Neurology in the Metabolic Hinterlands

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PhD, MRPC (UK) (Neurology), MBBS, BMedSci, MSc, NSFW

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www.LCLMH.com

Who is this guy?

- Clinical Neurologist – large NHS practice ~ 3700 patients a year
- PhD – Neuroimaging and Neuroinflammation
- Preventive Healthcare Physician @LCLMH
- Educator –students, doctors, public (especially ethnic minorities)

Conflicts of Interest

A. Small Private Clinic focused on Metabolic Health and Longevity

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D. No funding, completely independent

What do I discuss?

?Alzheimer's and Dementia – need at least 2 hours

What do I discuss?

?Alzheimer's and Dementia – need at least 2 hours

Neuroinflammation – needs at least 1 hour

Scope of Neurological Practice is HUGE

- Headaches
- Seizures
- Stroke
- Neurodegeneration

Scope of Neurological Practice is HUGE

- Neuroinflammation
- Movement Disorders
- Neuromuscular Disease
- Sleep Disorders

Common Neurological Presentations

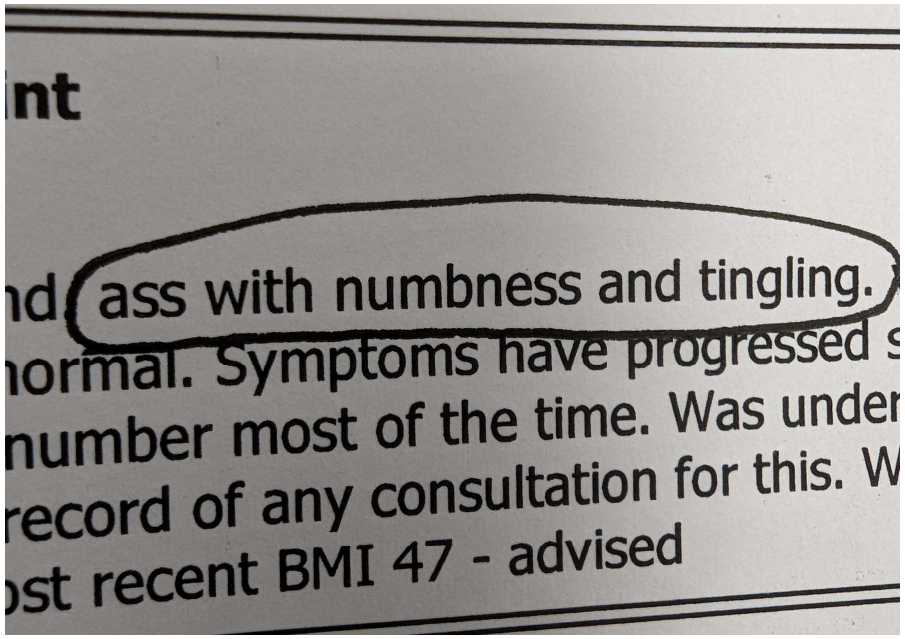
- Pain, including Headaches, Nerve pains
- Weakness, Numbness, Pins and Needles
- Muscle Twitches, Cramp
- Loss of Consciousness, Disorders of Sleep

