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BRAIN-GUT HEALTH

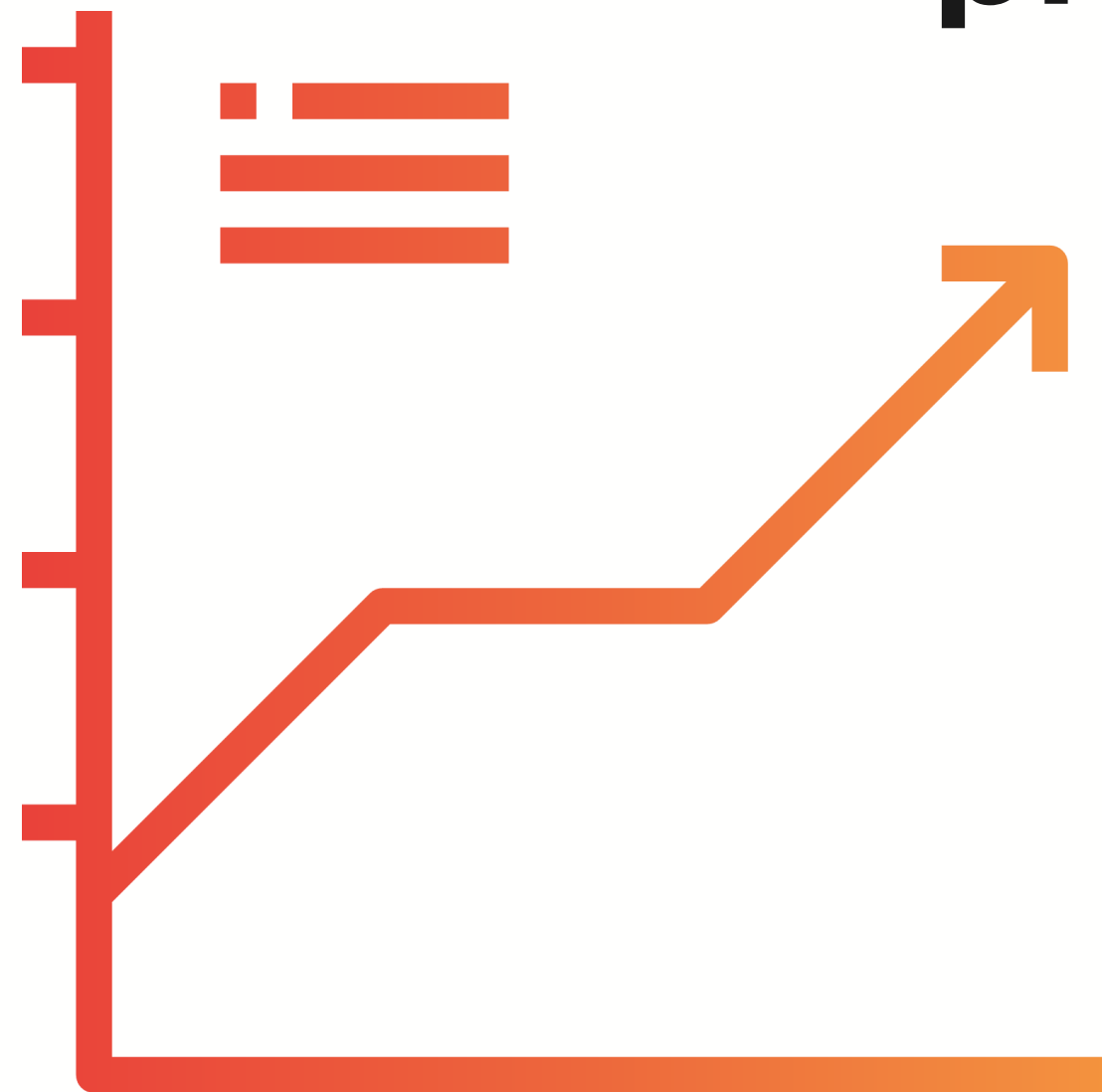
THE FUTURE OF PSYCHIATRY

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#1 Dear Psychiatry,

We have a big
problem!



[Insert psychiatric
diagnosis here]



#2 Cognitive Dissonance

"51% of trial deemed positive by FDA compared with 94% in the literature

32% overestimation of antidepressant benefit

Meta-Analysis > N Engl J Med. 2008 Jan 17;358(3):252-60. doi: 10.1056/NEJMSa065779.

Selective publication of antidepressant trials and its influence on apparent efficacy

Erick H Turner¹, Annette M Matthews, Eftihia Linardatos, Robert A Tell, Robert Rosenthal

The screenshot shows the top navigation bar of the BBC News website with links for Home, News, Sport, Weather, iPlayer, and Soam. Below the navigation bar is a red banner with the word 'NEWS' in white. Underneath the banner is a horizontal menu with links for Home, Cost of Living, War in Ukraine, Coronavirus, Climate, UK, World, Business, Politics, Tech, and Science. The 'Health' link is highlighted with a red underline. The main headline of the article is 'Nearly half a million more adults on antidepressants in England', dated 9 July. A red share icon is visible at the bottom left of the article preview.

Nearly half a million more adults in England are now taking antidepressants compared with the previous year, according to NHS figures.

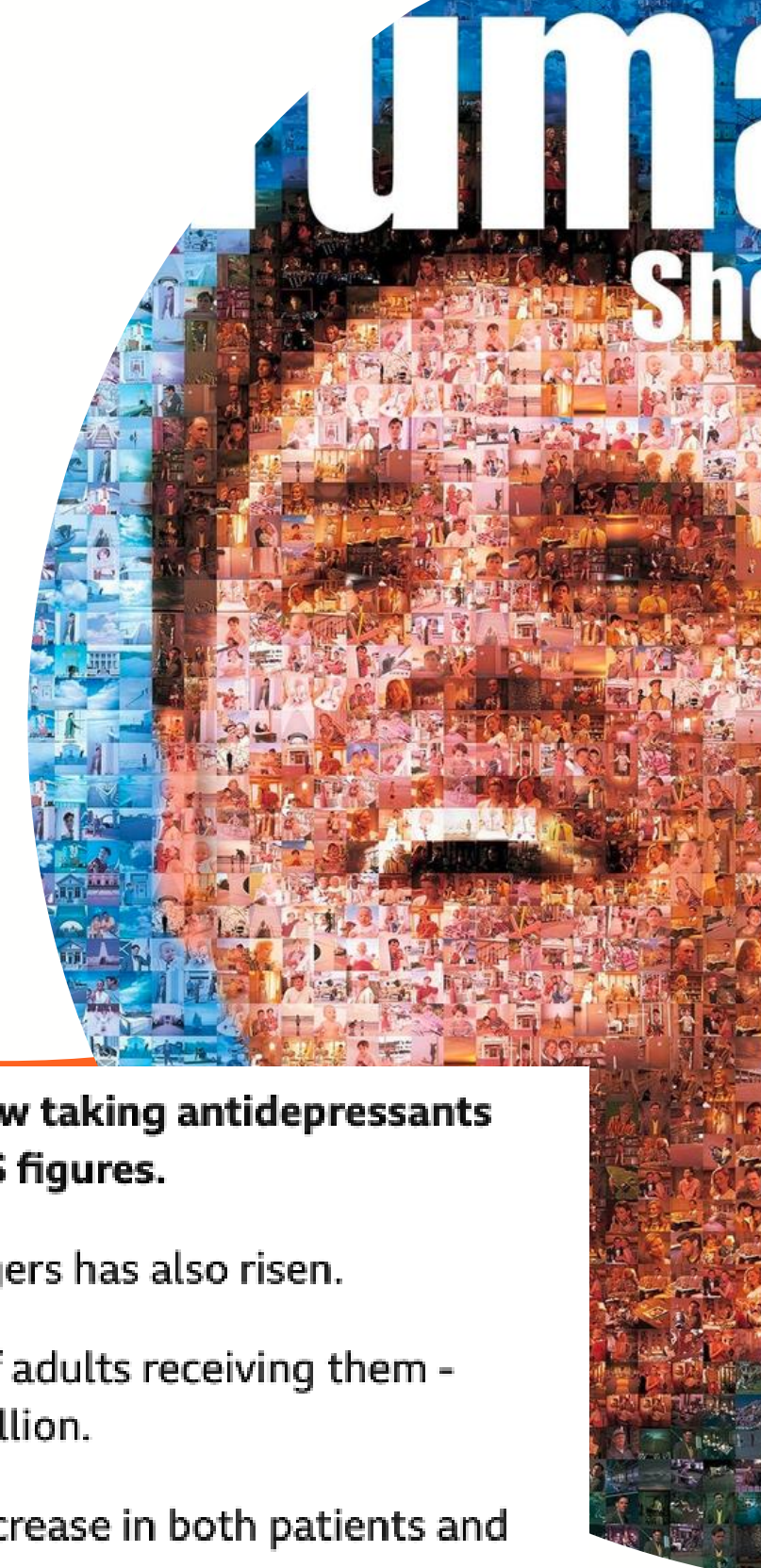
The number of prescriptions for children and teenagers has also risen.

