

NANYANG
TECHNOLOGICAL
UNIVERSITY
SINGAPORE

CC0007 Science and Technology for Humanity

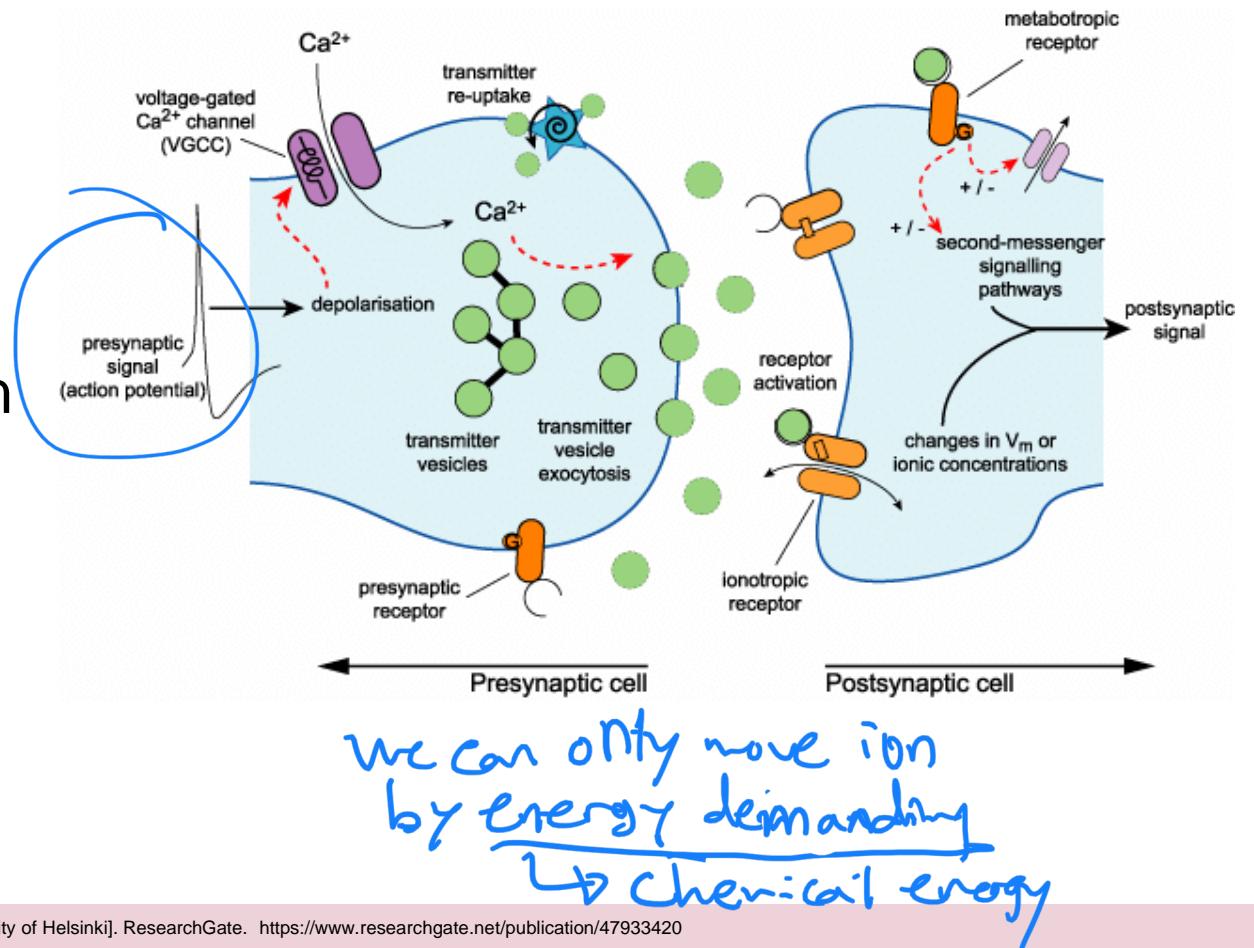
Metabolic Ageing: Brain, Microbiome and the Diet

Prof Zoltan Sarnyai, JCU (Australia)