Common Neurological Presentations

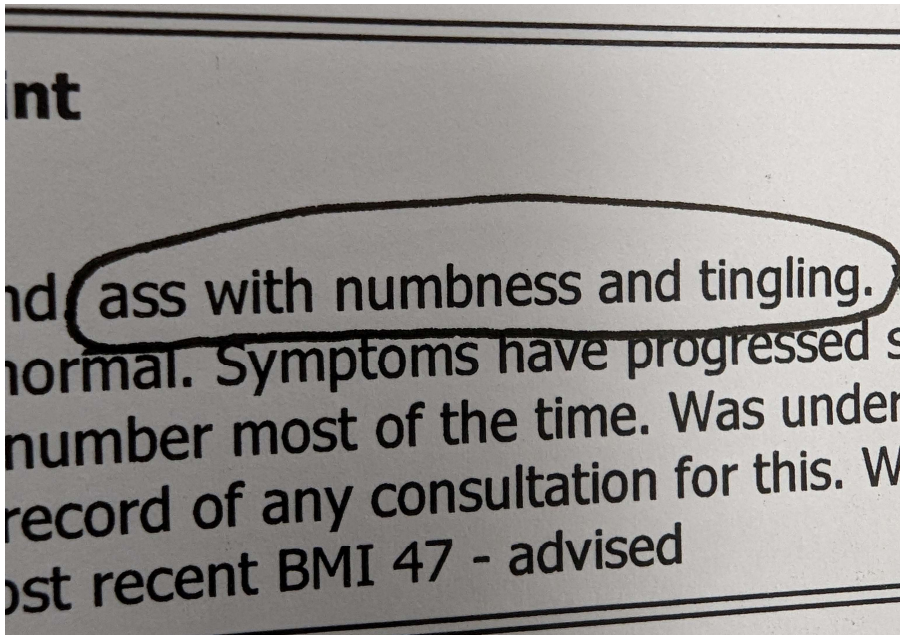
- Visual, Hearing, Speech, Swallow dysfunction
- Sphincter and Erectile dysfunction
- Gait, coordination, autonomic dysfunction
- Cognitive Symptoms, including memory