From 2021-22, there was a 5% rise in the number of adults receiving them - from 7.9 million in the previous 12 months to 8.3 million.

It is the sixth year in a row that there has been an increase in both patients and prescriptions.

An estimated 83.4 million antidepressant drug items were prescribed between 2021 and 2022, which marks a 5% increase from the previous year.

There was also a rise of just over 8% in youngsters taking the medication too - from 10,994 to 11,878 among 10 to 14-year-olds and from 166,922 to 180,455 in the 15 to 19-year-olds.



How Effective?



STAR-D Trial - 2006

4,041 outpatients with nonpsychotic depression at 23 psychiatric and 18 primary care sites

Citalopram/SSRI

28-33% remission (up to 14 weeks)

Less clinical effectiveness with 2nd, 3rd antidepressants



Mechanism Of Action?

Randomized Controlled Trial > *Biol Psychiatry*. 2010 Mar 1;67(5):439-45.

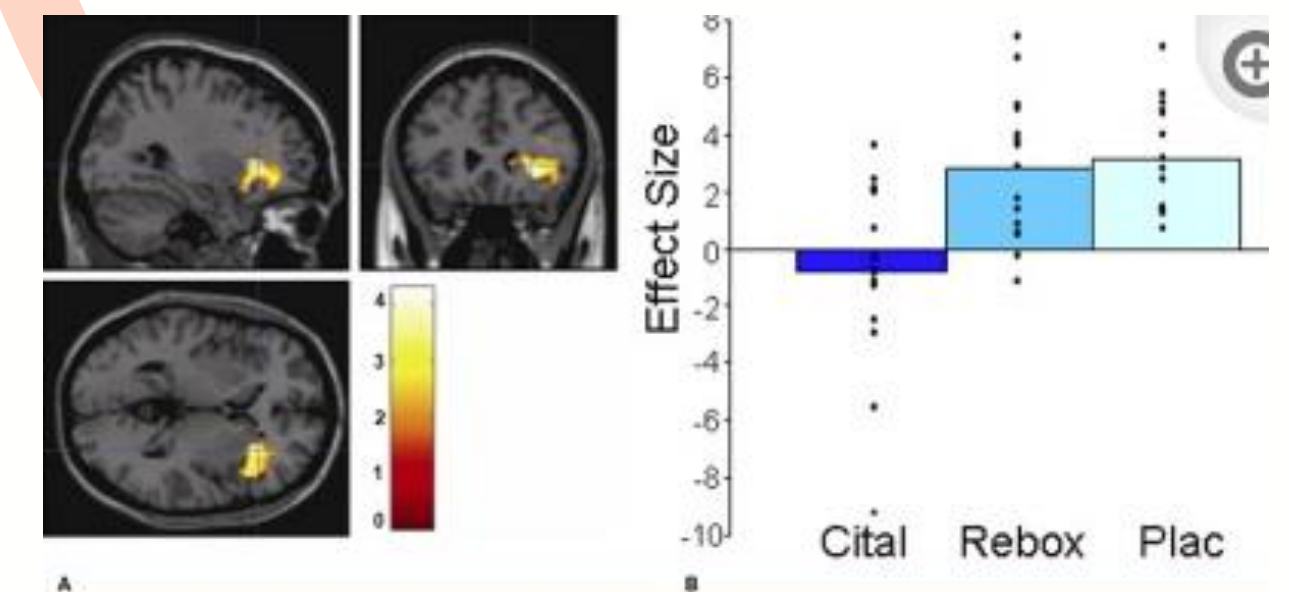
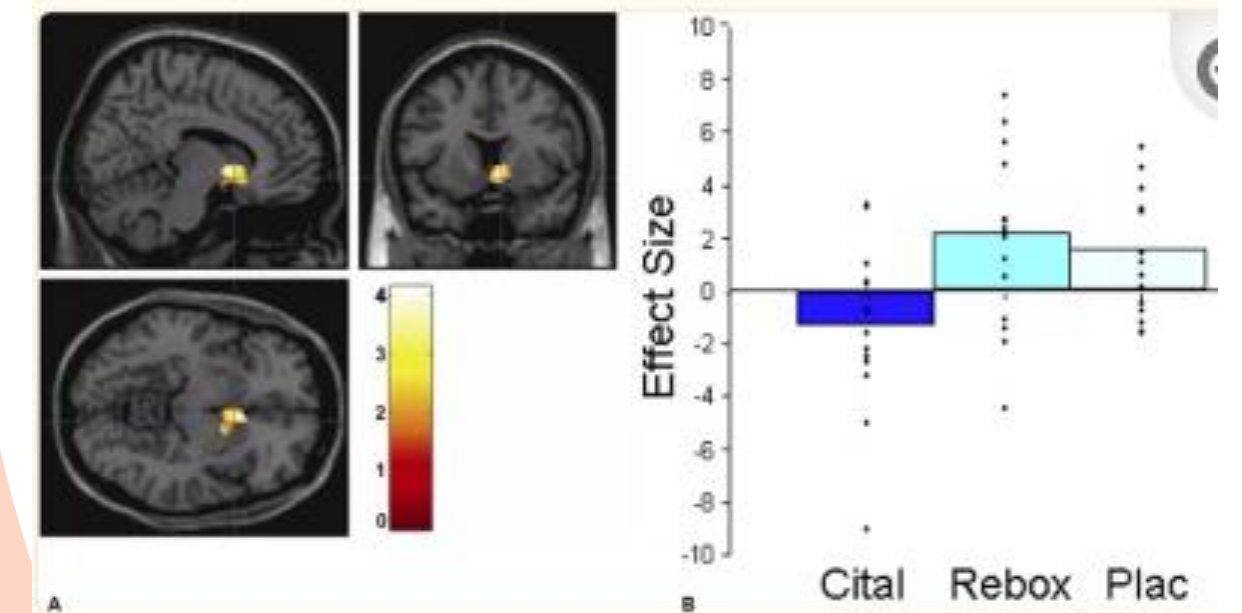
doi: 10.1016/j.biopsych.2009.11.001. Epub 2009 Dec 24.

