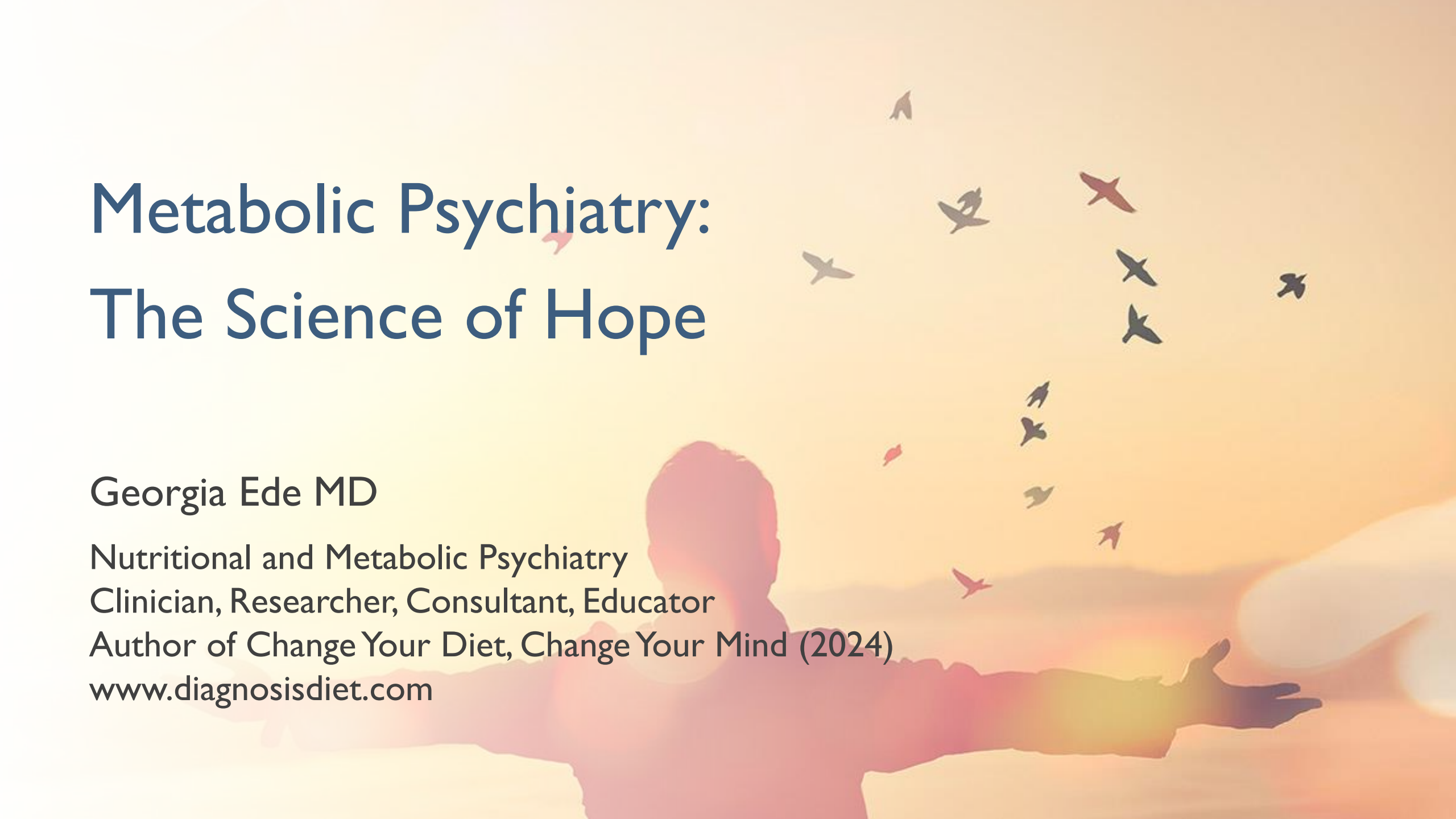


# Metabolic Psychiatry: The Science of Hope

A person is shown from the back, with their arms outstretched towards the horizon. The background is a warm, golden sunset sky with several birds in flight. The overall mood is one of hope and freedom.

