

# Nutrition and Mental Wellness:

how food affects the brain

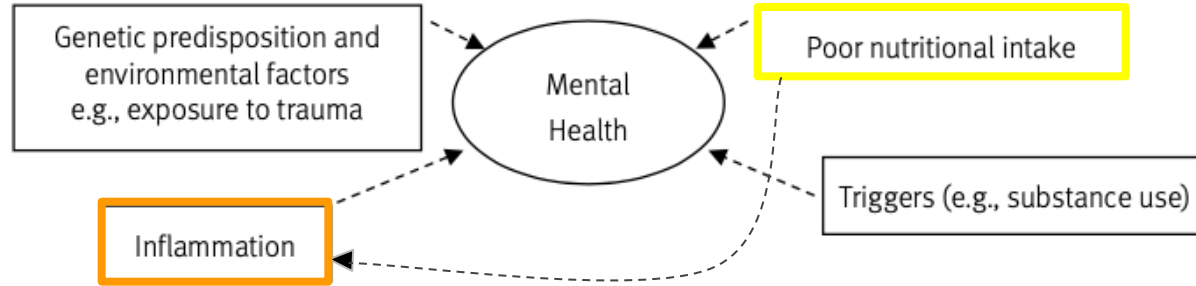
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## Outline

1. **Gut-brain axis**
2. **Fiber**
  - Inflammation and the brain
3. **Neurotransmitters**
  - Tryptophan
  - Tyrosine
4. **Micronutrients for brain functioning**
  - Omega-3 and -6
  - Vitamins B9 and B12
5. **Macronutrients for brain functioning**
  - Carbohydrates
  - Mediterranean diet
6. **Nutrition at the grocery store**
  - Food swaps
  - Frozen food

## A nutritional approach to mental health



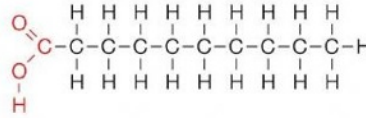
Composition, structure, and function of brain depend on availability of nutrients such as fats, amino acids, vitamins and minerals

- Food intake & quality impacts brain function → diet is a modifiable variable to target mental health, mood & cognitive performance
- Gut hormones, neurotransmitters, microbiota are all affected by diet composition

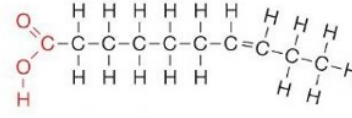
(Dickson et al 2019)

## Definitions

Saturated



Unsaturated



**Fatty acids** - a chain of carbons and hydrogens that make up what is referred to as 'fat' or 'oil' → can be saturated (animal fats) or unsaturated (plant fats)

**Amino acids** - the building block of proteins → the human body needs 20 in order to survive and make the proteins it uses to function (9 of these are essential and cannot be synthesized by the body)

**Neurotransmitter** - a chemical substance released between neurons (the cells in your nervous system) → act as signaling molecules to convey messages between cells

**Microbiome** - the collection of bacteria, viruses & fungi that live within and on the human body → varies between individuals but major groups are conserved

**Cytokines** - proteins used in cell signaling, particularly within the immune system → adipokines are cytokines secreted by adipose tissue (fat cells)

**Oxidative stress** - an imbalance between reactive oxygen species produced by the body and the amount that are being detoxified → toxic by-products from a variety of biological mechanisms that then need to be neutralized

Mental Disorder	Proposed Cause	Treatment	References	Type of Study
Major Depression	Serotonin deficiency	Tryptophan	[15] [32]	Human pilot clinical trial Double-blind, placebo controlled
	Dopamine/Noradrenaline deficiency	Tyrosine	[30] [36]	Double-blind, placebo controlled Randomized within or between subjects
	GABA deficiency	GABA	[29]	Clinical trial
	Omega-3 deficiency	Omega-3s	[39]	Clinical trial
	Folate/Vitamin B deficiency	Folate/Vitamin B	[9] [13]	Randomized controlled trial Clinical trial
	Magnesium deficiency	Magnesium	[14]	Cases studies
	SAM deficiency	SAM	[37]	Double-blind, placebo controlled
Bipolar Disorder	Excess acetylcholine receptors	Lithium orotate & taurine	[50]	Clinical trial
	Excess vanadium	Vitamin C	[45]	Double-blind, placebo controlled
	Vitamin B/Folate deficiency	Vitamin B/Folate	[47] [71]	Human pilot clinical trial Clinical trial
	L-Tryptophan deficiency	L-Tryptophan	[72]	Clinical trial
	Choline deficiency	Lecithin	[73]	Double-blind, placebo controlled
	Omega-3 deficiency	Omega-3s	[21] [48] [74] [75]	Double-blind, placebo controlled Clinical trial Clinical trial Double-blind, placebo controlled
Schizophrenia	Impaired serotonin synthesis	Tryptophan	[53]	Open-baseline controlled trial
	Glycine deficiency	Glycine	[54] [55] [56]	Double-blind, placebo controlled Human pilot open-label trial Clinical trial
	Omega-3 deficiencies	Omega-3s	[59] [60] [65]	Double-blind, placebo controlled Randomized, placebo controlled Open-label clinical trial
Obsessive Compulsive Disorder	St. John's wort deficiency	St John's wort	[69] [70]	Randomized, double-blind trial Double-blind, placebo controlled

