pain management, addiction medicine, and obesity medicine, and a certified Metabolic Health Practitioner. The Starved Brain is the first volume in his series The Brain. Makes claims about a neurodegenerative disease. Nothing in the distributed text should imply that any intervention prevents, treats, or reverses Alzheimer's disease. Compliance review recommended. The insulin-degrading enzyme competition is mechanistically well established, but its clinical weight is still debated; it is framed here as hypothesis-generating and must stay that way.

Gurpreet Singh Padda, MD
Regen.MD
+1 314-295-3000
email us here
Visit us on social media:
LinkedIn
YouTube

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