Georgia Ede MD

Nutritional and Metabolic Psychiatry

Clinician, Researcher, Consultant, Educator

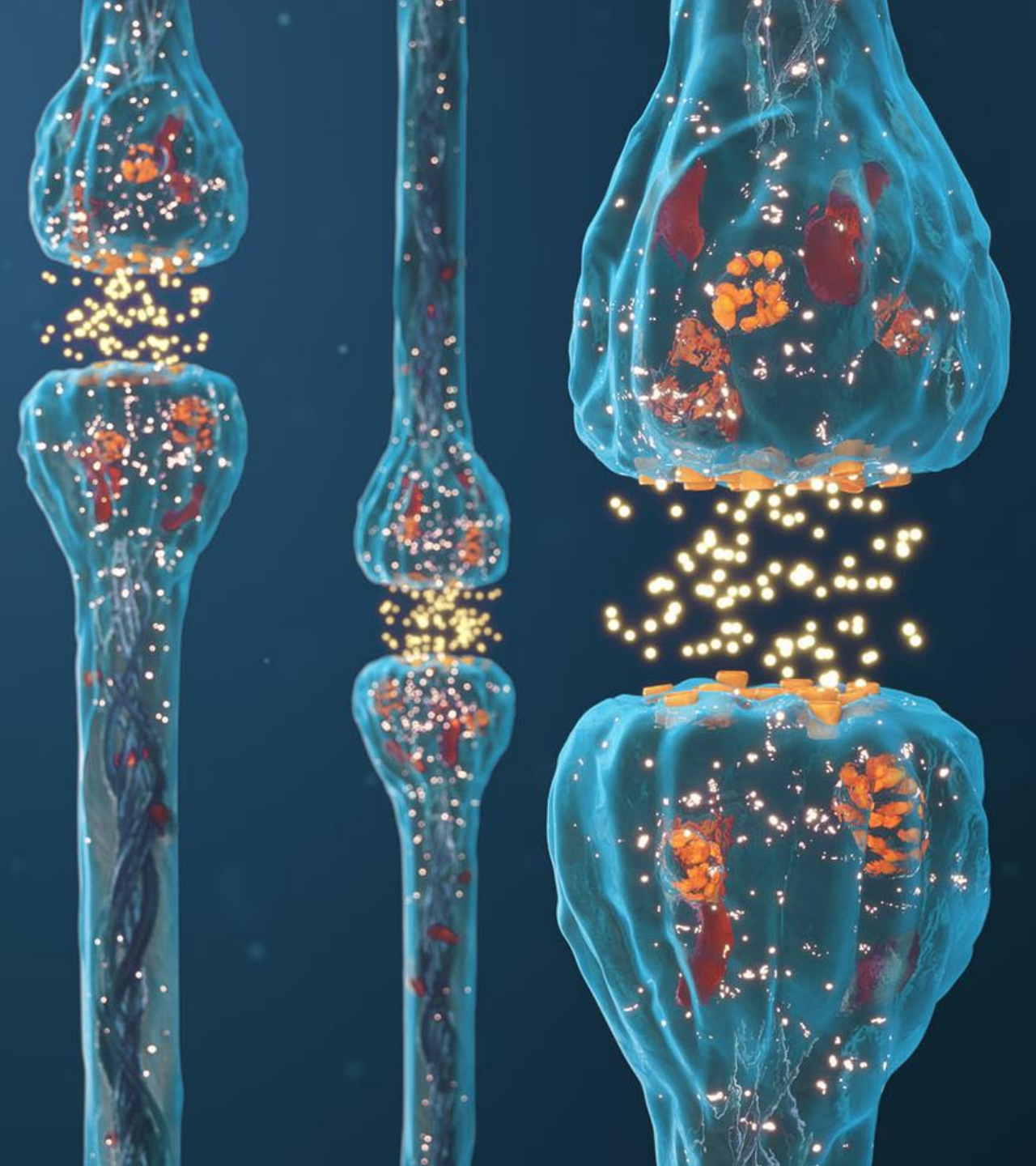
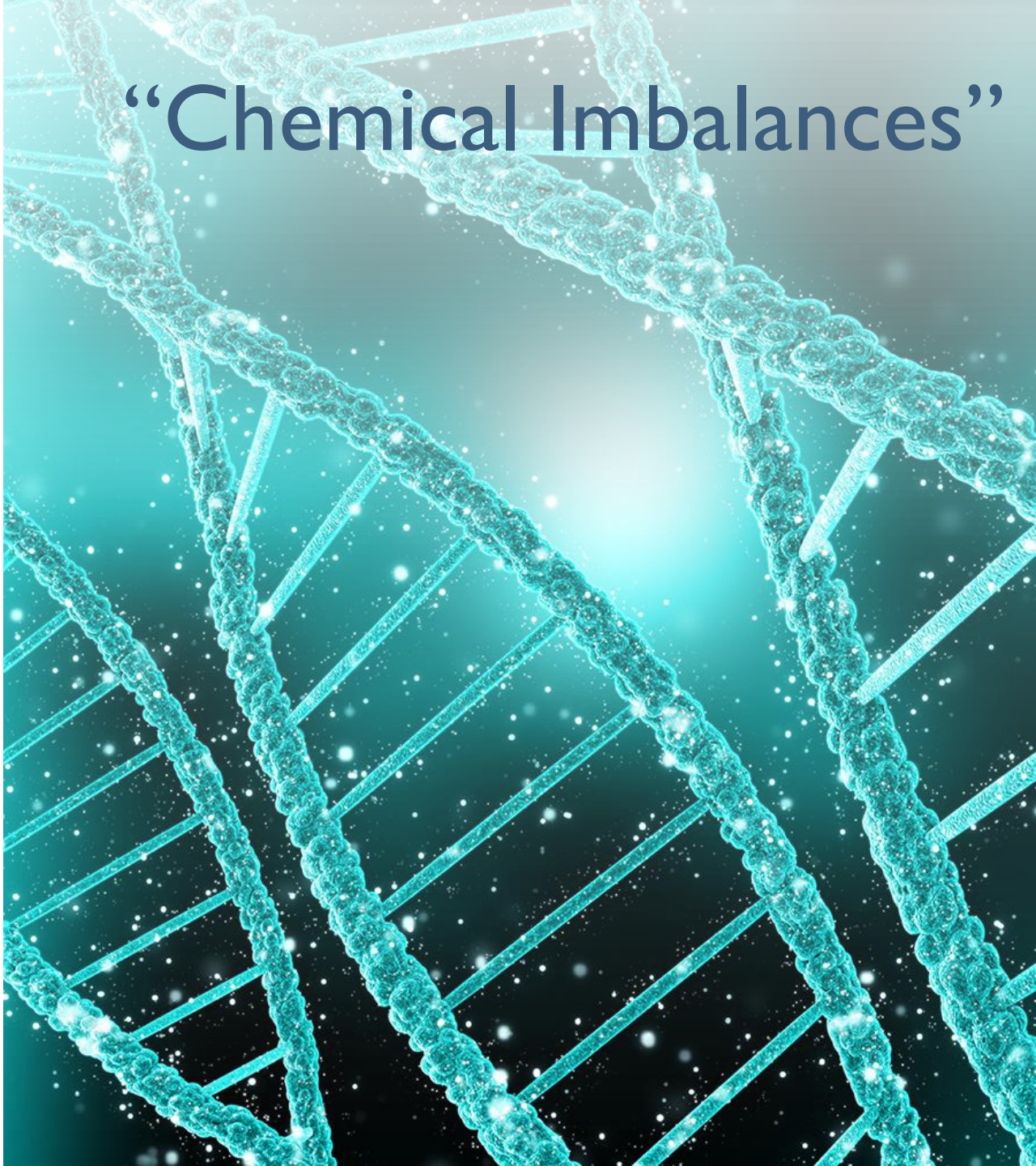
Author of Change Your Diet, Change Your Mind (2024)

[www.diagnosisdiet.com](http://www.diagnosisdiet.com)