(Lakhan and Vieira 2008)

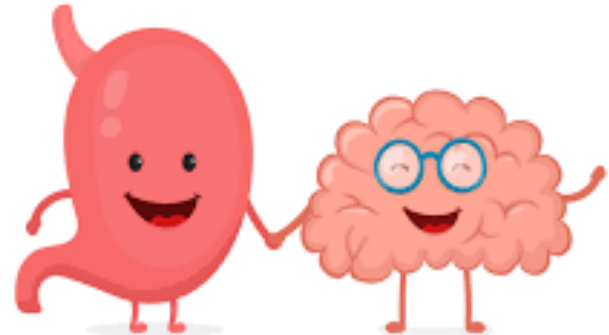
## Gut-brain axis

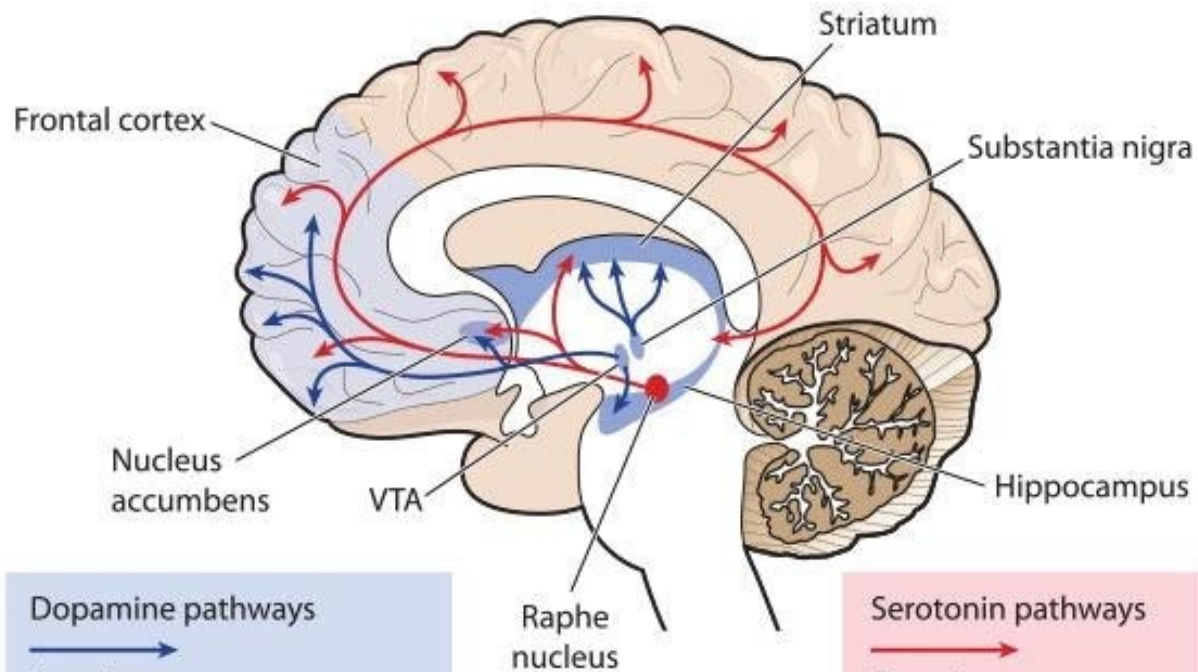
**Gut microbiome** → key mediating pathway for **inflammation**, **oxidative stress**, **neuroplasticity** (ability of the brain to change over time)