Diminished neural processing of aversive and rewarding stimuli during selective serotonin reuptake inhibitor treatment

Ciara McCabe¹, Zevic Mishor, Philip J Cowen, Catherine J Harmer

Results: Citalopram reduced activation to the chocolate stimuli in the ventral striatum and the ventral medial/orbitofrontal cortex. In contrast, reboxetine did not suppress ventral striatal activity and in fact increased neural responses within medial orbitofrontal cortex to reward. Citalopram also decreased neural responses to the aversive stimuli conditions in key "punishment" areas such as the lateral orbitofrontal cortex. Reboxetine produced a similar, although weaker effect.

Conclusions: Our findings are the first to show that treatment with SSRIs can diminish the neural processing of both rewarding and aversive stimuli. The ability of SSRIs to decrease neural responses to reward might underlie the questioned efficacy of SSRIs in depressive conditions characterized by decreased motivation and anhedonia and could also account for the experience of emotional blunting described by some patients during SSRI treatment.



#3 Cognitive & Behavioural Conditioning

- Usefulness of Psychiatrists
- Limited to 'Acute' & Secondary/Tertiary settings
- Medication ONLY Treatment
- Evidence-based medicine lip-service (top-down/guideline driven practice)
- Personalities: high compliant & risk adverse
- System-directed medicine NOT person-centred medicine
- Symptom management NOT root cause focused



#4 Time for a Paradigm-Shift



Brain Health NOT Mental Health

No longer limited to reducing symptoms with drugs

Grounded in improving 4 areas of brain health & empowering patients to take ownership of their health

Working collaboratively with patients to find solutions

Physiological



Psychological



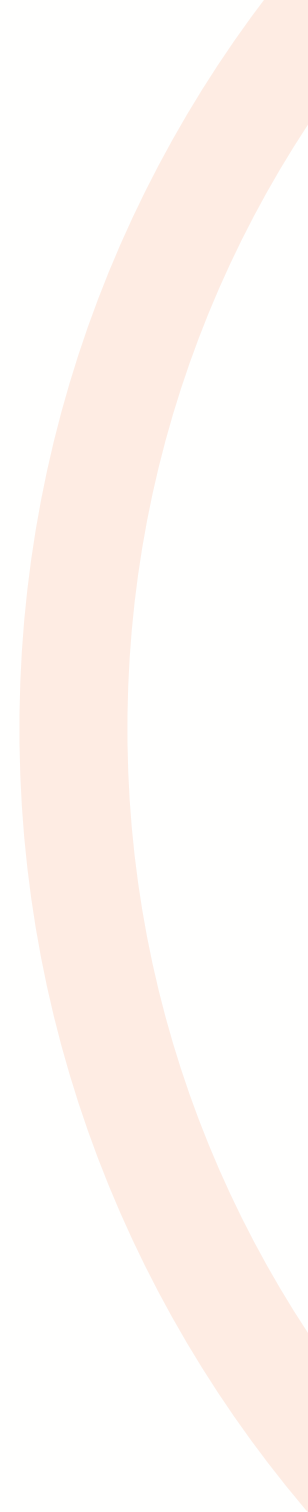
Social



Spiritual



Sublime Complexity

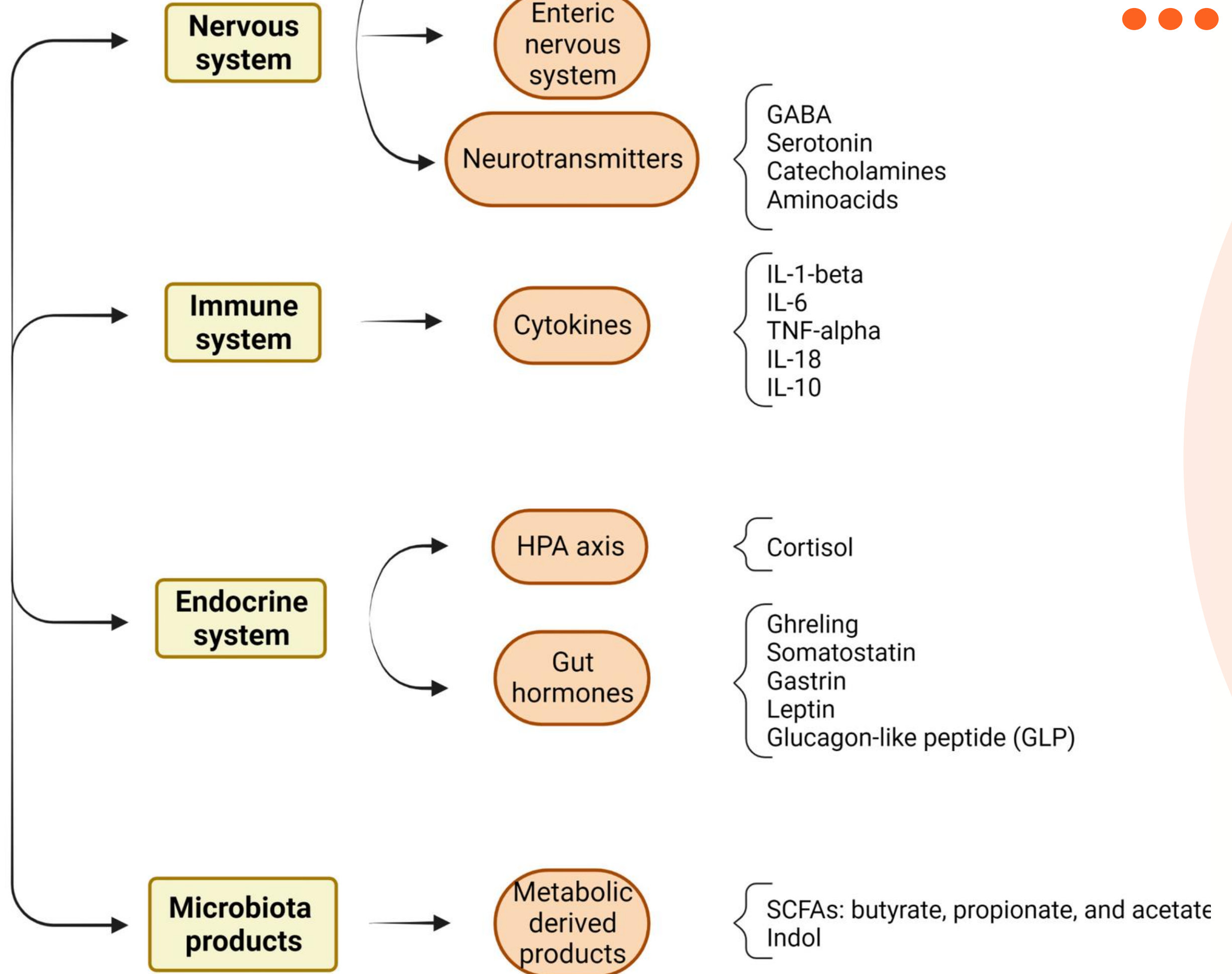
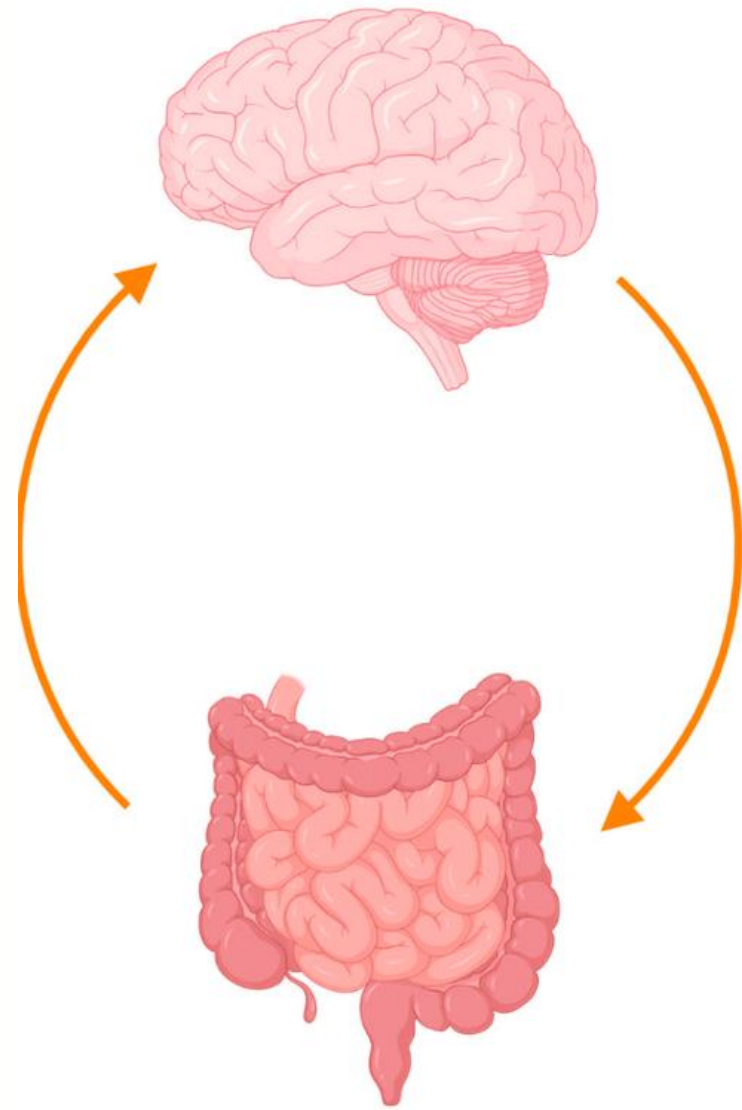