# The Usual Suspects



# “Chemical Imbalances”



# Usual Treatment



# Psychopharmacology

**Antidepressants: 50%**

Placebo: 40%

More than 1/2 are “treatment-resistant”<sup>1</sup>

**Antipsychotics: 23%**

Placebo: 14%

Up to 1/3 are “treatment-resistant”<sup>2</sup>



Antidepressants: McCormack J, Korownyk C. *BMJ*. 2018

Antipsychotics: Leucht S et al. *Am J Psychiatry*. 2017

1. Rush AJ et al. *Control Clin Trials*. 2004; 2. Siskind D et al. *Br J Psychiatry*. 2022.

# The Price of Relief

## Reduced Quality of Life

Sedation

**Sleepy**

Tremors

**Shaky**

Vertigo

**Dizzy**

Weight Gain

**Chubby**

Nausea

**Queasy**

Cognitive dulling

**Dopey**

Sexual dysfunction

**Floppy**

## Reduced Length of Life

Insulin Resistance

Type 2 Diabetes

Obesity

Cardiovascular Disease

Antipsychotics

**DOUBLE** risk of death  
(esp. from heart attacks and strokes)<sup>1</sup>



# Over a billion people living with mental health conditions – services require urgent scale-up

2 September 2025 | News release | Geneva | Reading time: 4 min (1035 words)

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## Mental Illness

59.3M adults

(23.1% of adult population)

## Serious Mental Illness

15.4M adults

(6% of adult population)

### Both sexes, All ages, DALYs per 100,000

Non-communicable diseases

#### 2023 rank

1 Cardiovascular diseases

2 Neoplasms

3 Musculoskeletal disorders

4 Substance use

5 Mental disorders

6 Diabetes & CKD

7 Neurological disorders

8 Chronic respiratory



## Depression

26M people

8.3% of US adults  
20% of US adolescents

**#1** cause of **disability**  
in the world



## Alzheimer's Dementia

7.2M people

**#6** cause of **death**  
in people over 65

# As goes the body, so goes the brain...



Inflammation

Oxidative Stress

**Insulin resistance**

# Our Ultra-Processed Planet

**United States: >60%<sup>1</sup>**

United Kingdom: 51%<sup>2</sup>

Ireland: 46%<sup>2</sup>

Germany: 46%<sup>2</sup>

Finland: 41%<sup>2</sup>

Australia: 39%<sup>3</sup>

Mexico: >30%<sup>4</sup>



1. Federation of American Societies for Experimental Biology. ScienceDaily. 2015;  
2. CA Monteiro et al. *Public Health Nutrition*. 2018; 3. Australia Bureau of Statistics. 2024;  
4. Marrón-Ponce JA et al. *Public Health Nutr*. 2018.

# Your Brain on Sugar: GLUCOTOXICITY

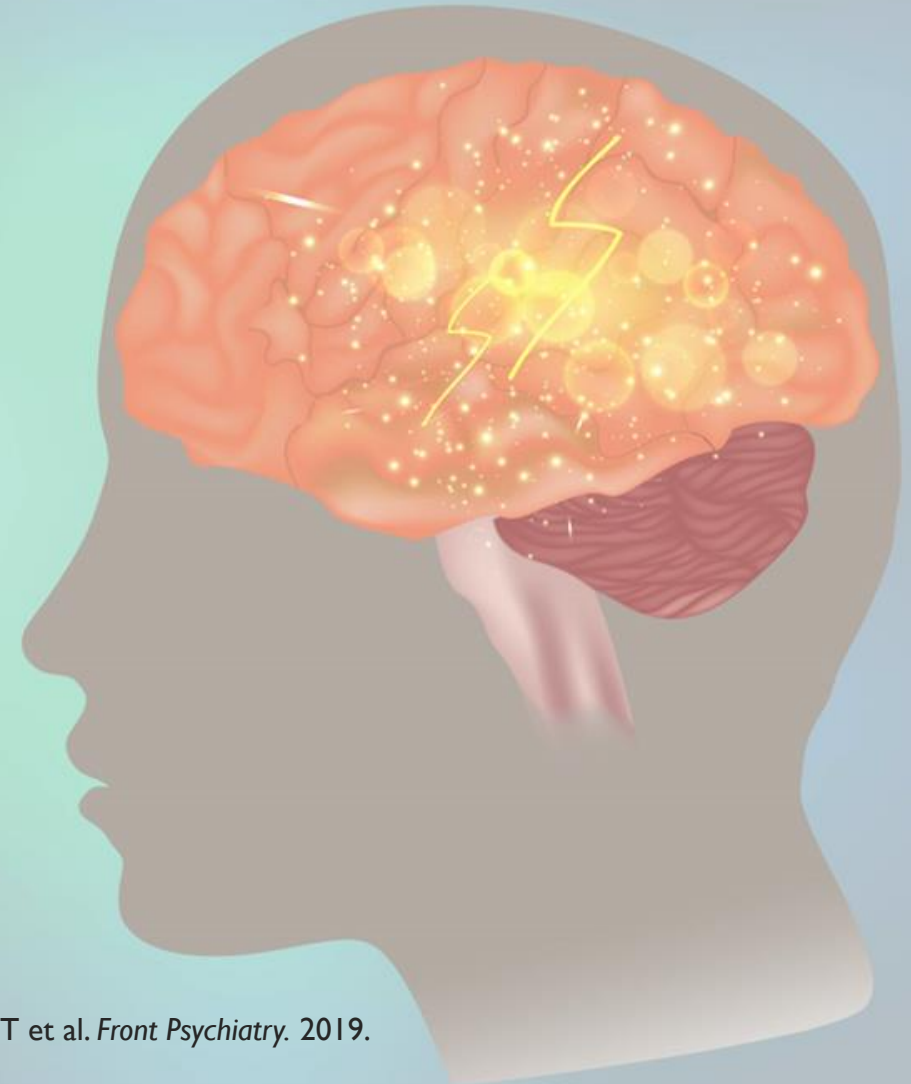
AGEs (advanced glycation end products)