- Largest immune and endocrine organ → 70-80% immune cells lie in gut and major source of serotonin and dopamine
- Diet is a *modifiable risk factor* for mental illness
  - Dietary patterns can affect mental illness via pathways independent of weight status

**Leaky gut** - changes in **intestinal permeability** (through high fat diet for example) cause bacterial toxins to activate immune cells in the intestinal wall

- elevated systemic inflammation
- inflammatory cytokines activate the hypothalamic-pituitary-adrenal axis (HPA) which mediates stress response





#### Dopamine pathways



#### Functions

- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

#### Serotonin pathways



#### Functions

- Mood
- Memory processing
- Sleep
- Cognition

## Fiber

The component of food that isn't broken down by your body

- **Soluble fiber** - dissolves in water, affects cholesterol and glucose absorption
- **Insoluble fiber** - doesn't dissolve in water, helps with movement of food

Plays role in **inflammation** → affects **microbiome** composition

- Microbes (bacteria) in gut ferment fiber to make short-chain fatty acids (SCFAs) → positive impact on immune functioning
- Markers of inflammation ↓ with high fiber diet
  - C-reactive protein (CRP)
  - Cytokines i.e. IL-6
- Anti-inflammatory adipokine ↑ with higher dietary fiber
- **Refined wheat** → **whole-grain wheat** = lowered inflammation
  - Whole grain foods rich in phytochemicals (protect against oxidative stress)

### SOLUBLE



OATS



NUTS



SEEDS



BEANS



APPLES



BERRIES

### INSOLUBLE



BROWN RICE



WHEAT BERRIES



RYE



KAMUT



SPELT



FRUITS & VEGGIES

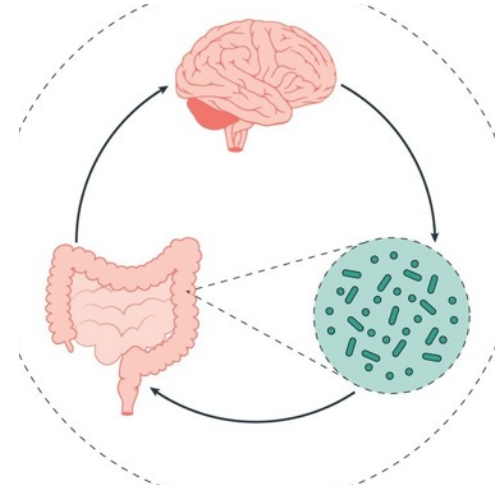


## Inflammation and the brain

### Depression frequently comorbid with inflammatory conditions

#### Inflammation acts as a mediator

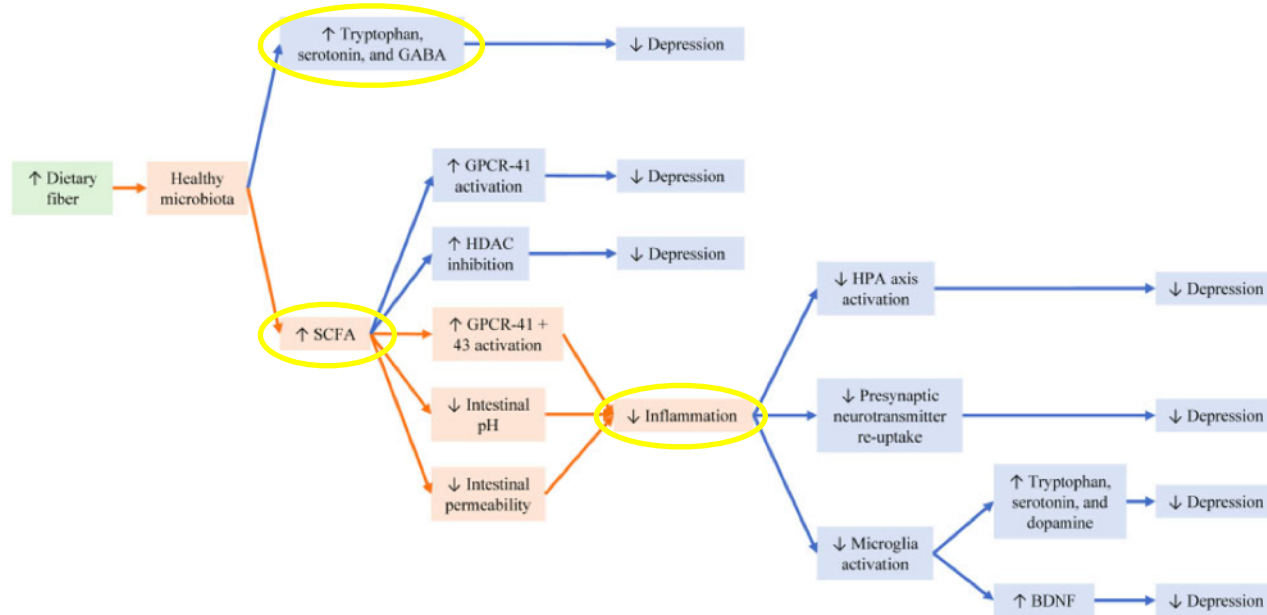
- Studies show parallel increases in inflammatory markers (CRP and IL-6) and depression
  - **Cytokines** induce depressive-like behaviours
- Lower concentrations of **adiponectin** also shown with increasing severity of depression
- Meta-analyses also showed schizophrenia and PTSD are both accompanied by activation of inflammatory pathways and cytokines