#5 (Brain) Health = Gut Health

- Scientific Reductionism vs Biological Reductionism
- Gut/GI Tract = 2nd brain - 100 million neurones (more than in SC or PNS)
- 30 feet of tubing with single layer of cells
- Primary function - includes nutrient supply



Communication pathways Gut-brain axis

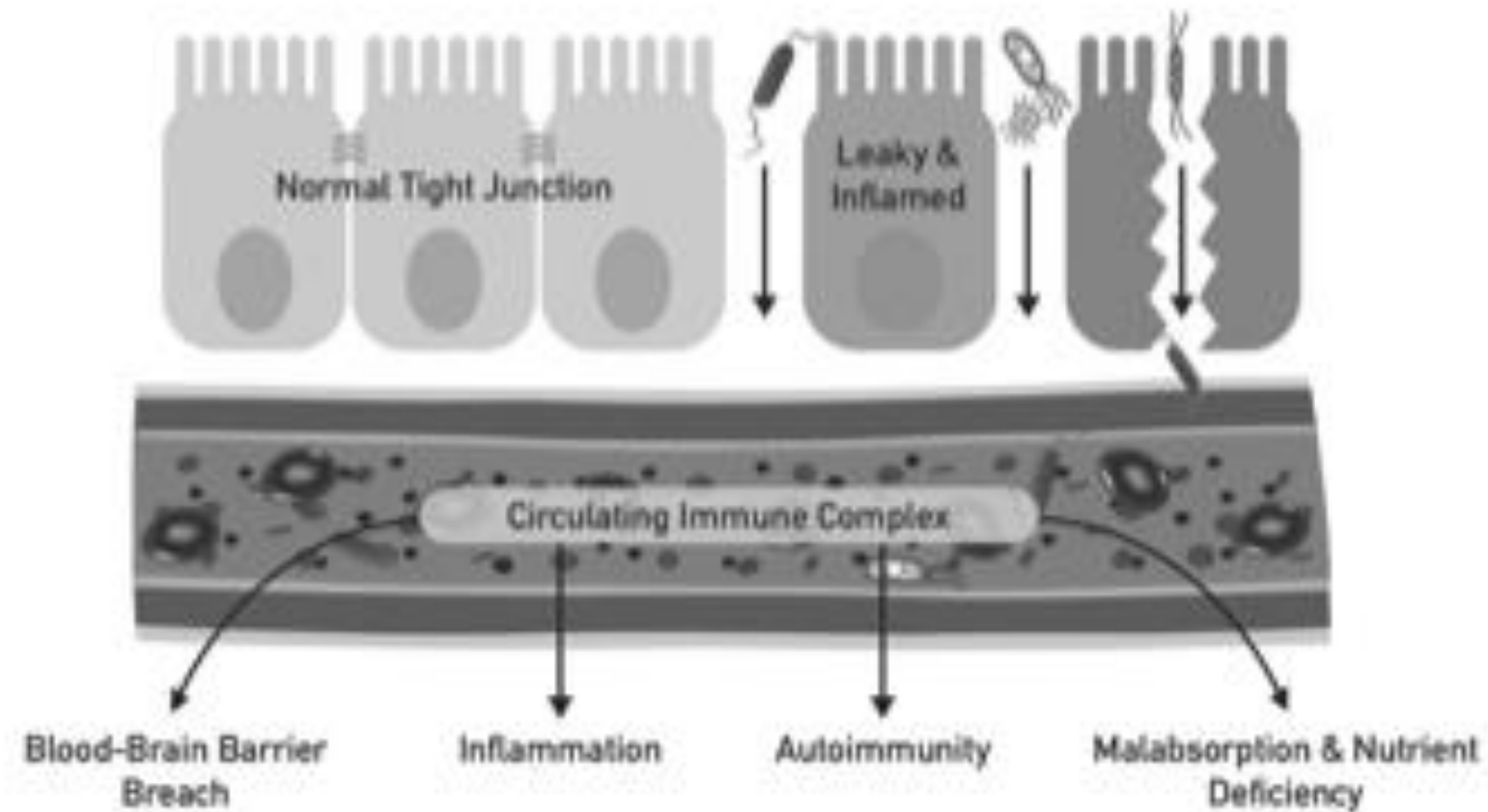


LEAKY GUT SYNDROME

TRIGGERS CAUSING INTESTINAL DAMAGE



INTESTINAL MUCOSAL CELL





Review

The Microbiota–Gut–Brain Axis in Psychiatric Disorders

Aleksandra Góralczyk-Bińkowska ^{1,*}, Dagmara Szmaida-Krygier ²  and Elżbieta Kozłowska ¹