Inflammation and oxidative stress

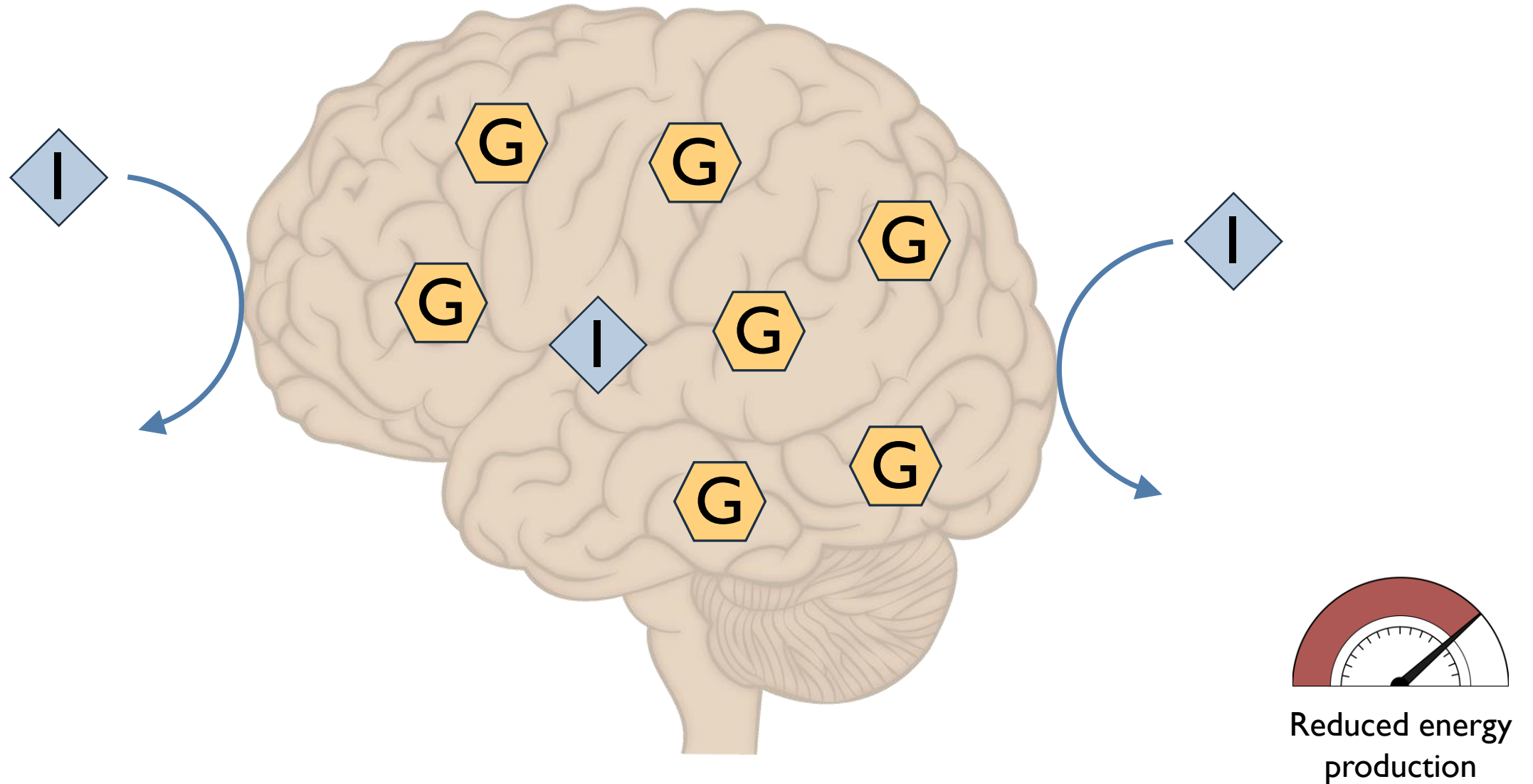


Neurotransmitter imbalances  
Damages proteins, lipids, DNA<sup>1</sup>  
Compromises blood-brain barrier<sup>2</sup>  
Shrinks the hippocampus<sup>3</sup>  
Injures mitochondria<sup>4</sup>



1. Brietzke E et al. *Neurosci Biobehav Rev.* 2018; Van Dyken P and LaCoste B. *Front. Neurosci.* 2018; Li CT et al. *Front Psychiatry.* 2019.
2. Calkin C et al. *Front Psychiatry.* 2021; Greene C et al. *Transl Psychiatry.* 2020.
3. Schmaal L et al. *Mol Psychiatry.* 2016;21; Haukvik UK et al. *Hum Brain Mapp.* 2022; Haukvik UK et al. *J Psychiatr Res.* 2018.
4. Maalouf M, Rho JM, Mattson MP. *Brain Res Rev.* 2009.

# Cerebral Glucose Hypometabolism



# IR and/or Cerebral Glucose Hypometabolism

Autism<sup>1</sup>

Attention deficit disorder<sup>2</sup>

Anxiety disorders in obese children<sup>3</sup>

Post-traumatic stress disorder<sup>4</sup>

Borderline personality disorder<sup>5</sup>

Obsessive-compulsive disorder<sup>6</sup>

**Major depression<sup>7</sup>**

**Bipolar disorder<sup>8</sup>**

**Schizophrenia<sup>9</sup>**

**Alzheimer's disease<sup>10</sup>**

# Metabolic Dysfunction and Mental Health

Pre-diabetes

**2.7 X**

more likely to develop  
**major depression<sup>1</sup>**

Newly diagnosed  
**bipolar disorder**

**3.5 X**

more likely to have  
**metabolic syndrome<sup>2</sup>**

Newly diagnosed  
**schizophrenia**

**3.7 X**

more likely to have  
**insulin resistance<sup>3</sup>**

# Alzheimer's Disease = Type 3 Diabetes

Journal of Diabetes Science and Technology

Volume 2, Issue 6, November 2008

© Diabetes Technology Society

REVIEW ARTICLE

## Alzheimer's Disease Is Type 3 Diabetes—Evidence Reviewed

Suzanne M. de la Monte, M.D., M.P.H.<sup>1-3</sup> and Jack R. Wands, M.D.<sup>3</sup>

