Nutrition and Mental Wellness: how food affects the brain

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Outline

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3. **Neurotransmitters**
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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

**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
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(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
- Brown rice
- Nuts
- Wheat berries

**INSOLUBLE**

- Seeds
- Rye
- Beans
- Apples
- Berries
- Fruits & veggies

(helloglow.co)
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, γ-aminobutyric acid; GPCR, G-protein–coupled receptor; HDAC, histone deacetylase; HPA, hypothalamic-pituitary-adrenal; SCFA, short-chain fatty acids; †, increased; ‡, 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)

![Diagram]

- Tryptophan $\rightarrow$ serotonin
- Phenylalanine $\rightarrow$ tyrosine $\rightarrow$ dopamine, norepinephrine
Tryptophan → 5-HTP → Serotonin

Proteins

N-acetyl-serotonin

Kynurenine → Niacin

5-HIAA

Melatonin

Salmon, chicken, eggs, bananas, peanuts, seeds, oatmeal, cheese
Phenylalanine $\xrightarrow{L} \text{Tyrosine} \xrightarrow{\text{TH}} \text{3,4-dihydroxyphenylalanine (DOPA)} \xrightarrow{\text{DDC}} \text{Dopamine} \xrightarrow{\text{N} \beta \text{AS}} \text{Norepinephrine} \xrightarrow{\text{D} \beta \text{H}} N-\beta\text{-alanyl dopamine}
Omni-6

Omega-3

Arachidonic acid

Eicosapentaenoic acid

Docosahexaenoic acid

Prostaglandins

Leukotriens

Pro-inflammatory

Lipoxins AT-LXs

E-series Resolvins

Protectin 1

D-series Resolvins

Anti-inflammatory Pro-resolving

(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

- Brain structure and mass
- Signal transmission within neurons
- Memory, focus, and attention
- Prevents brain shrinkage
- Lowers risk of dementia
Omega-6/omega-3 ratio

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

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<td>Pistachios</td>
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Also eggs, soybeans, tuna, cauliflower

(GH Healthwatch)
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

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)
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

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

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)
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
QUESTIONS?