- **Short-chain fatty acids (SCFA)** change intestinal pH which changes the composition of the microbiome
  - Dietary fiber alters the SCFA and bacterial toxin production
- Inflammatory cytokines can increase reuptake and decrease synthesis of neurotransmitters (serotonin and dopamine)

(Oddy et al 2020)

## Potential mechanism for this relationship



**Figure 1 Simplified overview of pathways from dietary fiber intake to inflammation and depression.** Abbreviations and symbols: BDNF, brain-derived neurotrophic factor; GABA,  $\gamma$ -aminobutyric acid; GPCR, G-protein-coupled receptor; HDAC, histone deacetylase; HPA, hypothalamic-pituitary-adrenal; SCFA, short-chain fatty acids;  $\uparrow$ , increased;  $\downarrow$ , decreased.

## Protein-neurotransmitter pathway

Most common nutritional deficiencies found in people with mental illness are omega-3 fatty acids, B vitamins, minerals, and amino acid precursors to neurotransmitters

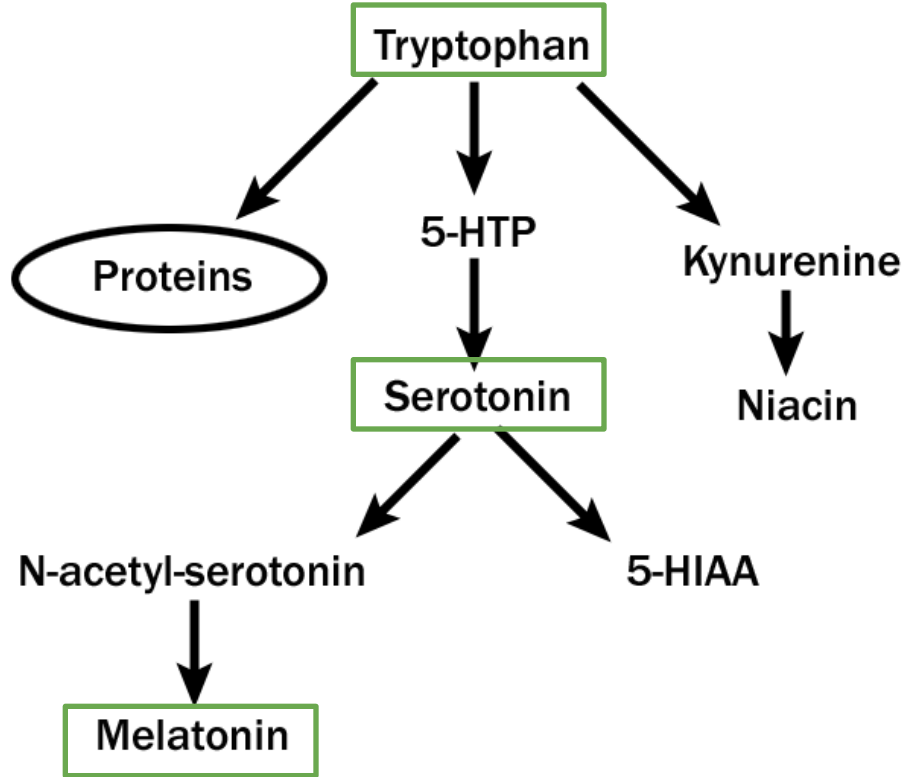
(Lakhan and Vieira, 2008)