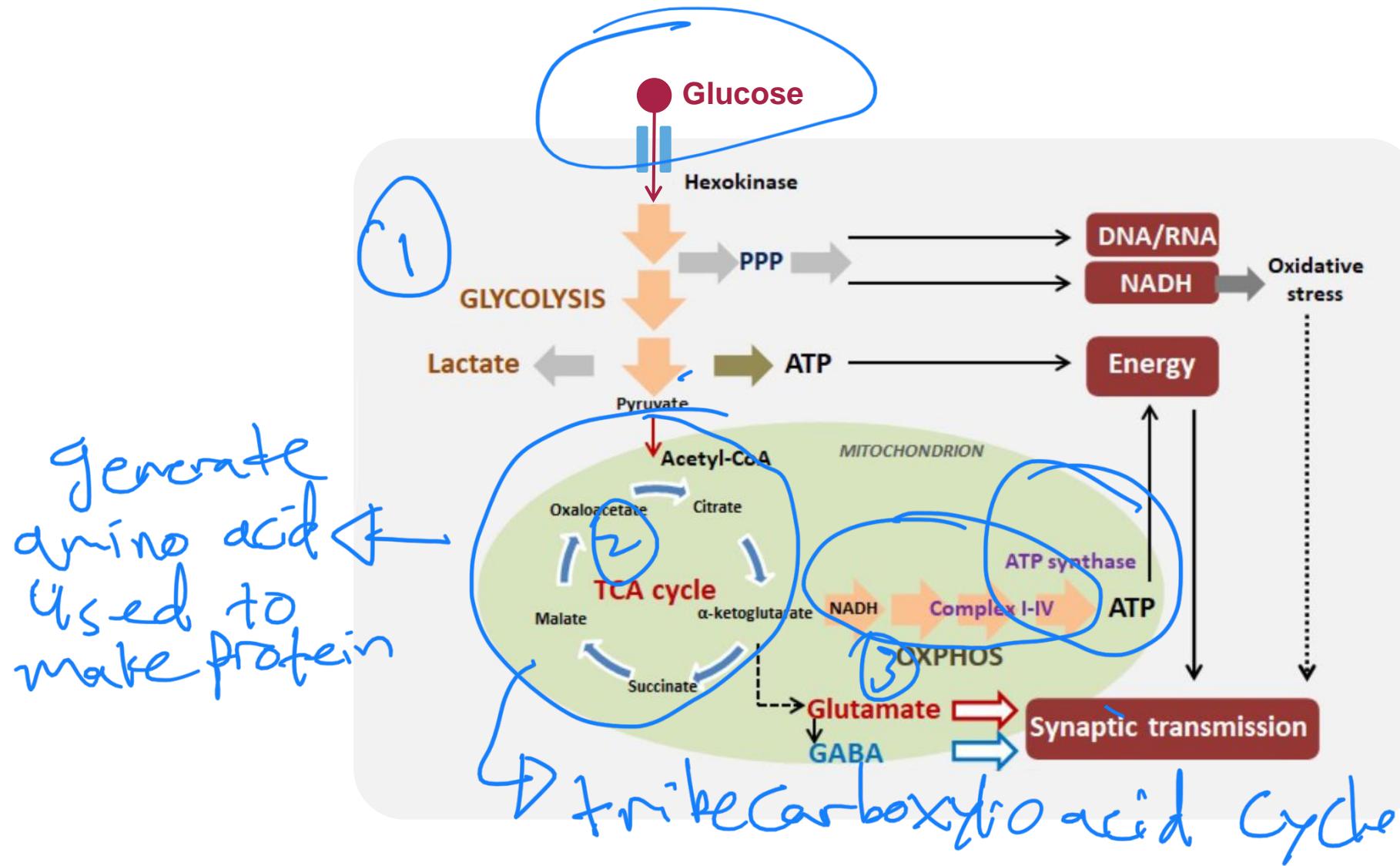
The Brain is a Very Expensive Organ to Fuel

- Cognition is costly!
- 20% of the whole body's energy budget
 - Brain is 1/50 of the whole body
- Where does the energy go?
 - To maintain communication between nerve cells (synaptic transmission)
 - Movement of ions across the cell membrane require chemical energy (ATP)