### Abstract

Alzheimer's disease (AD) has characteristic histopathological, molecular, and biochemical abnormalities, including cell loss; abundant neurofibrillary tangles; dystrophic neurites; amyloid precursor protein, amyloid- $\beta$  (APP-A $\beta$ ) deposits; increased activation of prodeath genes and signaling pathways; impaired energy metabolism; mitochondrial dysfunction; chronic oxidative stress; and DNA damage. Gaining a better understanding of AD pathogenesis will require a framework that mechanistically interlinks all these phenomena. Currently, there is a rapid growth in the literature pointing toward insulin deficiency and insulin resistance as mediators of AD-type neurodegeneration, but this surge of new information is riddled with conflicting and unresolved concepts regarding the potential contributions of type 2 diabetes mellitus (T2DM), metabolic syndrome, and obesity to AD pathogenesis. Herein, we review the evidence that (1) T2DM causes brain insulin resistance, oxidative stress, and cognitive impairment, but its aggregate effects fall far short of mimicking AD; (2) extensive disturbances in brain insulin and insulin-like growth factor (IGF) signaling mechanisms represent early and progressive abnormalities and could account for the majority of molecular, biochemical, and histopathological lesions in AD; (3) experimental brain diabetes produced by intracerebral administration of streptozotocin shares many features with AD, including cognitive impairment and disturbances in acetylcholine homeostasis; and (4) experimental brain diabetes is treatable with insulin sensitizer agents, i.e., drugs currently used to treat T2DM. We conclude that the term "type 3 diabetes" accurately reflects the fact that AD represents a form of diabetes that selectively involves the brain and has molecular and biochemical features that overlap with both type 1 diabetes mellitus and T2DM.

*J Diabetes Sci Technol* 2008;2(6):1101-1113

“Disturbances in brain insulin and IGF signaling mechanisms could account for the majority of molecular, biochemical and histopathological lesions in Alzheimer's Disease”

—Dr. Suzanne de la Monte  
Brown University, 2008

# Whole Foods for ALL

# Ketogenic Diet for ?



# What Is a Ketogenic Diet?

**ANY** way of eating that lowers **insulin** levels enough to switch on **fat burning** and generate **clinically meaningful levels of ketones** in the blood ( $\geq 0.5$  mM BHB)

**Very low carbohydrate (~5%)**  
**Adequate protein**  
**Remainder of calories from fat**

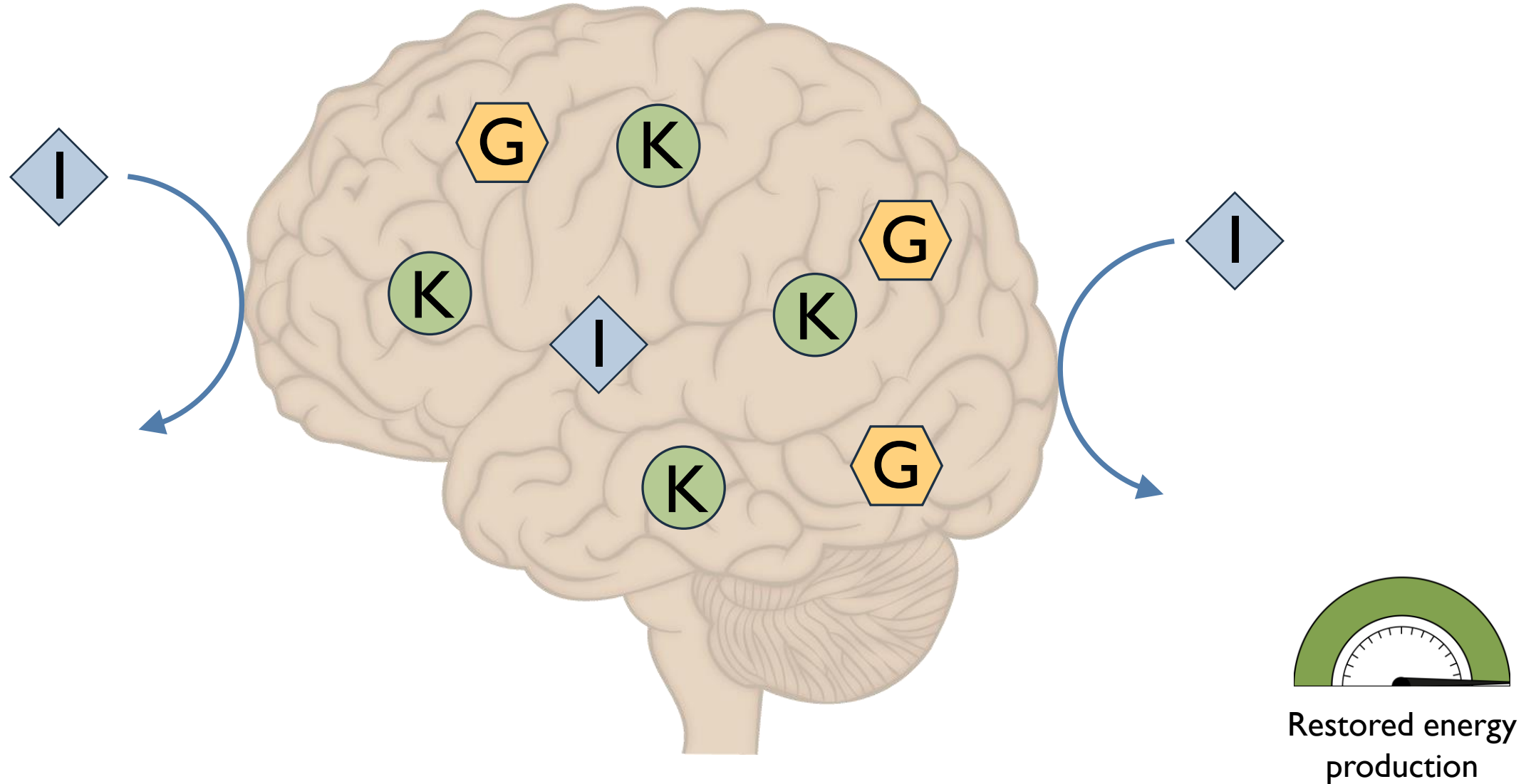


# “The Brain Is a Hybrid Engine”

—Professor Stephen Cunnane

<b>Ketones</b>	<b>Glucose</b>
Clean and efficient	More inflammation/oxidation
Slower energy, more ATP	Faster energy
Most brain cell operations prefer ketones over glucose; can meet 60%+ of brain's needs	Certain brain functions require glucose
Burn well under low-insulin conditions	Insulin-dependent processing