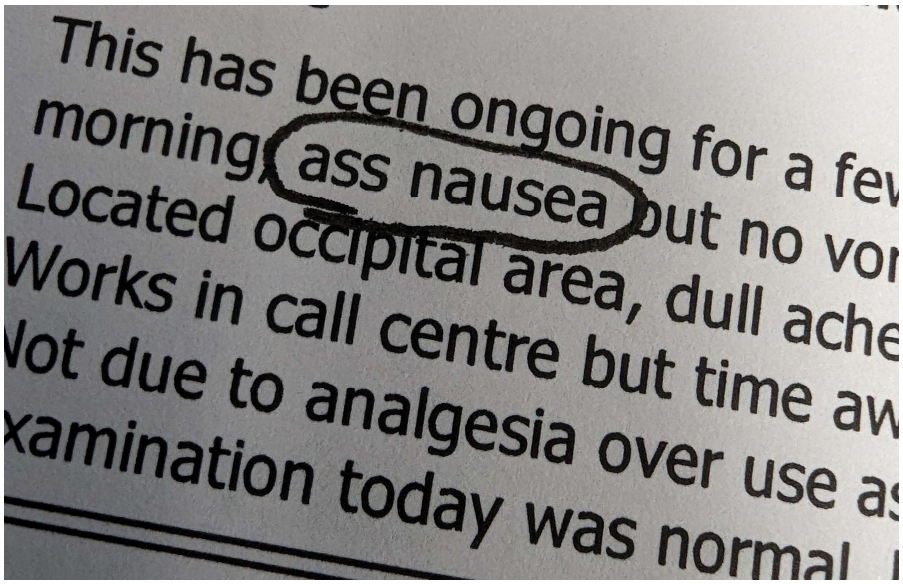
Real GP referrals

Real GP referrals



Real GP referrals





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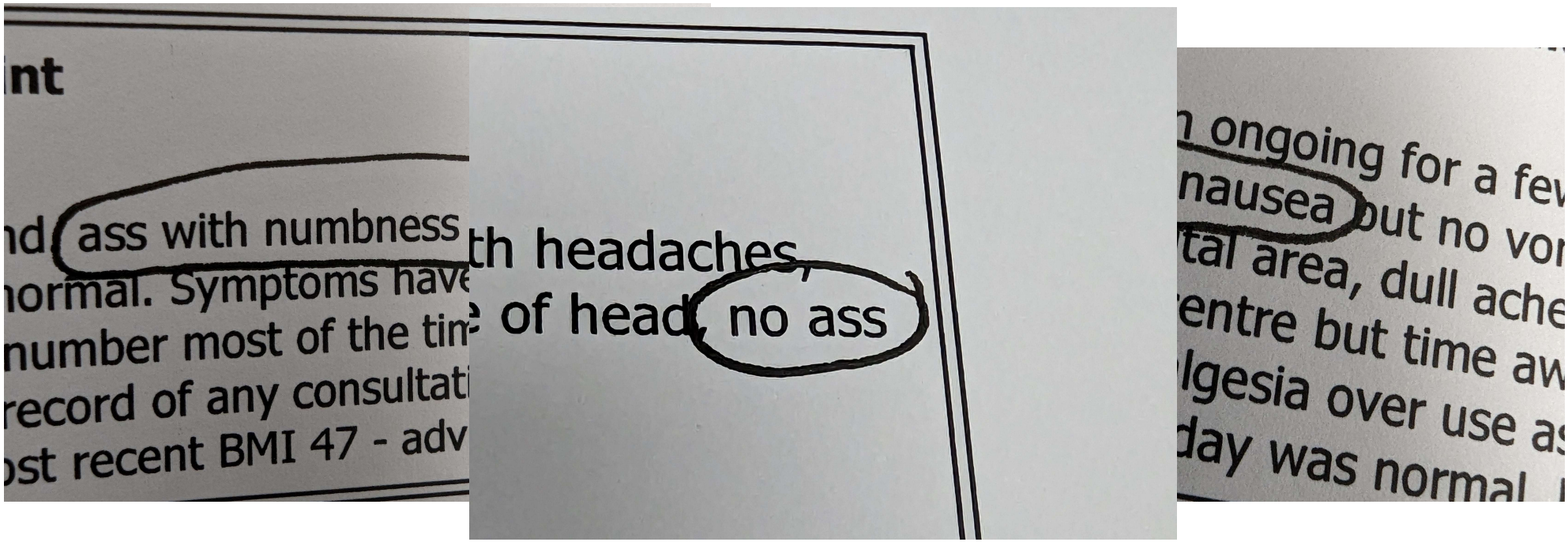


Large Number of Worried Well

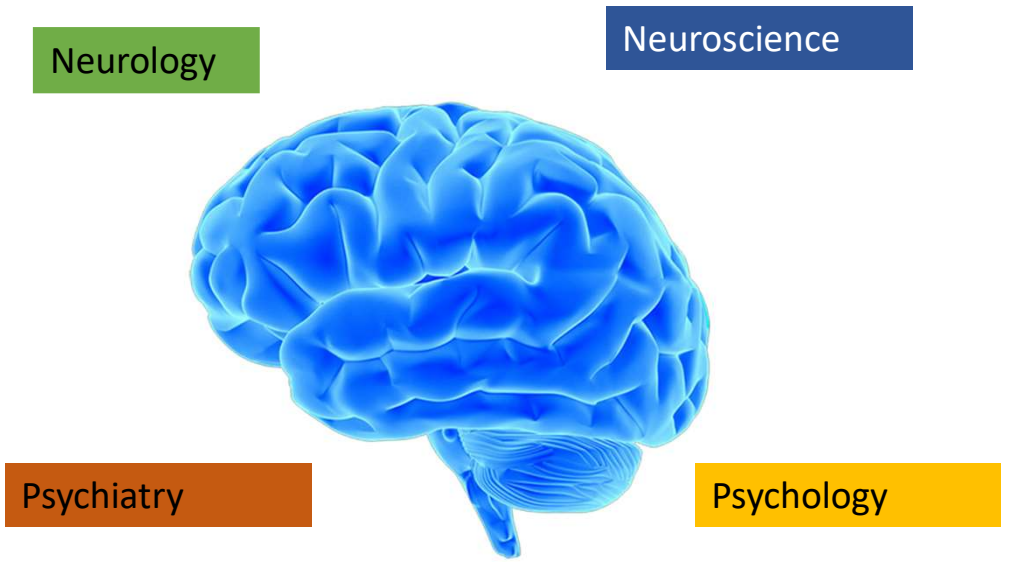
- Headaches: “Do I have a brain tumour?”
- Pain, Pins and Needles: “Do I have Multiple Sclerosis?”
- Twitches and Cramps: “Do I have Motor Neurone Disease?”
- Brain Fog: “Do I have Dementia?”