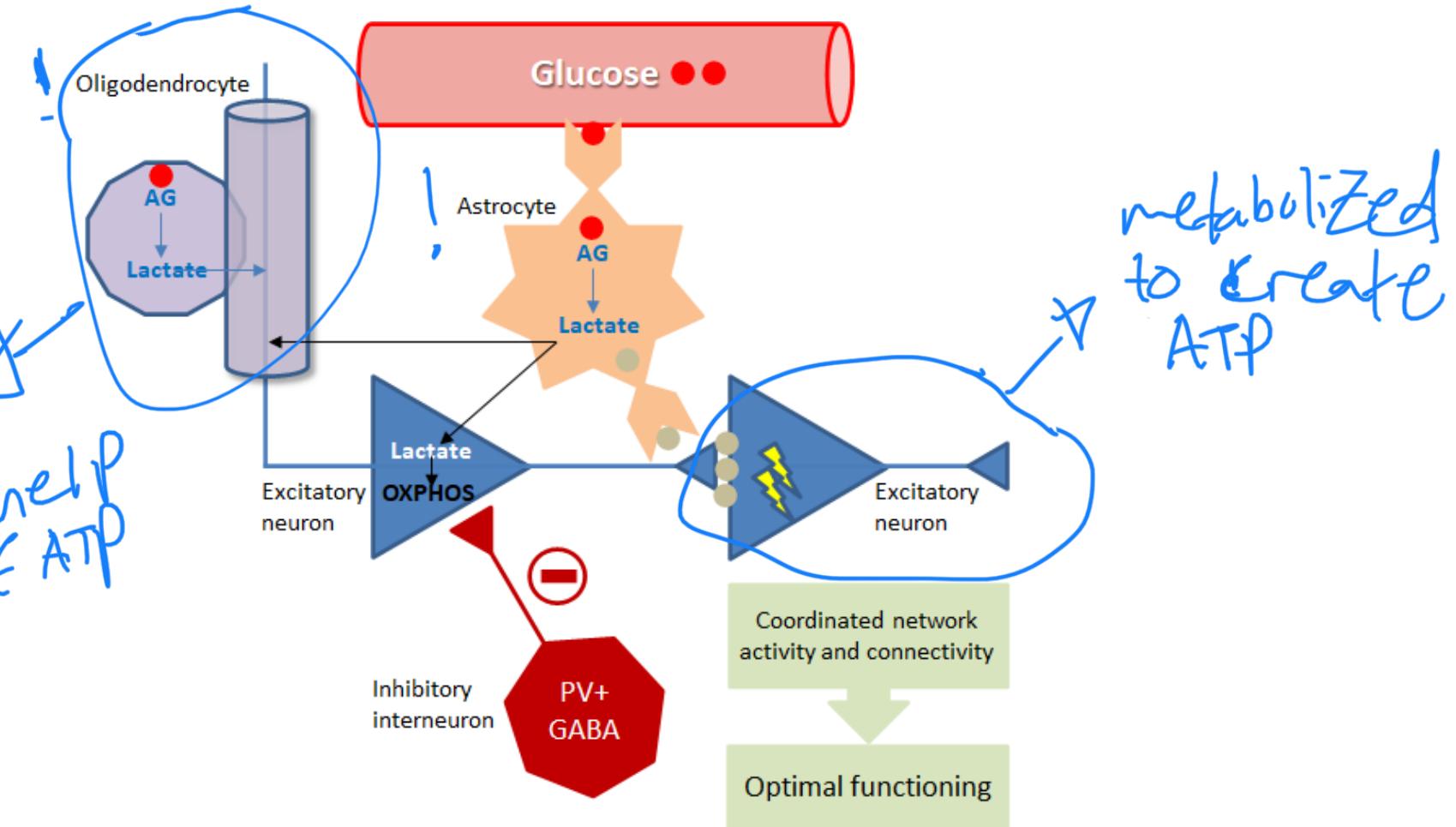
Uusisaari , M. (2003). GABAergic mechanisms of excitation and hypersynchrony in adult rat hippocampus [Doctoral dissertation, University of Helsinki]. ResearchGate. <https://www.researchgate.net/publication/47933420>

Glucose is the Main Source of the Chemical Energy



Different Cells Work Together to Fuel the Brain

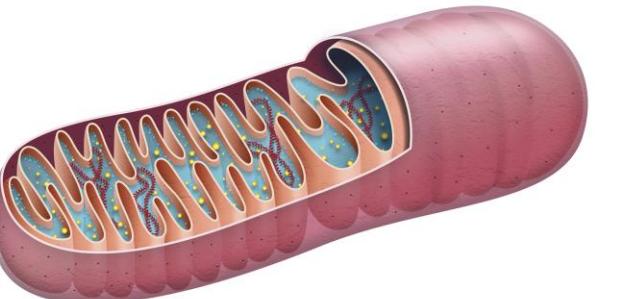
digesting
FOR inhibitory
molecule for help
generation of ATP