# Ketones Rescue Failing Brain Metabolism



# Emerging Evidence in Psychiatric Disorders

## Randomized Controlled Trials

Alcohol withdrawal (1)

Autism (1)

Alzheimer's disease (4)

Treatment-Resistant Depression (1)

## Uncontrolled Trials (# of studies)

Bipolar disorder (3)

Schizophrenia (2)

Major depression (2)

Autism (2)

## Case Reports and Case Series (n)

Schizophrenia (10)

Bipolar disorder (5)

Binge eating disorder (3)

Major depression & gen anxiety d/o (5)

Down syndrome w/ dementia (1)

Severe underweight anorexia (3)

[carnivore diet]

Weight-restored anorexia (6)

[ketogenic diet + ketamine]

PTSD (4)

OCD (4)

# Ketogenic Diets for Cognitive Decline

“To the extent a treatment effect has been demonstrated, [the KD] is **comparable to some pharmaceutical interventions** in AD.”  
—Grese, 2026

“**The KD can enhance the mental state and cognitive function of those with AD.**”  
—Rong 2024

“[Ketosis] appears **promising in improving both acute and long-term cognition** among patients with Alzheimer’s Disease or mild cognitive impairment.”  
—Gamma, 2022

“Ketogenic interventions **are probably effective for cognitive improvement** in patients with mild-to-moderate AD who are APO $\epsilon$ <sub>4</sub>- and in patients with MCI.”  
—Bohnen, 2023

“There is evidence that the KD and exogenous ketone supplementation **may provide treatment benefits** in AD patients”  
—Hersant & Grossberg, 2022

# Fran (67 yo) with Impending Dementia





# KD for Serious Mental Illness

Can eating a ketogenic diet improve symptoms of serious mental illness?