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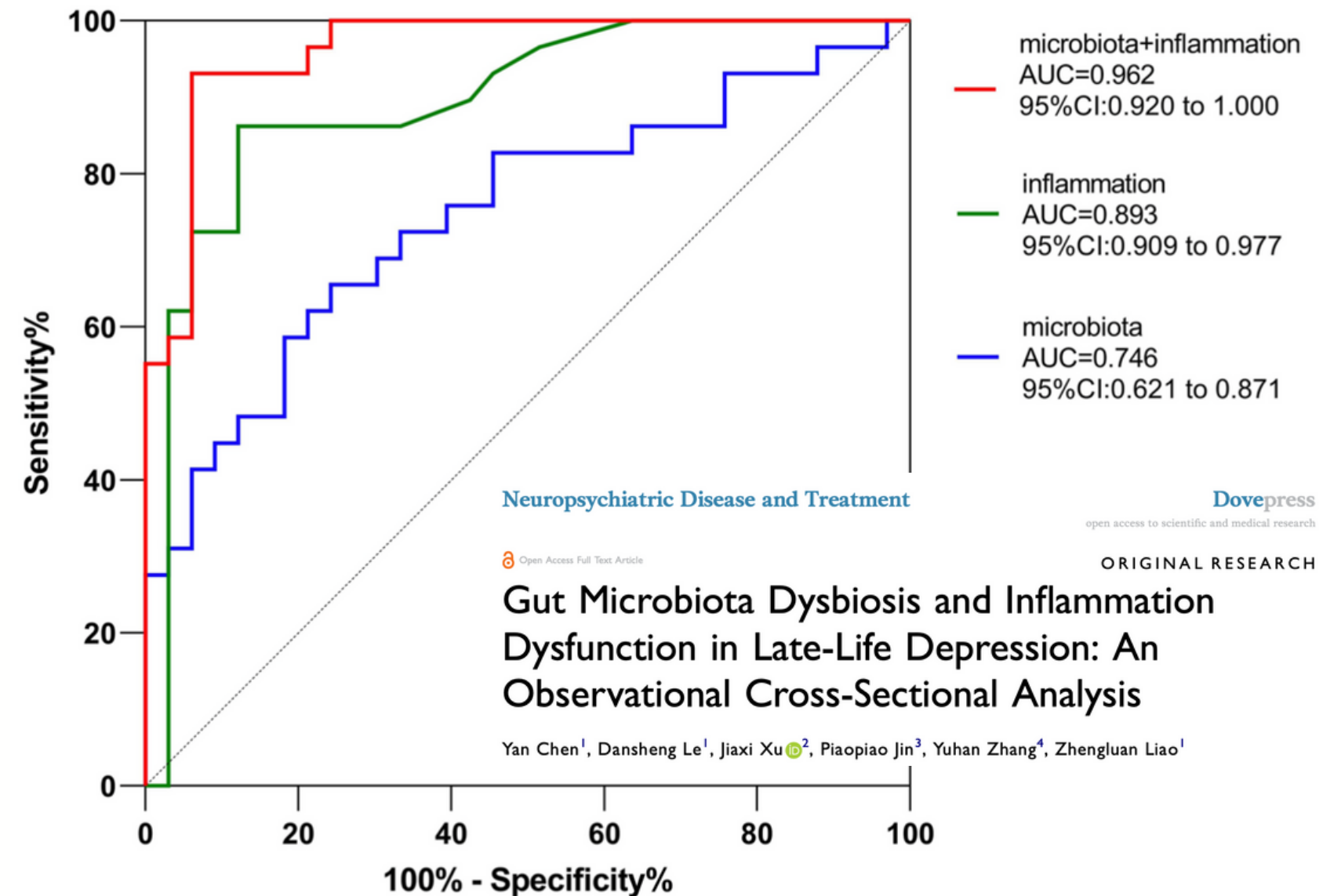
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Int. J. Mol. Sci. **2022**, *23*, 11245. <https://doi.org/10.3390/ijms231911245>

#6 Evolving Understanding of Pathophysiology & biomarkers

- LLD Depression Study (Chen et al, 2024)
- 29 untreated LLD, 36 HCs
- Serum inflammatory markers & faecal analysis
- IL-6, Akkermansia & Sutterella = predictors of LLD
- IL-6, IFN gamma, Akkermansia, Verrucomicrobia = predictors of LLD severity

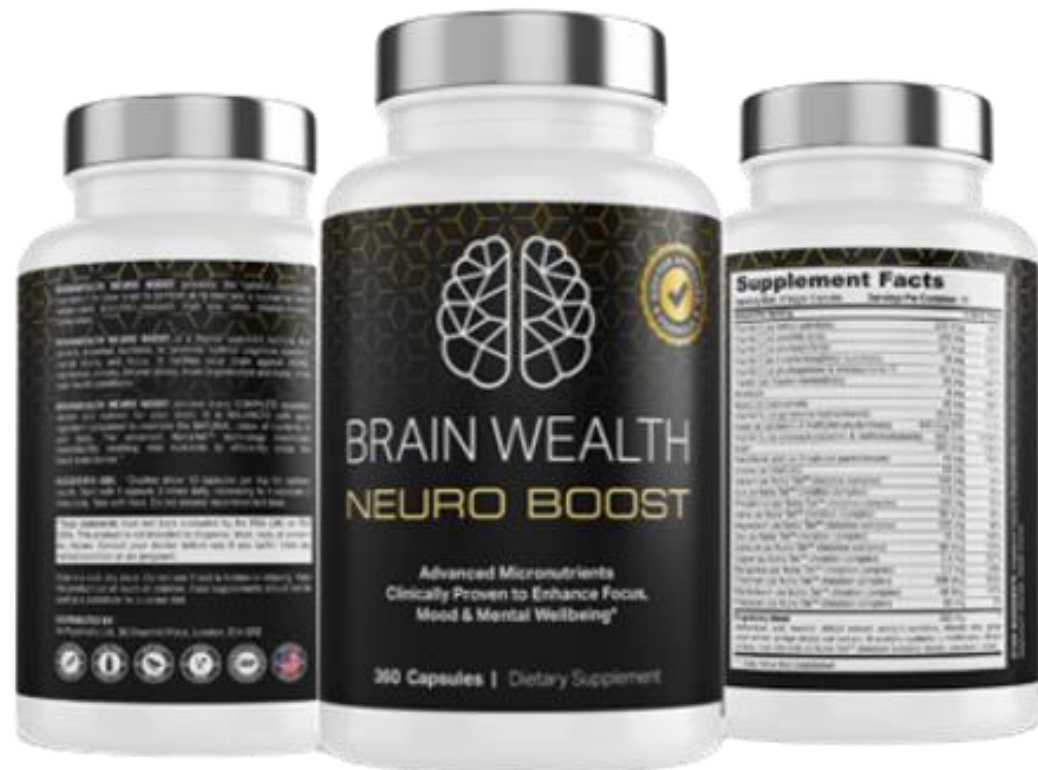


#7 Probiotics & Prebiotics as Viable Treatment Options?