Real Pathology Increasing

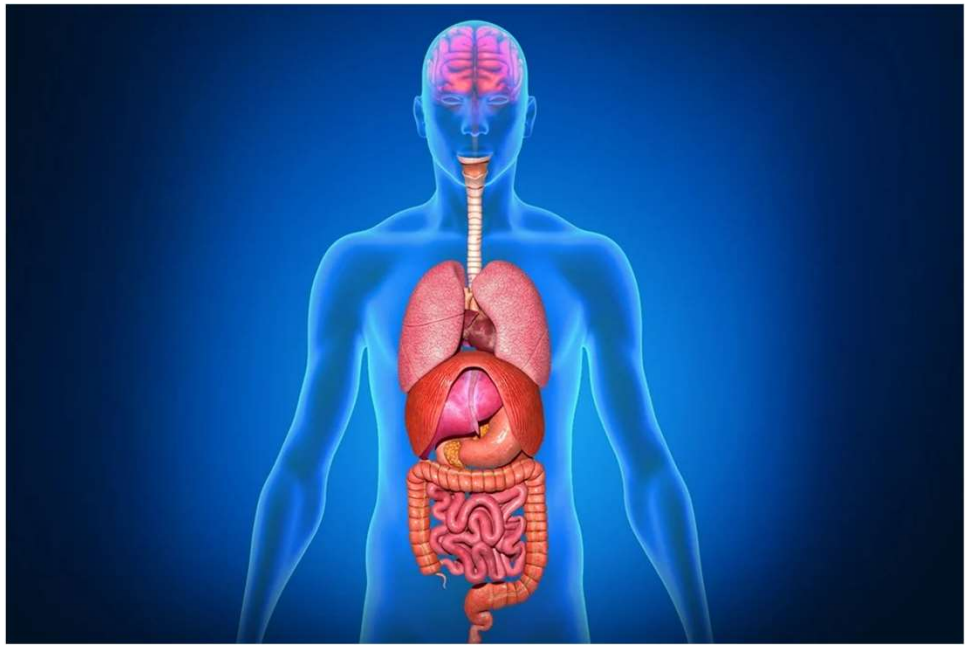
- Neurodegenerative Disease
- Stroke
- Neuroinflammation
- Neuropsychiatric conditions

Modern Neurology (Medicine as a whole)

- Tunnel Vision
- Short-sighted
- Compartmentalised



Modern Neurology (Medicine as a whole)