Tryptophan → serotonin

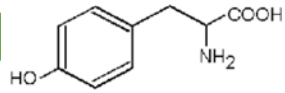


Phenylalanine → tyrosine → dopamine, norepinephrine



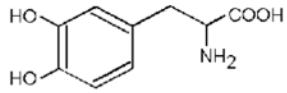


Phenylalanine



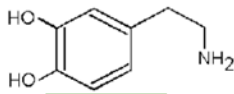
Tyrosine

TH



3,4-dihydroxyphenylalanine (DOPA)

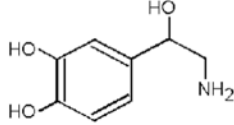
DDC



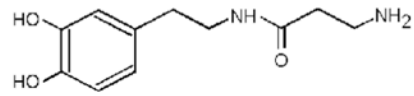
Dopamine

NβAS

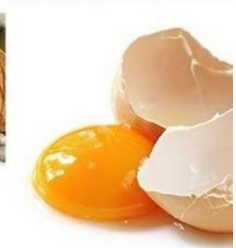
DβH

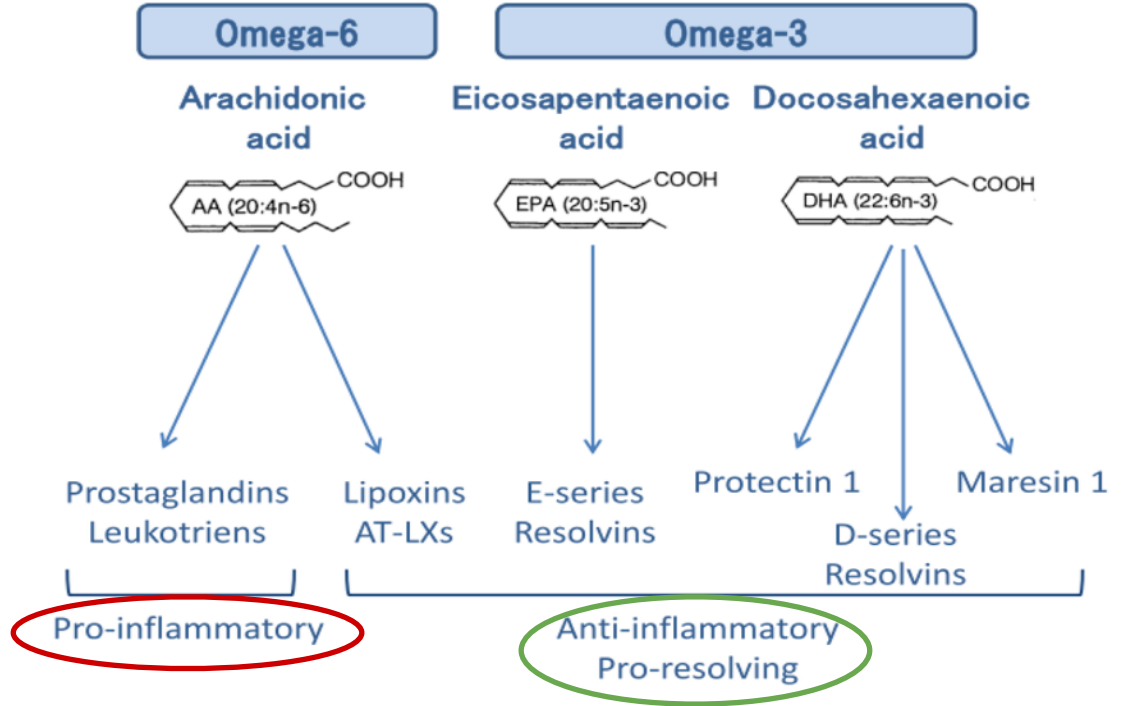


Norepinephrine



N-β-alanyl dopamine



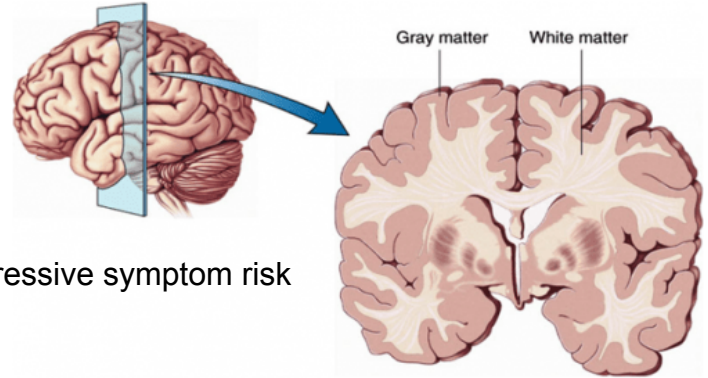


(Hirahashi, 2017)