- Depression - 1008
- Anxiety - 699
- ADHD - 57
- Autism - 345
- Dementia - 265



#7 Focus on Micronutrients





Effects of nutrients (in food) on the structure and function of the nervous system: update on dietary requirements for brain. Part 1: micronutrients

J M Bourre ¹

Affiliations + expand

PMID: 17066209

Abstract

The objective of this update is to give an overview of the effects of dietary nutrients on the structure and certain functions of the brain. As any other organ, the brain is elaborated from substances present in the diet (sometimes exclusively, for vitamins, minerals, essential amino-acids and essential fatty acids, including omega-3 polyunsaturated fatty acids). However, for long it was not fully accepted that food can have an influence on brain structure, and thus on its function, including cognitive and intellectual. In fact, most micronutrients (vitamins and trace-elements) have been directly evaluated in the setting of cerebral functioning. For instance, to produce energy,

- Micronutrients in the one carbon cycle play a vital role in mediating epigenetic processes.
- An imbalance in micronutrients reduced mRNA levels of BDNF, NGF, TrkB and CREB.
- Prenatal omega-3 supplementation to an imbalanced diet normalized all mRNA levels.
- An imbalanced diet adversely programmes brain development/function in the offspring.

[Nat Rev Neurosci](#). Author manuscript; available in PMC 2010 Jan 12.

Published in final edited form as:

[Nat Rev Neurosci. 2008 Jul; 9\(7\): 568-578.](#)

doi: [10.1038/nrn2421](#)

PMCID: PMC2805706

NIHMSID: NIHMS162299

PMID: [18568016](#)



International Journal of Developmental
Neuroscience

Volume 34, May 2014, Pages 24-32



Maternal micronutrient imbalance alters gene expression of BDNF, NGF, TrkB and CREB in the offspring brain at an adult age

[Pratiksha Sable](#), [Anvita Kale](#), [Asmita Joshi](#), [Sadhana Joshi](#)  

Brain foods: the effects of nutrients on brain function

[Fernando Gómez-Pinilla](#)

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The publisher's final edited version of this article is available at [Nat Rev Neurosci](#)

Abstract

[Go to: ▶](#)

It has long been suspected that the relative abundance of specific nutrients can affect cognitive processes and emotions. Newly described influences of dietary factors on neuronal function and synaptic plasticity have revealed some of the vital mechanisms that are responsible for the action of diet on brain health and mental function. Several gut hormones that can enter the brain, or that are produced in the brain itself, influence cognitive ability. In addition, well-established regulators of synaptic plasticity, such as brain-derived neurotrophic factor, can function as metabolic modulators, responding to peripheral signals such as food intake. Understanding the molecular basis of the effects of food on cognition will help us to determine how best to manipulate diet in order to increase the resistance of neurons to insults and promote mental fitness.

[Home](#) > [Media release](#) > The

The Hidden Young Health

January 18, 2021

*Soaring numbers of teens
with situation getting worse*

The diets of British teenage
leading to a worrying risk of
report commissioned by the
which found seriously inadequate

“

WITH NUTRIENT INTAKES HAVING
DECLINED SUBSTANTIALLY OVER THE
LAST 20 YEARS, THESE VITAMIN AND
MINERAL SHORTFALLS ARE NOT LIKELY
TO DISAPPEAR ANY TIME SOON

”

Leading healthcare professionals, including a nutritionist, pharmacist and two GPs, assessed the latest evidence from the National Diet and Nutrition Survey – the government’s official diet check. They found not only that intakes of vitamins and minerals have been steadily declining over the past decade but that increasing numbers of young people are now at risk of deficiency – indicating a need for more targeted

STATE OF THE NATION

DIETARY
TRENDS IN
THE UK
REARS ON

AND WHERE ARE WE GOING?



ENZYME CO-FACTORS

A co-factor is non-protein chemical compound (primarily vitamins) or metallic ion that is required for an enzyme's role as a catalyst (a substance that increases the rate of a chemical reaction)