Clinique du Castelvieu  
Castelmarou, France

**28**  
inpatients



Bipolar disorder  
n=12

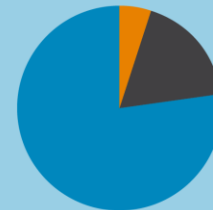


Major depression  
n=6

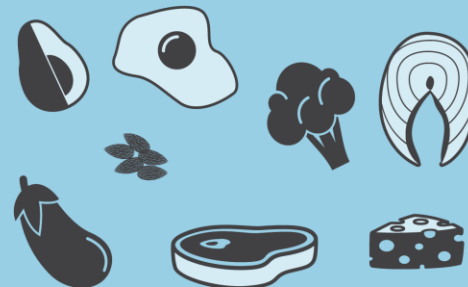


Schizophrenia  
n=10

Ketogenic Diet



**75-80%** fat  
**15-20%** protein  
**5%** carbohydrate



**43%**  
achieved  
clinical  
remission



symptoms  
improved in  
**100%**  
of patients

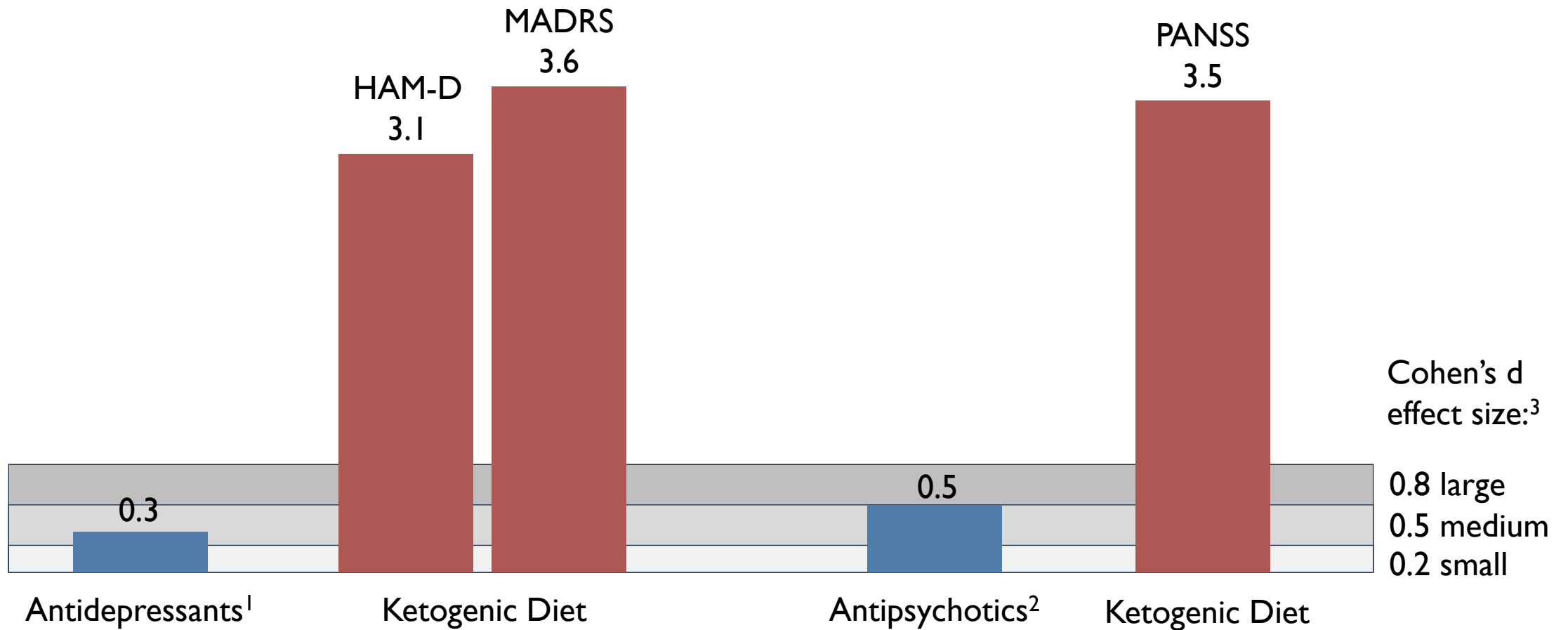


**96%**  
of patients  
lost weight



**64%**  
of patients  
were discharged  
on **less** medication

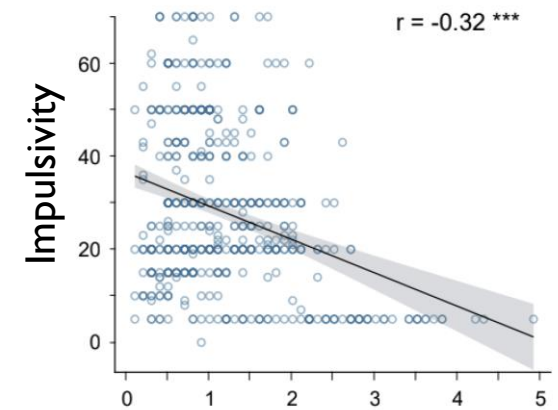
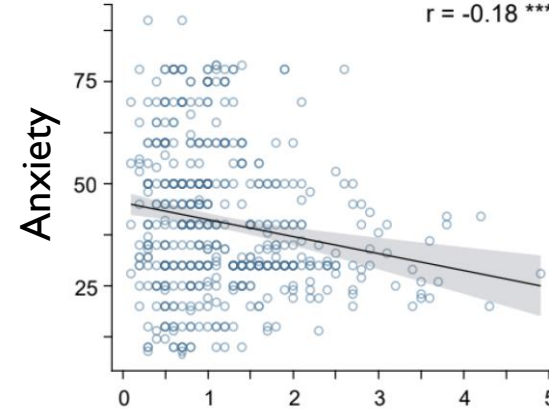
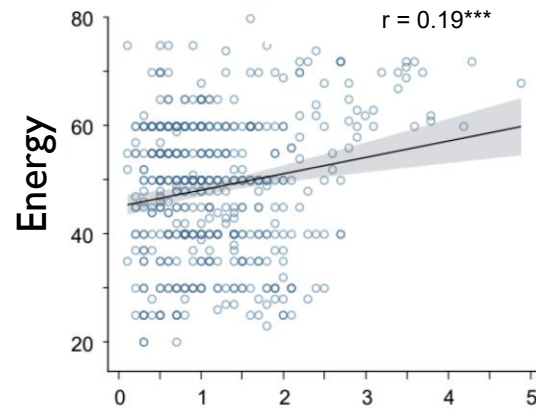
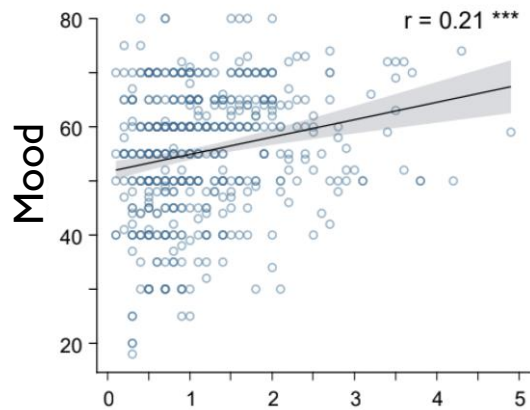
# Effect Sizes Compared to Medication



1. Hengartner MP, Plödel M. *Front Psychiatry*. 2018; 2. Leucht S et al. *Schizophr Bull*. 2022; 3. Lakens D. *Front Psychol*. 2013.

# Ketogenic Diets for Bipolar Disorder

8-week pilot study; 20 adults w bipolar disorder  
In ketosis 91% of the time (mean BHB = 1.3 mM)



Ketone Level (BHB)

**7/20 refused to discontinue the diet!**

Decreased brain glutamate on MRS of 9 to 13% — **largest ever recorded!**

# KD for Bipolar Disorder and Schizophrenia

## 21 participants

with serious mental illness and metabolic abnormalities

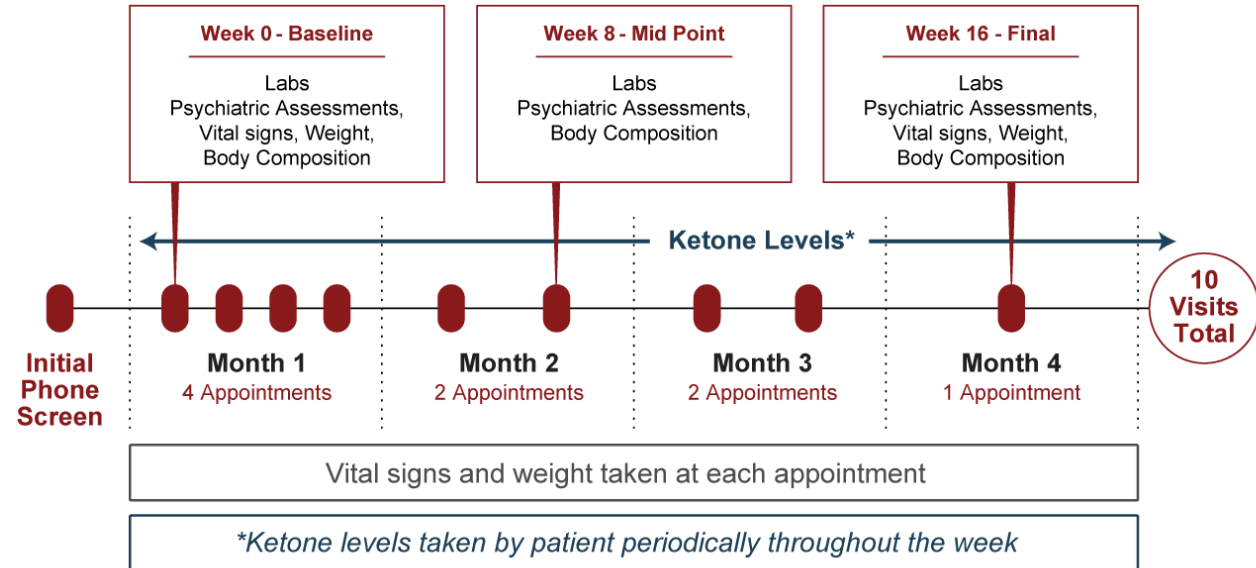


**Bipolar disorder (n=16)**



**Schizophrenia (n=5)**

## Ketogenic diet for 4 months



**79%**

of participants had a clinically meaningful psychiatric improvement\*



**100%**

reversal of metabolic syndrome\*\*



**10%**

average weight loss



**Adherence Trend**

a larger effect or benefit with higher dietary adherence level

\*Defined as a 1 point or more change in Clinical Global Impression (CGI)