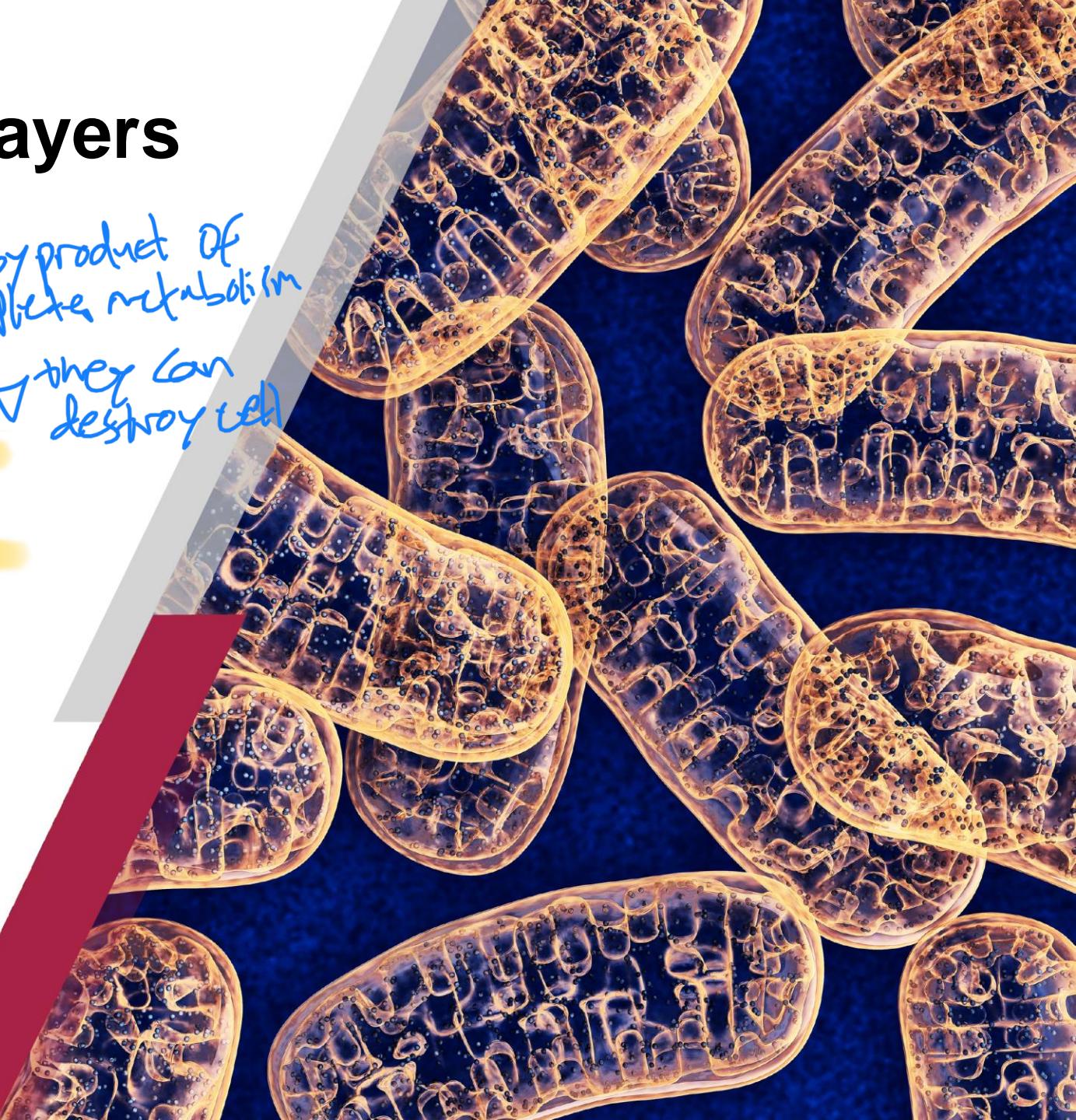
! Mitochondria are Key Players in Brain Bioenergetics

- ATP (energy) production
- Reactive Oxygen Species (ROS)
- Neurotransmitter (glutamate and GABA) production