25-50% of all enzymes cannot function without co-factors

3000 identified enzymes that require Magnesium to function



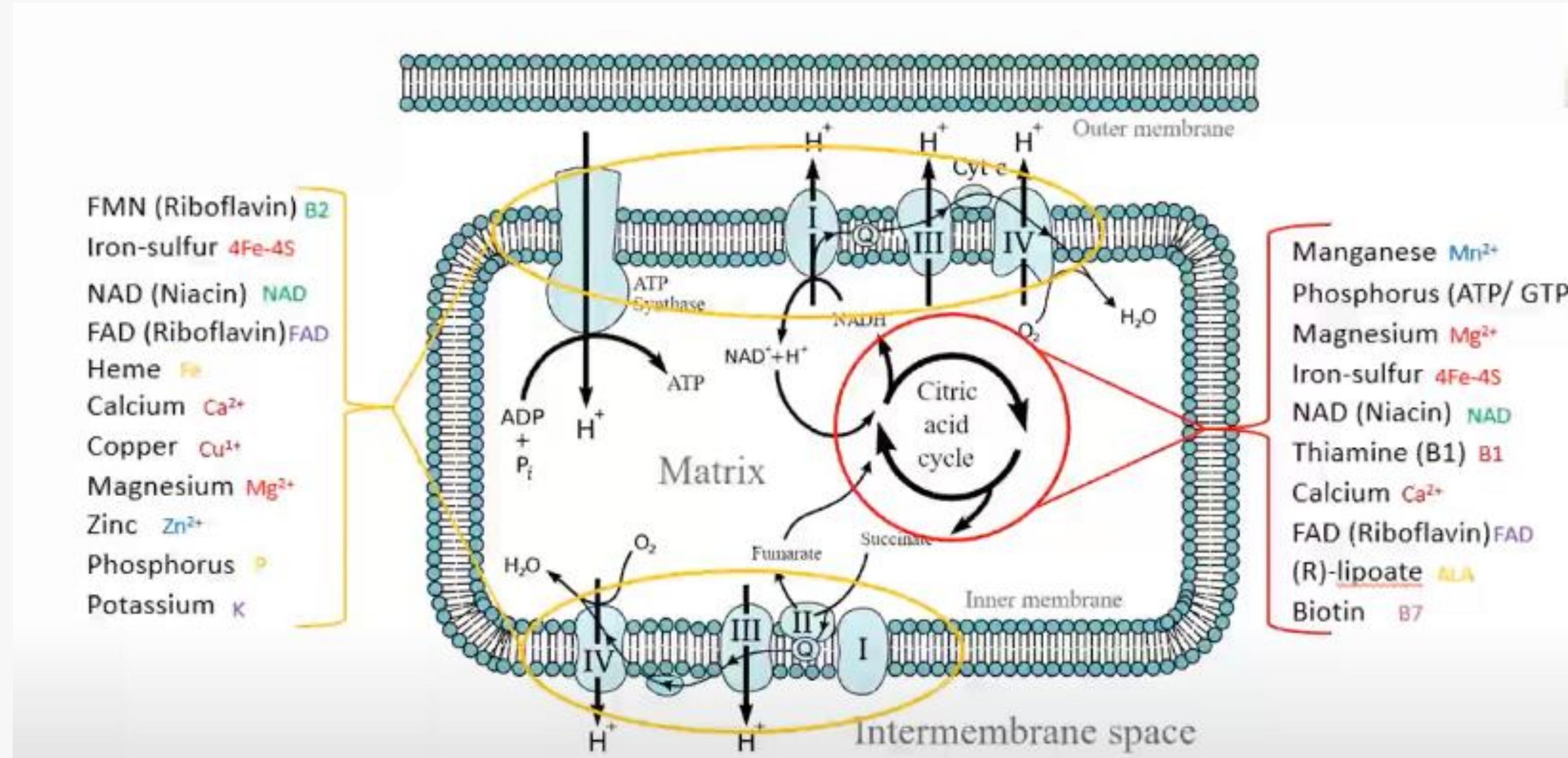
THE MARVEL OF MITOCHONDRIA

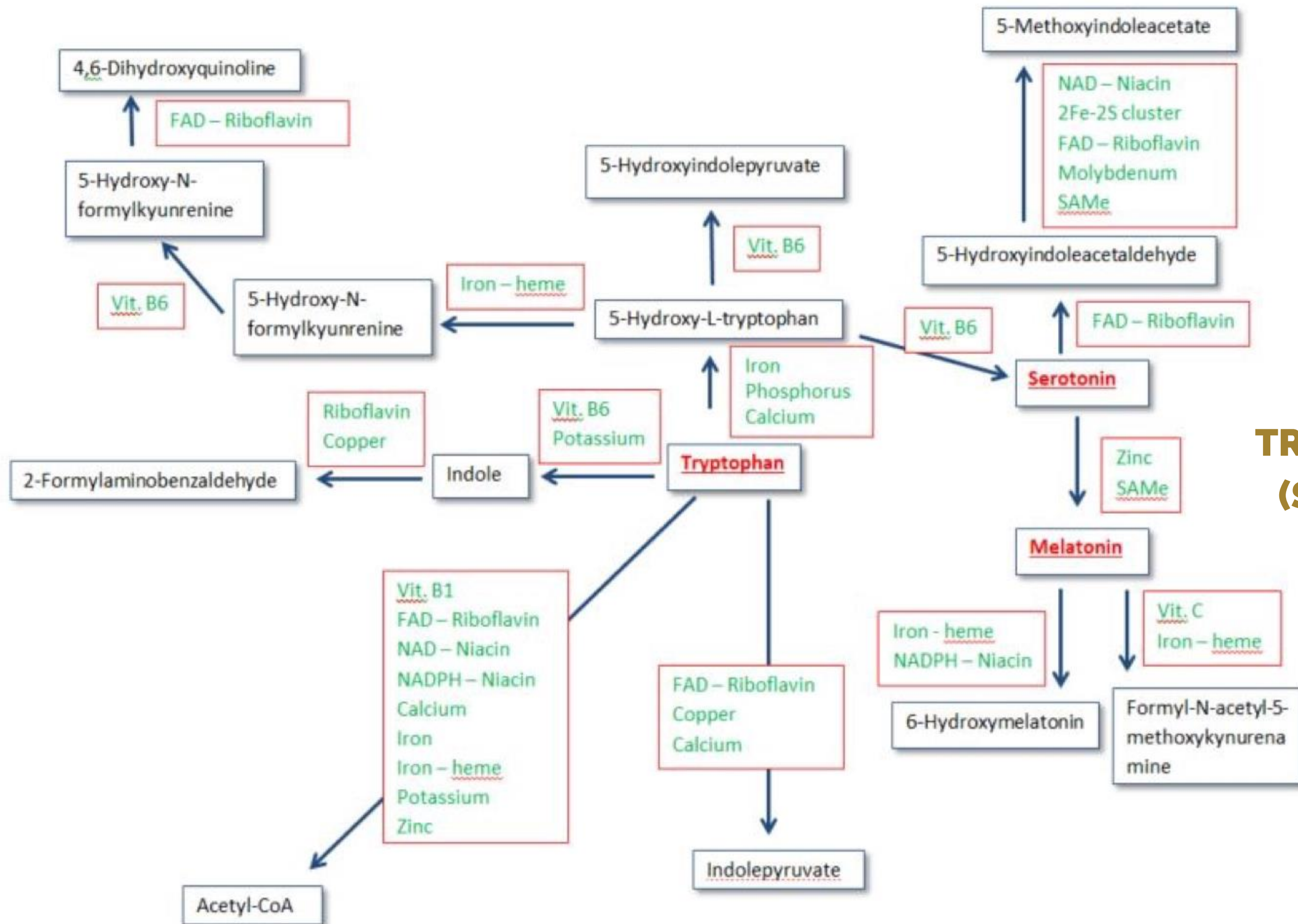
Each mitochondria has 17,000 assembly lines for making ATP

This diagram depicts two

There are an estimated 100,000 trillion mitochondria in the human

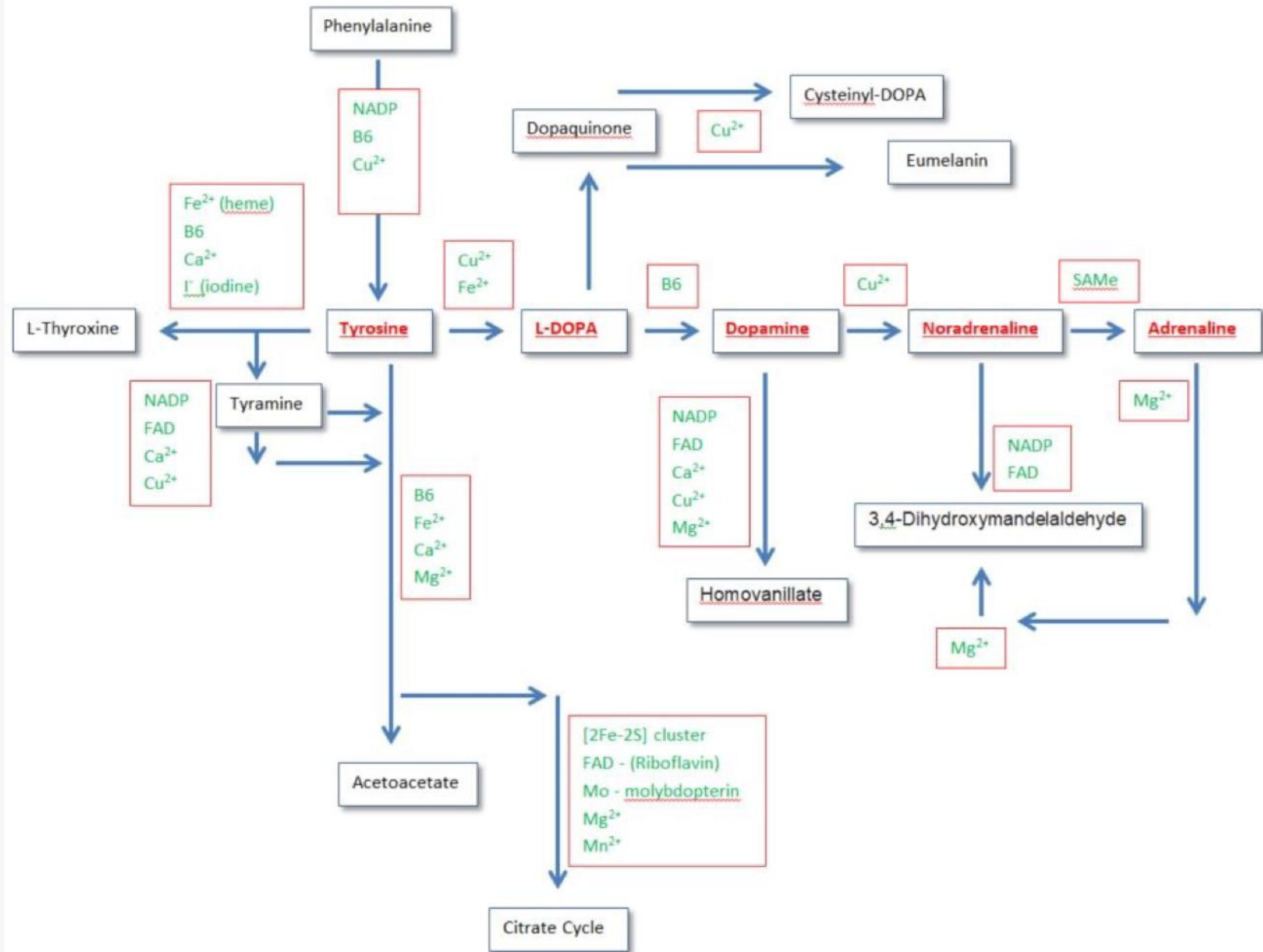
Mitochondrial turnover is about 100 days, this would mean that around 2 billion mitochondria are made every second