\*\*Of n=6 participants with metabolic syndrome at study start

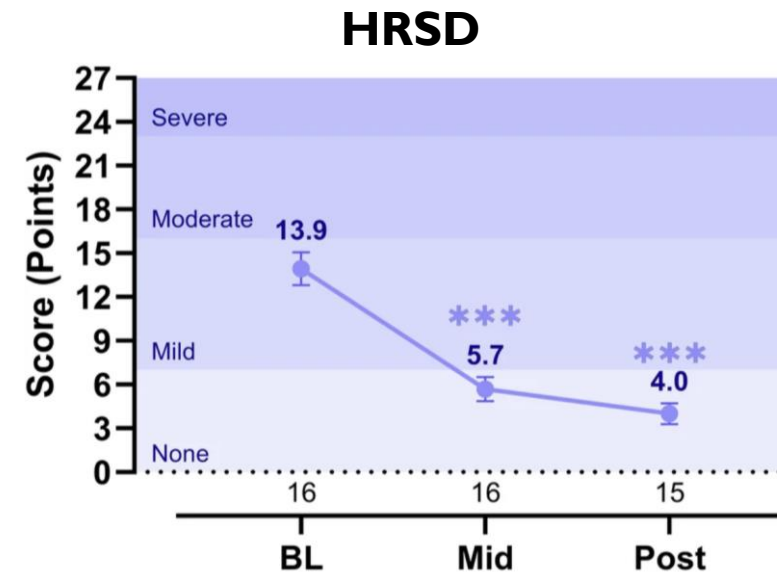
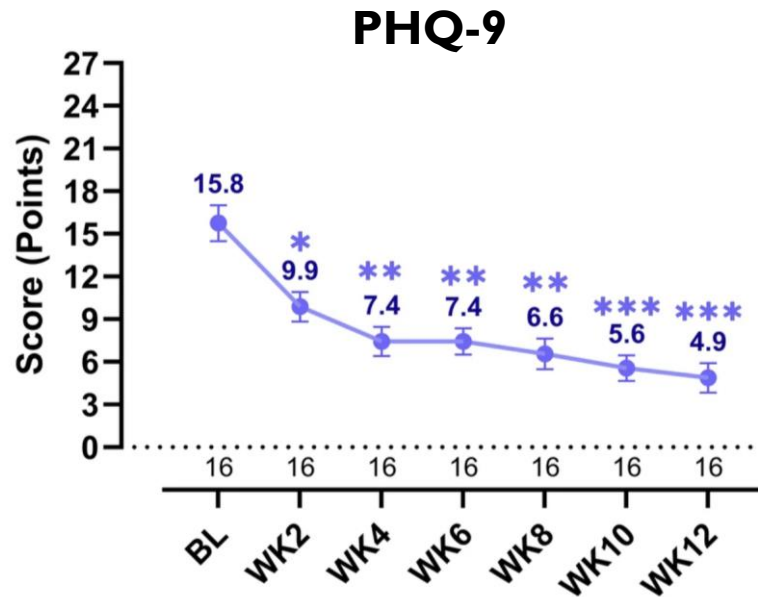
# KD for Major Depression in College Students

**2025 uncontrolled pilot, n=24 OSU students w/ mild-mod MDD**

Well-supported KD added to standard care x 10-12 weeks

16/24 completed the trial (Avg BHB = 0.7 mM; in ketosis 73% of the time)

100% of completers improved. ~70% reduction in depression scores



compared to baseline:

- \* =  $p < 0.05$
- \*\* =  $p < 0.01$
- \*\*\* =  $p < 0.001$

# Oxford RCT: Treatment-Resistant Depression

**2026 RCT, n=88 adults w/ mod-severe TR-MDD, on medication**

**KD vs. “Phyto Diet” x 6 weeks (+ option to continue for 6 more wks)**

## **Keto Diet**

Free prepared foods\*

(≤ 30 g carb, 15-20% cals from protein)

\*or £25 / week in food vouchers

## **Phyto Diet**

+1 colorful fruit or vegetable /day

Added fats/cooking oils → olive oil

Improvement in depression symptoms (PHQ-9):

**Overall: ↓ 10 points** (2-point difference)

**Severe depression: 5-point difference**

**↓ 8 points**

# Studies Under Way

## **Bipolar Disorder**

G. Keferstein, MOJO Institute, Germany

K. Lara-Breitinger, Mayo Clinic, US

M. Phillips, University of Pittsburgh, US

## **Bipolar Disorder in Children & Adolescents:**

E. Errico, CMHRC Hawaii, US (2)

D. Miklowitz, UCLA, US

## **Psychosis**

A. Ruusunen, Kuopio University Hospital, Finland

D. Kelly, University of Maryland, US

## **Schizophrenia and Bipolar Disorder**

Northern California Institute of Research and Education, US

C. Longhitano & Z. Sarnyai, James Cook University, Australia

S. Sethi, Stanford University, US

V.A. Chouinard, McLean Hospital (Harvard), US

## **Major Depressive Disorder**

E. Brietzke, Queens University, Canada

T. Liwinski, University of Basel, Switzerland

## **Autism**

S. Gulati, All India Institute of Medical Sciences

Qilu Hospital of Shandong University, China

## **MCI/Alzheimer's Disease**

R. Swerdlow, University of Kansas, US

S. Craft, Wake Forest University, US

M. Lilimand, Hôpitaux de Paris, France

J. Sheffler, Florida State University, US

J. Jia, Capital Medical University, China

L. Jia, Xuanwu Hospital, China

L. Hanoglu, Istanbul Medipol University Hospital, Turkey

## **Anorexia Nervosa**

G. Frank, UC San Diego, US (3)



# Hope Is on the Menu