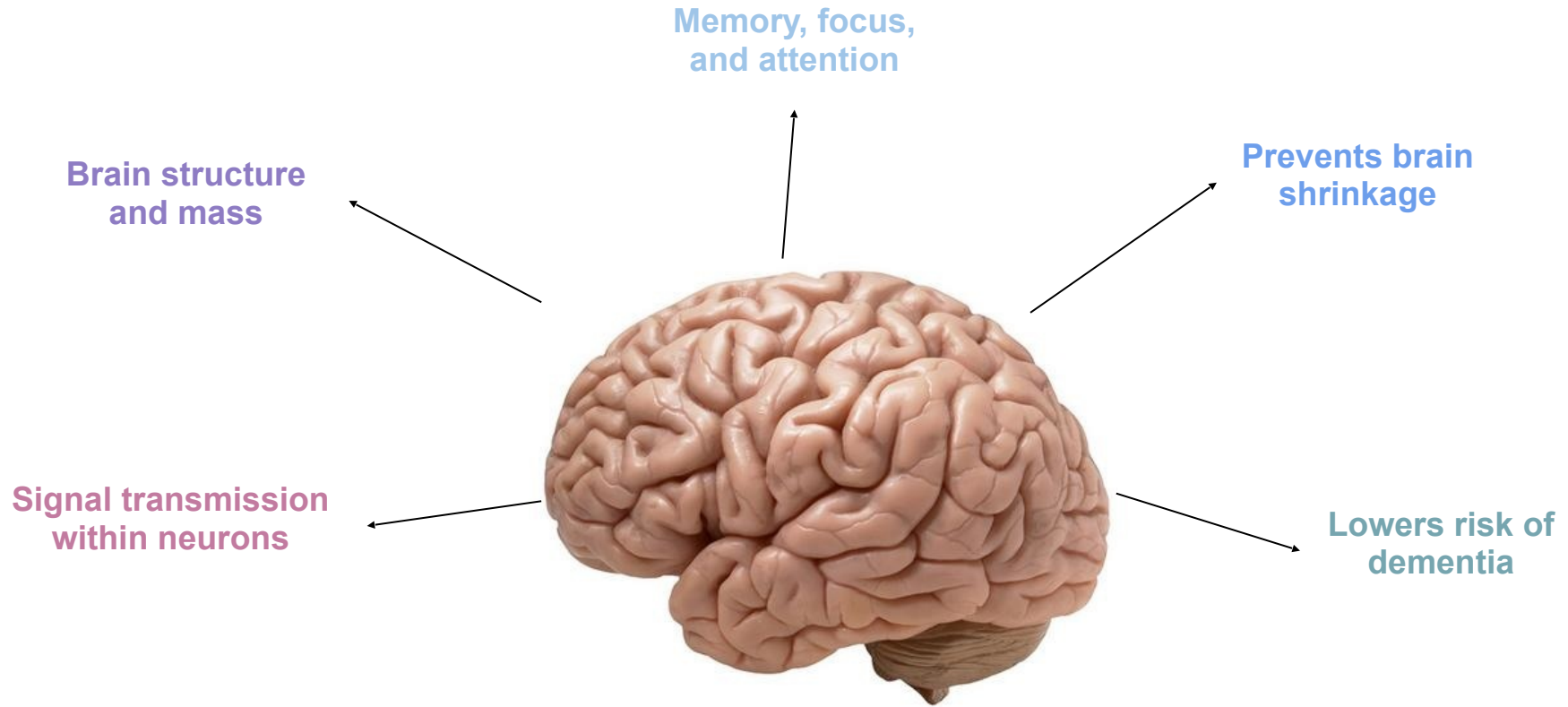
## Nutrients for brain functioning - Omega-3

Essential fatty acid → cannot be synthesized by body

- Brain lipids make up **neuronal membranes**
  - Omega-3s make up 33% of grey matter in brain
  - Higher plasma omega-3 level = less death of grey matter with age (particularly in **hippocampus** and **amygdala**)
  - Higher omega-3 = lower cognitive decline, dementia risk, depressive symptom risk in elderly
- Fatty acid composition in brain is unique
  - Main poly-unsaturated fatty acid (PUFA) is DHA (from omega-3 fatty acid) → **neuroprotective**
  - Endogenous synthesis of these fatty acids are low; relies on **dietary sources** in plasma (blood)