by product of
complete metabolism
↑ they can
destroy cell



Mitochondria

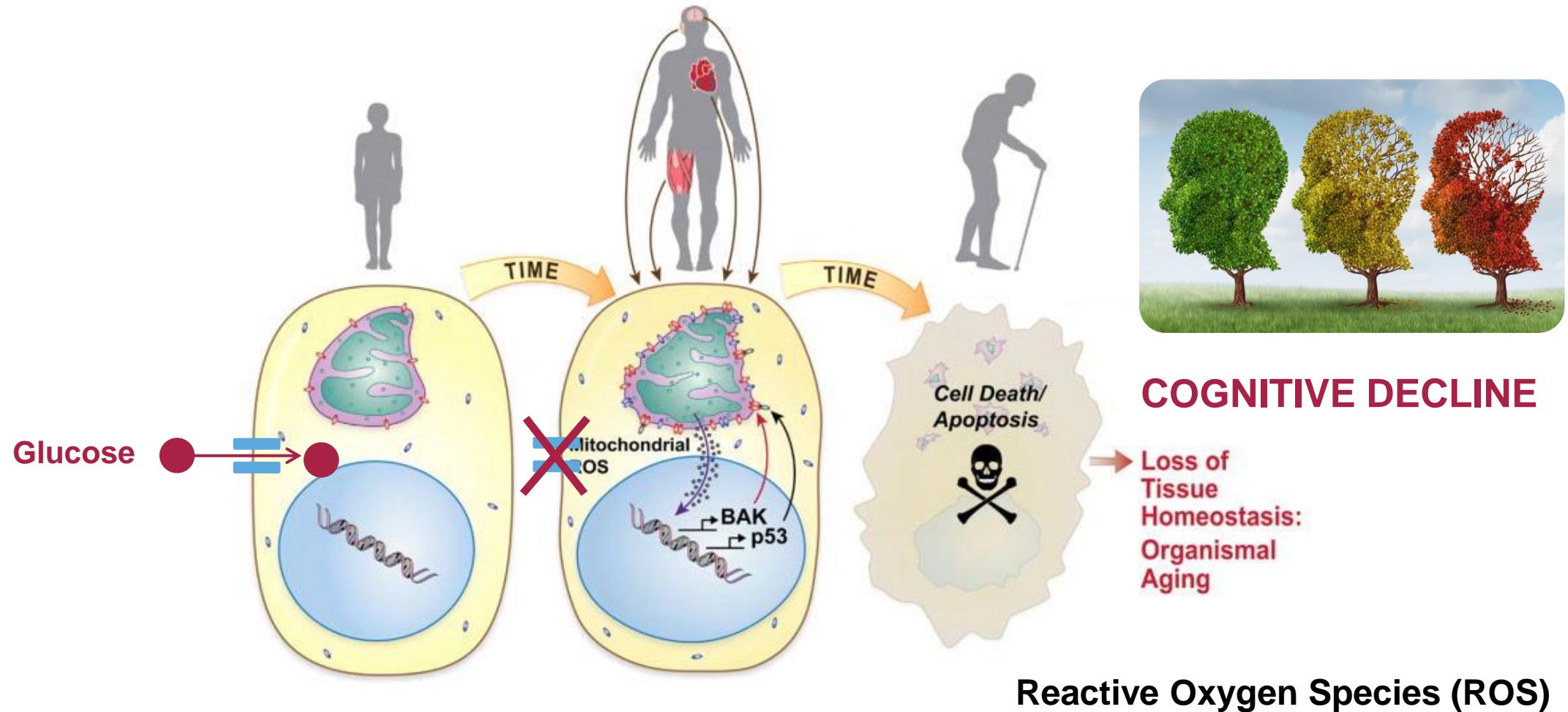


Metabolic Brain Ageing

- Ageing is characterized by **bioenergetic failure** and is accompanied by the **impairment of mitochondrial dynamics** and mitochondrial quality control pathways, leading to excessive production of **reactive oxygen species (ROS)**, which are harmful to cell proteins, lipids, and DNA.