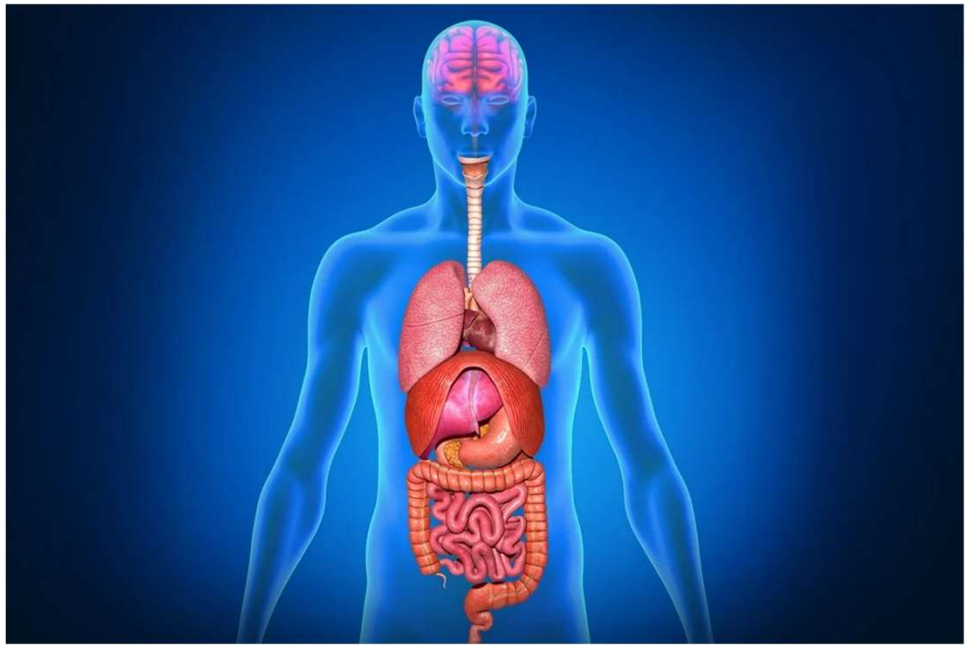
Neurology

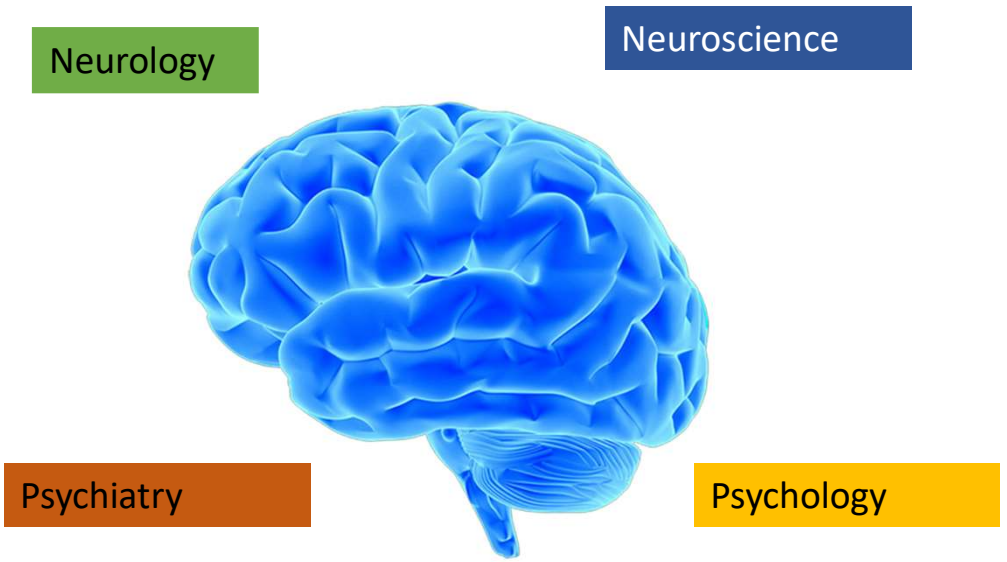
Neuroscience

Psychiatry

Psychology

Modern Neurology (Medicine as a whole)