TRYPTOPHAN METABOLISM (SEROTONIN SYNTHESIS)

TYROSINE METABOLISM (DOPAMINE SYNTHESIS)



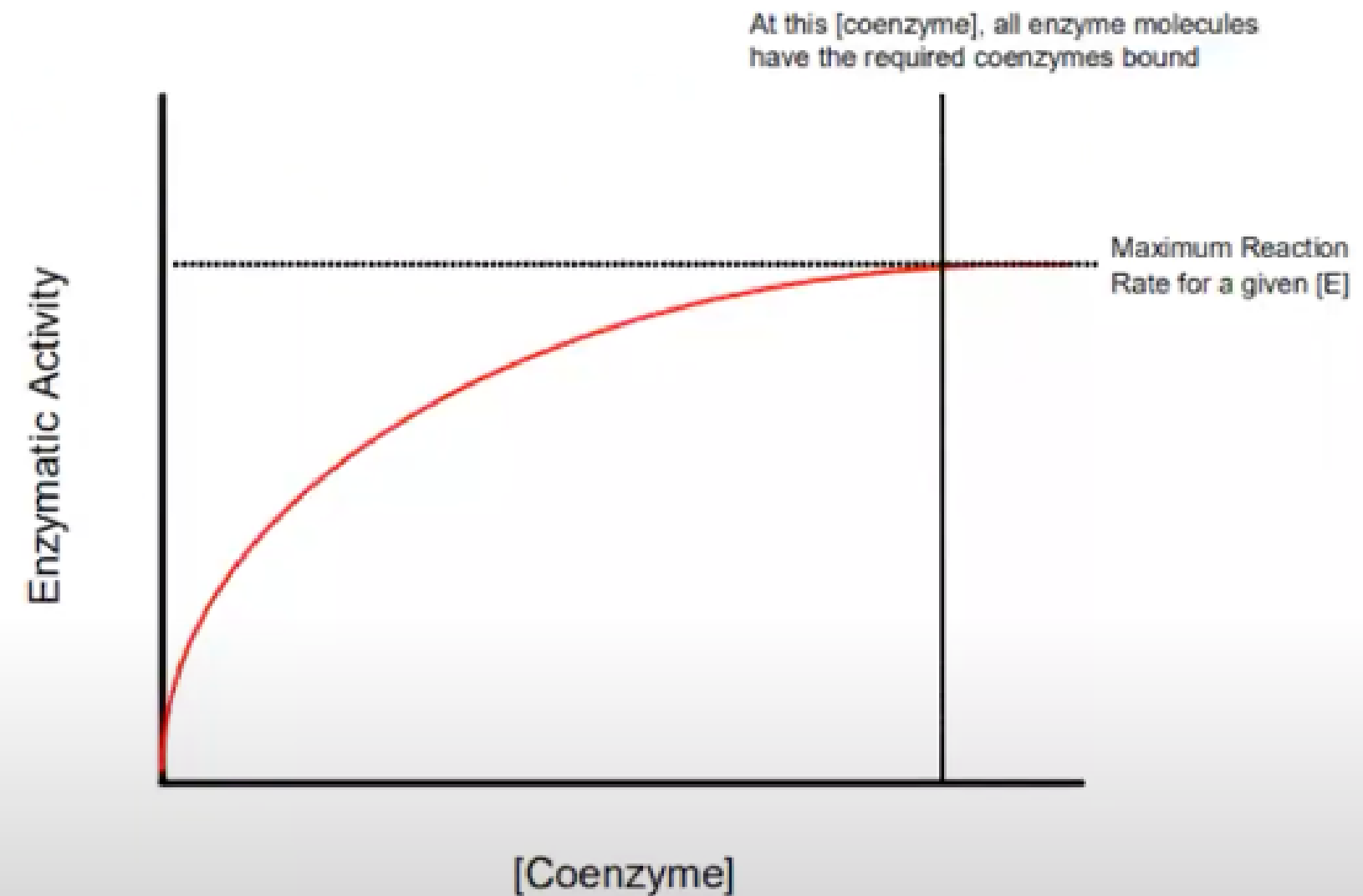
Dose-dependant improvements in previously suboptimal pathways, leading to functional improvement

Resulting in a broad up-regulation of central nervous system function

Not just affecting the individual pathways but entire ecosystem of the brain - pathways are interconnected and interdependent, not exist in isolation

The idea of a 'magic bullet' as a single compound or molecule simply does not match the reality of the complexity of the human brain

Cofactor Concentration is Proportional to Reaction Rate



Lab #4: Enzymes – ResearchGate. Retrieved 18 Nov 2021

<https://www.researchgate.net/file.PostFileLoader.html?id=565e7f15860614b54dc8b4567&assetKey=AS%3A302082802814980>

NUTRIENTS & MICROBIOME DIVERSITY

Increase in OTUs (operational taxonomic units) – a measure of community diversity

May support a more diverse microbiome or protect against fluctuations

Randomized Controlled Trial > Sci Rep. 2019 Jul 12;9(1):10128.

doi: 10.1038/s41598-019-46146-3.

Human gut microbiome changes during a 10 week Randomised Control Trial for micronutrient supplementation in children with attention deficit hyperactivity disorder

Aaron J Stevens¹, Rachel V Purcell², Kathryn A Darling³, Matthew J F Eggleston⁴, Martin A Kennedy⁵, Julia J Rucklidge³

It has been widely hypothesized that both diet and the microbiome play a role in the regulation of attention-deficit/hyperactivity disorder (ADHD) behaviour. However, there has been very limited scientific investigation into the potential biological connection. We performed a 10-week pilot study investigating the effects of a broad spectrum micronutrient administration on faecal microbiome content, using 16S rRNA gene sequencing. The study consisted of 17 children (seven in the placebo and ten in the treatment group) between the ages of seven and 12 years, who were diagnosed with ADHD. We found that micronutrient treatment did not drive large-scale changes in composition or structure of the microbiome. However, observed OTUs significantly increased in the treatment group, and showed no mean change in the placebo group. The differential abundance and relative frequency of Actinobacteria significantly decreased post- micronutrient treatment, and

CONSEQUENCES OF NUTRIENT DEFICIENCY OR INSUFFICIENCY



DNA DAMAGE

e.g. B12, B6, C, E, Zinc can cause single or double strand breaks and/or oxidative lesions mimicking radiation damage



GENETIC POLYMORPHISMS

can lead to poorer binding affinity between mutant enzyme and co-factor – can recover function with high doses of co-factor (vitamins/minerals)



MITOCHONDRIAL DECAY & OXIDANT LEAKAGE

resulting in accelerated ageing and neuronal damage e.g. iron, biotin