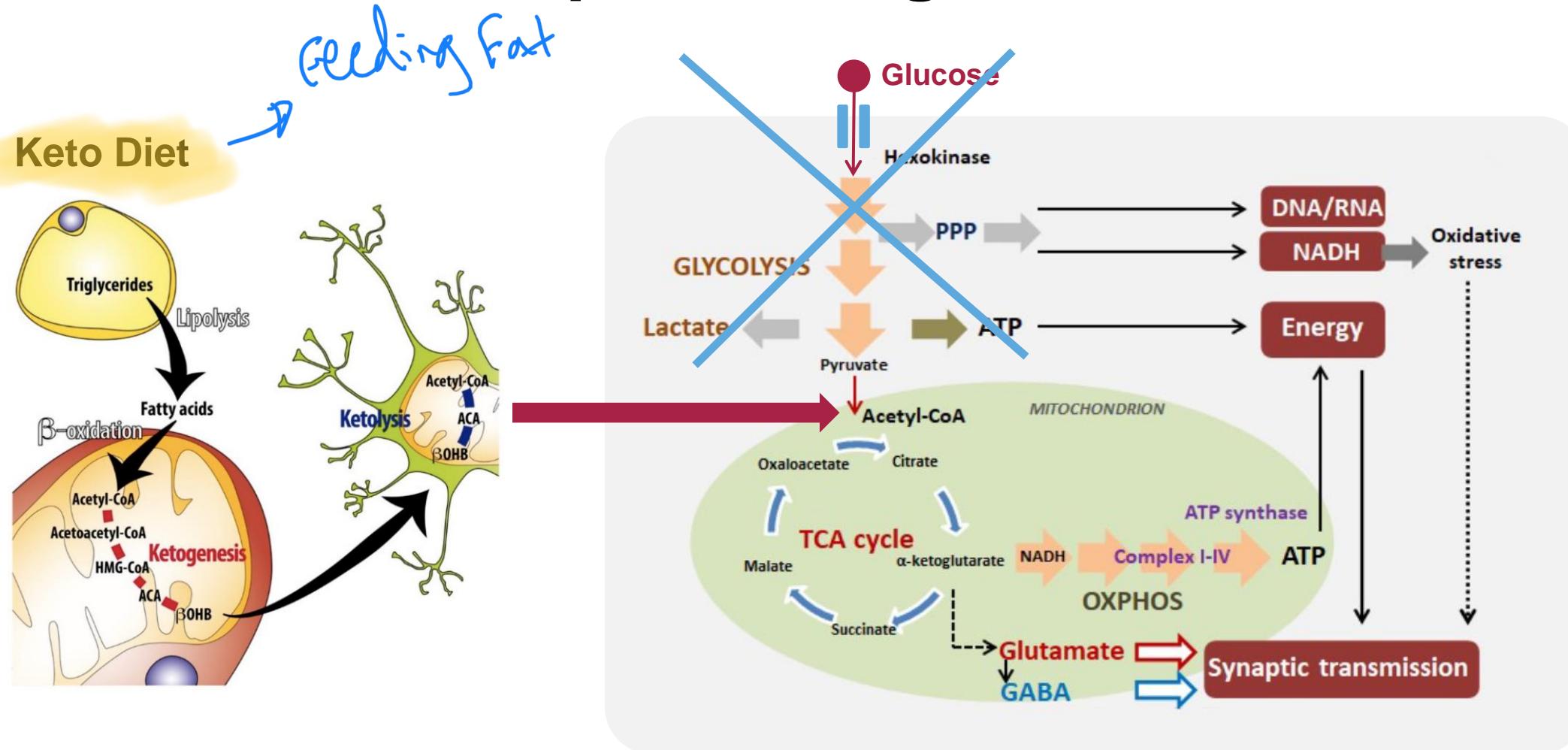


Bioenergetic Deficit → No Energy → ROS↑ → Cell Death



Someya, S. & Prolla, T. A. (2010). Mitochondrial oxidative damage and apoptosis in age-related hearing loss. *Mechanisms of Ageing and Development*, 131(7-8), 480–486. <https://doi.org/10.1016/j.mad.2010.04.006>

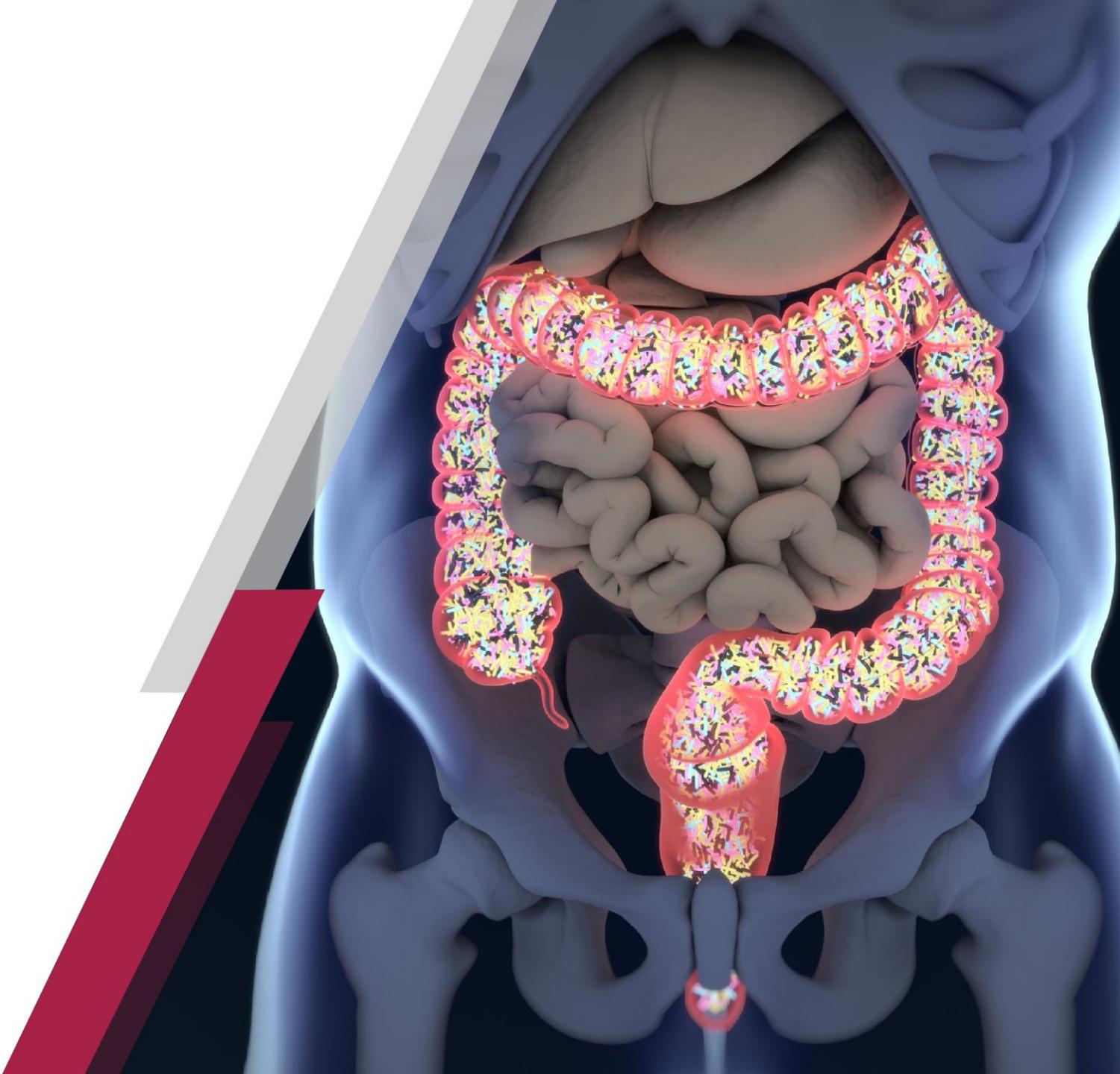
How Can a Diet Help Bioenergetics?