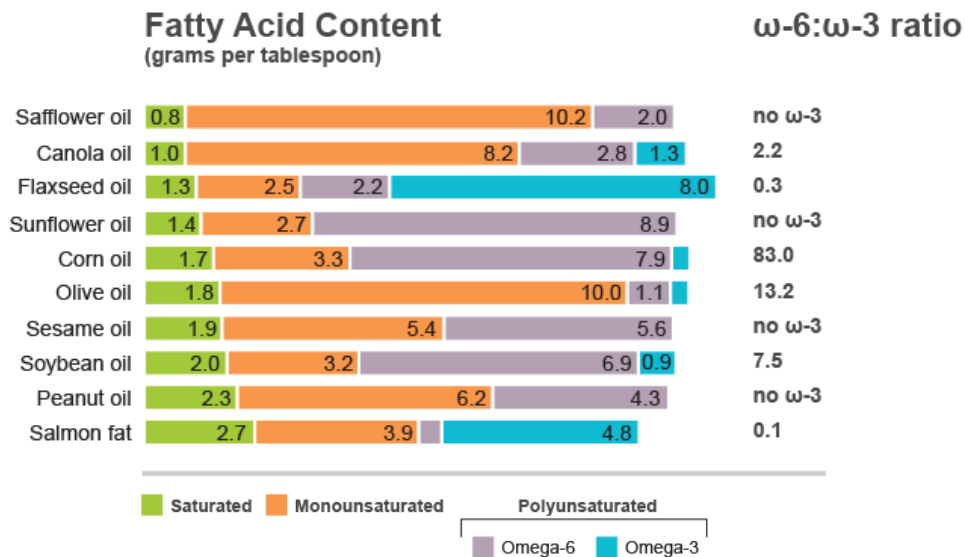




# OMEGA-3 EFFECTS ON THE BRAIN



## Omega-6/omega-3 ratio



(GB Healthwatch)

Ideally aiming for 1:1  
Average modern diet = 16:1

Nut	Omega6:3 ratio
Flaxseed	0.26
Chia seed	0.33
Walnuts	4.2
Macadamias	6.3
Pecans	20.9
Cashews	48.3
Pistachios	53.7

Also eggs, soybeans, tuna, cauliflower

# Nutrients for brain functioning - vitamins

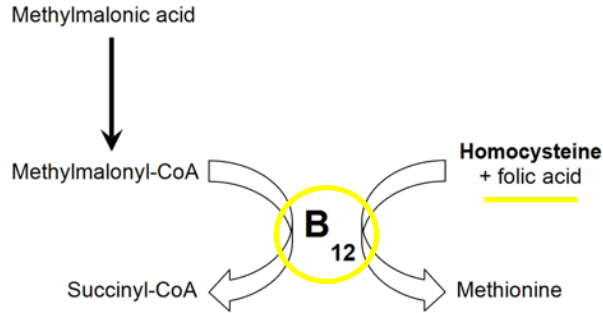
## Vitamin B9 - Folate

- Study participants with depression have blood folate levels on average 25% lower than healthy controls
  - Folate deficiency associated with low levels of serotonin metabolite
  - Converts a chemical called homocysteine to **methionine** - important for DNA synthesis and other pathways in brain
- Can lead to poor outcome with antidepressant therapy - 500mcg folic acid shown to enhance effectiveness of medication

(Young,  
2007)



# Nutrients for brain functioning - vitamins



## Vitamin B12

- Studies have shown that participants with vitamin B12 deficiencies are more likely to have depressive symptoms
- Necessary for synthesis of **methionine** → essential for myelin and neurotransmitters (prevents build-up of homocysteine as well)
- Used to synthesize myelin (coating around neurons)
- Deficiency causes **neurological** and **psychiatric** problems
  - Brain shrinkage accelerated, likely due to increasing homocysteine

(Deth et al 2017)