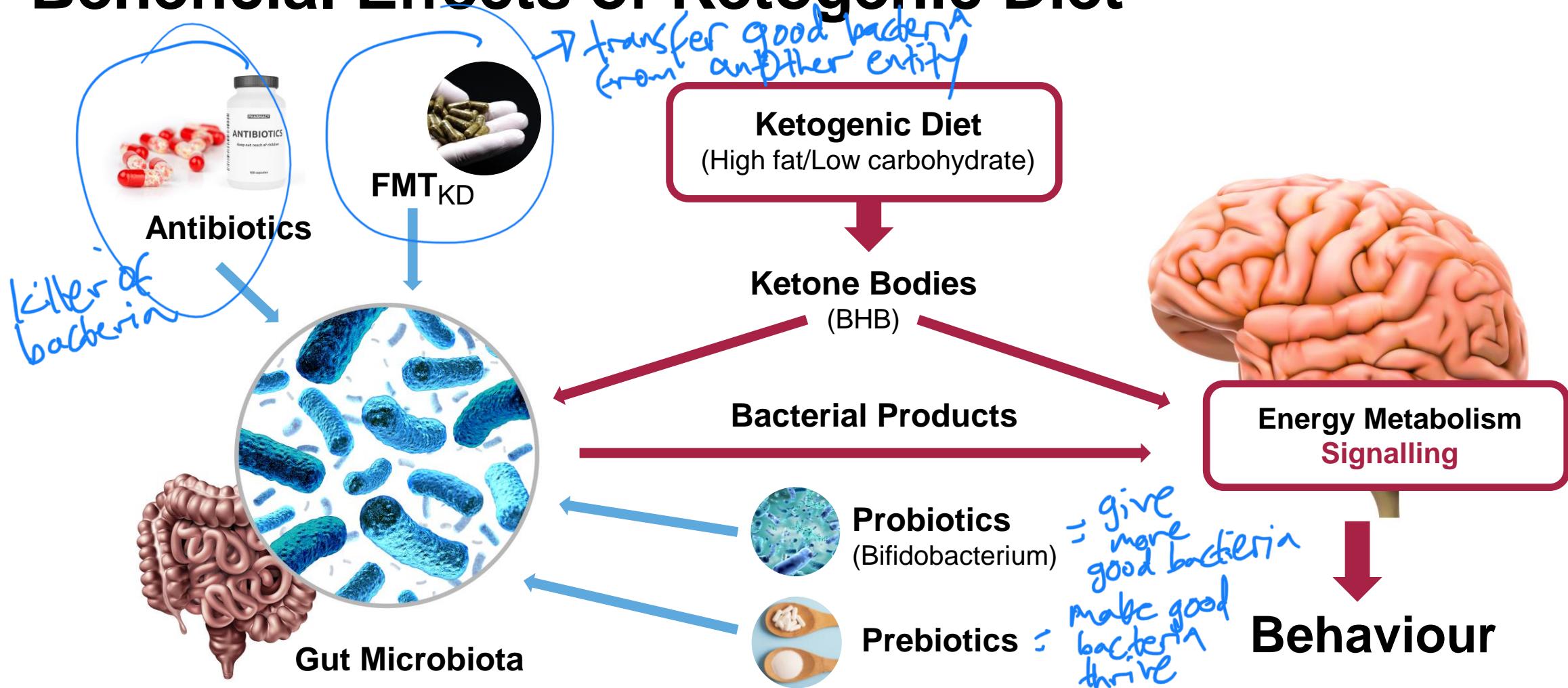
Longo, R., Peri, C., Cricri, D., Coppi, L., Caruso, D., Mitro, N., De Fabiani, E. & Crestani, M. (2019). Ketogenic Diet: A New Light Shining on Old but Gold Biochemistry. *Nutrients*, 11(10), 2497. <https://doi.org/10.3390/nu11102497>

The Gut Microbiome

- 100 trillions of bacteria
($10 \times$ of all human cells)
- > 1000 different species
- > 3 million genes
($150 \times$ of human genes)
- Weigh up to 2 kg
- Altered by **nutrients**



Gut Microbiome and Brain Mediate the Beneficial Effects of Ketogenic Diet



Ketogenic Diet Improves Cognition During Ageing

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

A ketogenic drink improves cognition in mild cognitive impairment: Results of a 6-month RCT

Conclusions: This kMCT drink improved cognitive outcomes in MCI, at least in part by increasing blood ketone level. These data support further assessment of MCI progression to Alzheimer's disease.

Received: 21 May 2020 | Revised: 3 September 2020 | Accepted: 16 September 2020

DOI: 10.1002/alz.12206

FEATURED ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

A ketogenic drink improves cognition in mild cognitive impairment: Results of a 6-month RCT

Mélanie Fortier¹ | Christian-Alexandre Castellano¹ | Valérie St-Pierre¹ |
Étienne Myette-Côté^{1,2} | Francis Langlois³ | Maggie Roy^{1,2} | Marie-Christine Morin¹ |
Christian Bocti^{1,2} | Tamas Fulop^{1,2} | Jean-Philippe Godin⁴ | Carla Delannoy⁵ |
Bernard Cuenoud⁵ | Stephen C. Cunnane^{2,6}

¹ Research Center on Aging, CIUSSS de l'Estrie–CHUS, Sherbrooke, Quebec, Canada

² Department of Medicine, Université de Sherbrooke, Sherbrooke, Quebec, Canada

³ CIUSSS de l'Estrie–CHUS, Sherbrooke, Quebec, Canada

⁴ Nestlé Health Science, Vevey, Switzerland

⁵ Nestlé Health Science, Vevey, Switzerland

⁶ Department of Analytical Chemistry, University of Bern, Bern, Switzerland

Correspondence
Mélanie Fortier, Research Center on Aging,
CIUSSS de l'Estrie–CHUS, 1036 Belvedere St
Sherbrooke, QC, J1H 4C4, Canada.
melanie.fortier2@sherbrooke.ca

Supporting information
Additional Supporting Information may be found in the online version of this article:
DOI: 10.1002/alz.12206

Program - Alzheimer Society Canada; Fonds de Recherche en Santé du Québec (FRQS);

Abstract

Introduction: Counteracting impaired brain glucose metabolism with ketones may improve cognition in mild cognitive impairment (MCI).

Methods: Cognition, plasma ketone response, and metabolic profile were assessed before and 6 months after supplementation with a ketogenic drink containing medium chain triglyceride (ketogenic medium chain triglyceride [kMCT]; 15 g twice/day; n = 39) or placebo (n = 44).

Results: Free and cued recall (Trial 1; P = .047), verbal fluency (categories; P = .024), Boston Naming Test (total correct answers; P = .033), and the Trail-Making Test (total errors; P = .017) improved significantly in the kMCT group compared to placebo (analysis of covariance; pre-intervention score, sex, age, education, and apolipoprotein E4 as covariates). Some cognitive outcomes also correlated positively with plasma ketones. Plasma metabolic profile and ketone response were unchanged.

Conclusions: This kMCT drink improved cognitive outcomes in MCI, at least in part by increasing blood ketone level. These data support further assessment of MCI progression to Alzheimer's disease.

KEY WORDS

acetoacetate, Alzheimer's disease, beta-hydroxybutyrate, cognition, episodic memory, executive function, ketone, language, medium chain triglyceride, mild cognitive impairment

No part of this video shall be filmed, recorded, downloaded, reproduced, distributed, republished or transmitted in any form or by any means without written approval from the University.