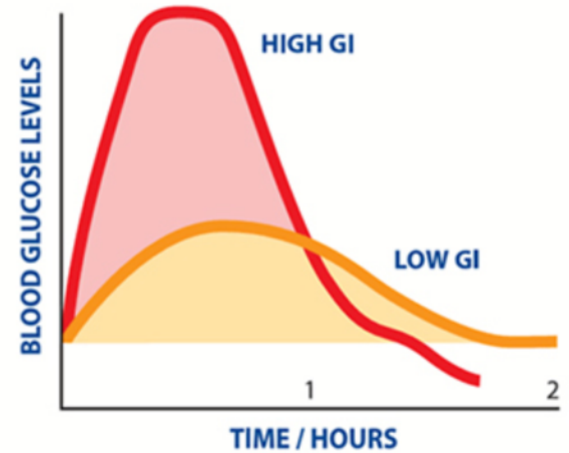
Randomized controlled trials have shown that 0.8mg folic acid/day or 0.4mg vitamin B12/day decreased depression symptoms (Lakhan and Vieira 2008)

## Carbohydrates

Carbohydrates cause a release of insulin → helps tryptophan enter the brain

- Serotonin/tryptophan production triggered by carb rich foods
- **Glycemic Index** → ranking of carbohydrates based on their effect on blood glucose levels
  - Low GI foods more likely to provide moderate + lasting effect on brain chemistry, mood and energy than high GI foods
  - Study with middle aged, healthy women found high GI diet associated with higher levels of CRP (inflammatory marker)

(Rao et al 2008)



**Beneficial nutrients:** monounsaturated fatty acids, high fiber, low omega 6:3 ratio, antioxidants (vitamins C and E), polyphenols

## Mediterranean Diet

What is the Mediterranean diet?

- **Plant-based**, high in **fruits** and **vegetables**, minimally processed foods
  - **Olive oil** main source of added fat
- Focus on **whole-grains**, legumes, nuts & seeds
- Moderate amounts of dairy products, low-moderate fish & poultry, low red meat

Health benefits related to **anti-inflammatory** and **anti-oxidative** properties of the diet

- Lower levels of inflammatory markers
- Higher levels of adiponectin (insulin-sensitizing hormone)
- Protects from oxidative stress

(Scarmeas et al 2015)

Many studies have shown an association between Mediterranean diet and lower levels of cognitive decline

- Systematic review combining 41 studies showed Mediterranean diet induced a protective effect against depression

(Lassale et al 2018)

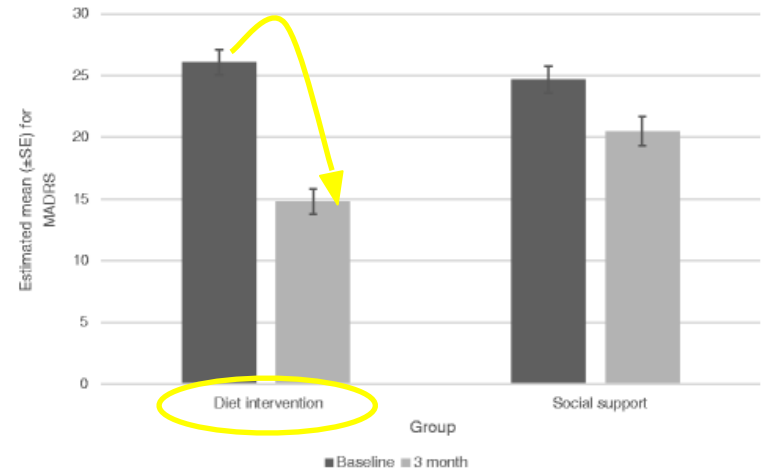


**A randomized controlled trial of dietary improvement  
for adults with major depression  
(the SMILES trial)**

## Mediterranean Diet

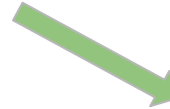
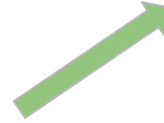
- 'ModiMedDiet' intervention → based on Mediterranean diet
  - included whole grains, vegetables, fruit, legumes, low-fat unsweetened dairy, raw unsalted nuts, fish, lean red meats, chicken, eggs, olive oil
  - reduce sweets, refined cereals, fried food, fast-food, processed meats, sugary drinks
- Participants had to have experienced a major depressive episode and have a baseline diet rated as being poor quality
- Diet intervention group showed significantly greater improvement in MADRS scores at 3 months (Depression Rating Scale), independent of other factors
- Improvements in depressive symptoms were independent of weight change

(Opie et al 2017)





## Food swaps



## Food swaps





## Frozen food

- Great alternative to fresh produce
- Frozen foods retain same nutrients as they had at the time of freezing
  - Some studies have shown frozen fruits and vegetables with higher levels of certain vitamins and antioxidants than the refrigerated counterpart
- Try to stick to individual food items rather than pre-prepared meals for nutritional and economical benefits



## Resources

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QUESTIONS?