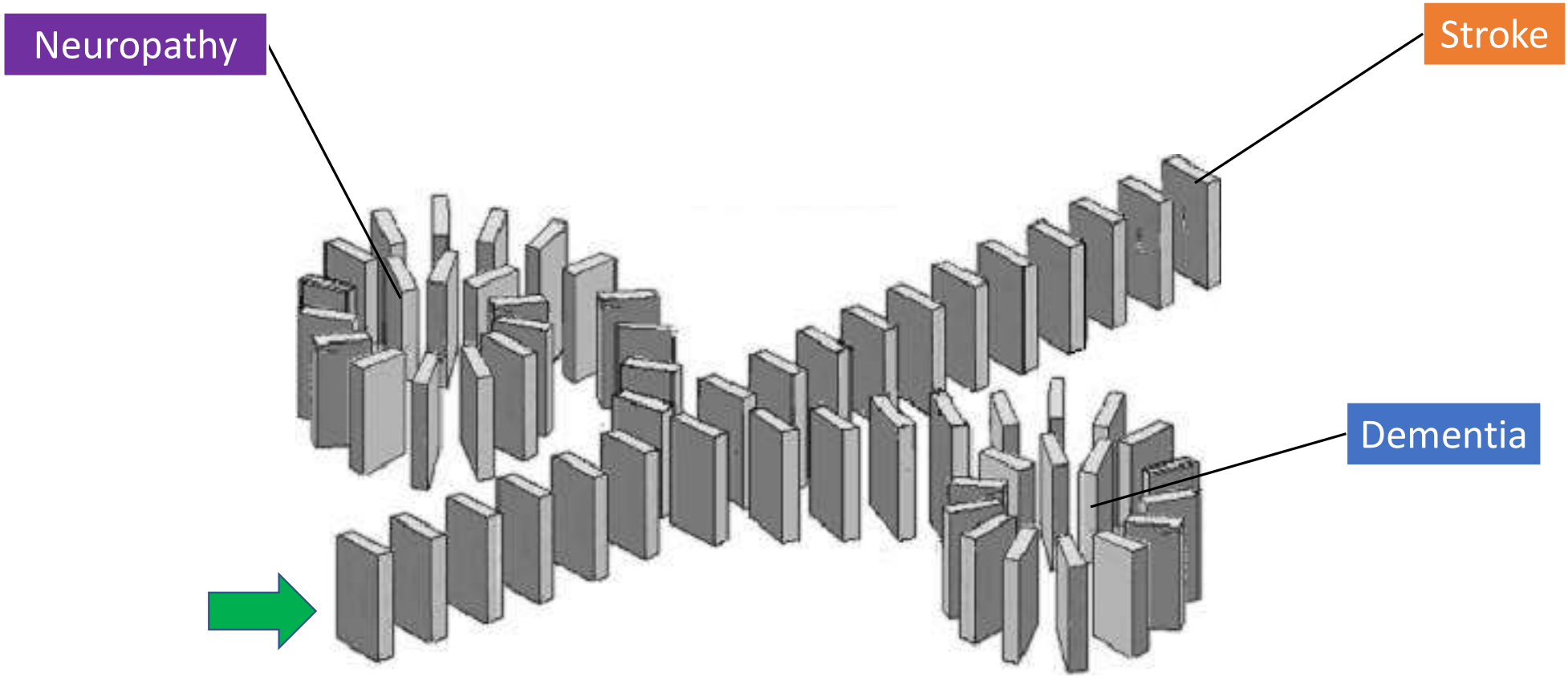


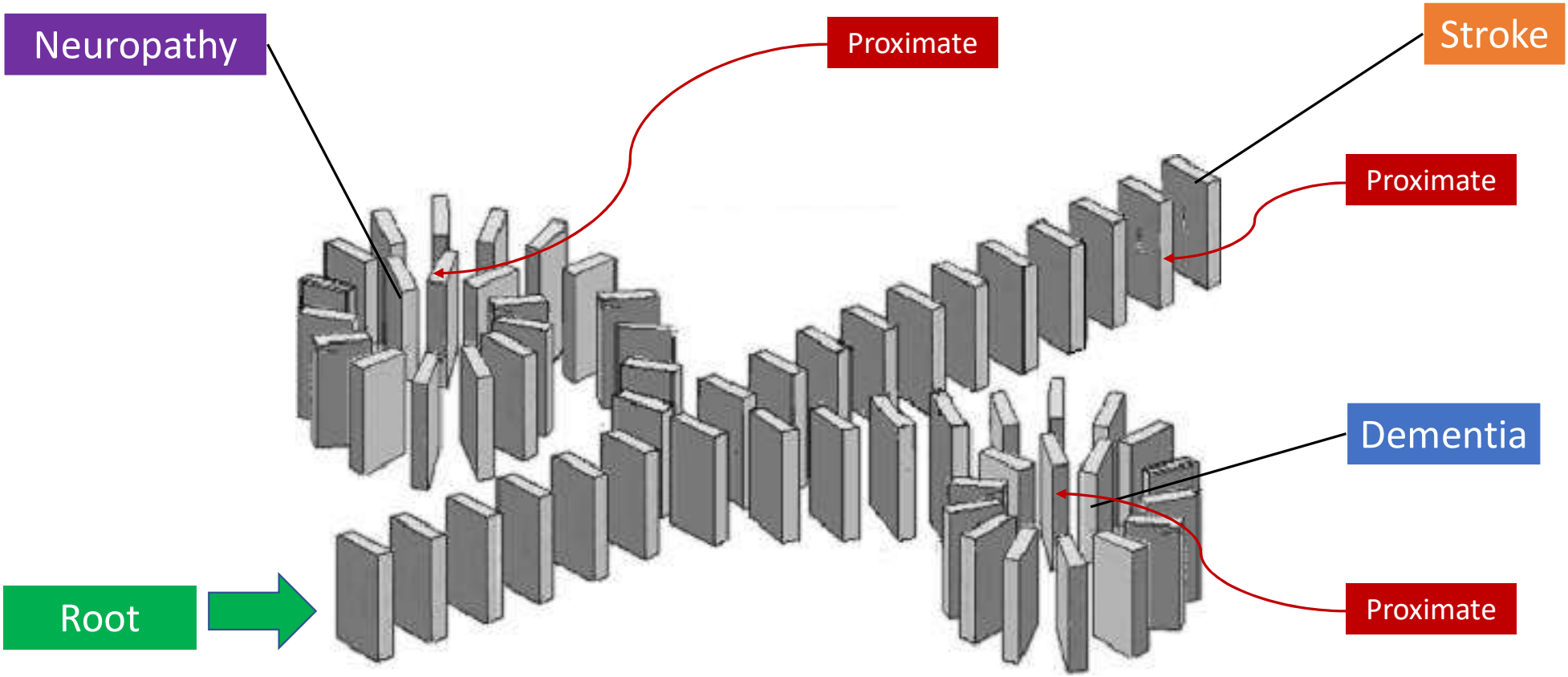


Need a **whole-systems** approach to medicine

Modern Neurology (Medicine as a whole)

- Patients mainly seen once disease has started
- Focused on **Proximate** rather than **Root** cause


Neuropathy
Stroke
Dementia


Neuropathy
Proximate
Stroke
Proximate
Dementia
Proximate
Root

Modern Neurology (Medicine as a whole)

- Focused on either

Pharmacological intervention

or

No intervention at all

Root Cause Approach to Neurology

- Significant **Metabolic Dysfunction** is seen in many pathologies
  - Common, non-sinister presentations
  - Sinister Pathologies

Metabolic Dysfunction

- Disruption of normal physiological infrastructure and processes:
  - Excess/Inappropriate Inflammatory pathway signalling
  - Vitamin, Mineral and Electrolyte Imbalances
  - Hormonal Disruption/Dysregulation
- Inherited – very rare
- Acquired – very common

Metabolic Dysfunction (Non-Sinister)

- Migraine
  - Strong association with Oestrogen – 30-40% of women will suffer migraine at some-point during their menstruating years
  - Common with gynaecological disorders
  - Also common with disruption of normal physiological Insulin, Cortisol, Oestrogen, Testosterone balance
  - Folate Deficiency strongly associated with Migraine + aura

Metabolic Dysfunction (Non-Sinister)

- Peripheral Neuropathy (Axonal Sensory-predominant)
  - Diabetes Mellitus
  - Alcohol (doesn't have to be excess…)
  - B12/Folate Deficiency
  - 80% no cause found ("idiopathic")
    - Large proportion will develop Type 2 DM in the next 5 years
    - More sophisticated B12/Folate testing often demonstrates deficiency despite "normal" serum levels

Metabolic Dysfunction (Sinister)

- Dementia (especially Alzheimer's and Vascular)
- Stroke
- **Numbers are rising**

Rising Neurology-Adjacent Conditions

- ~10% of patients attending Neurology clinic
- Fibromyalgia
- Chronic Fatigue Syndrome

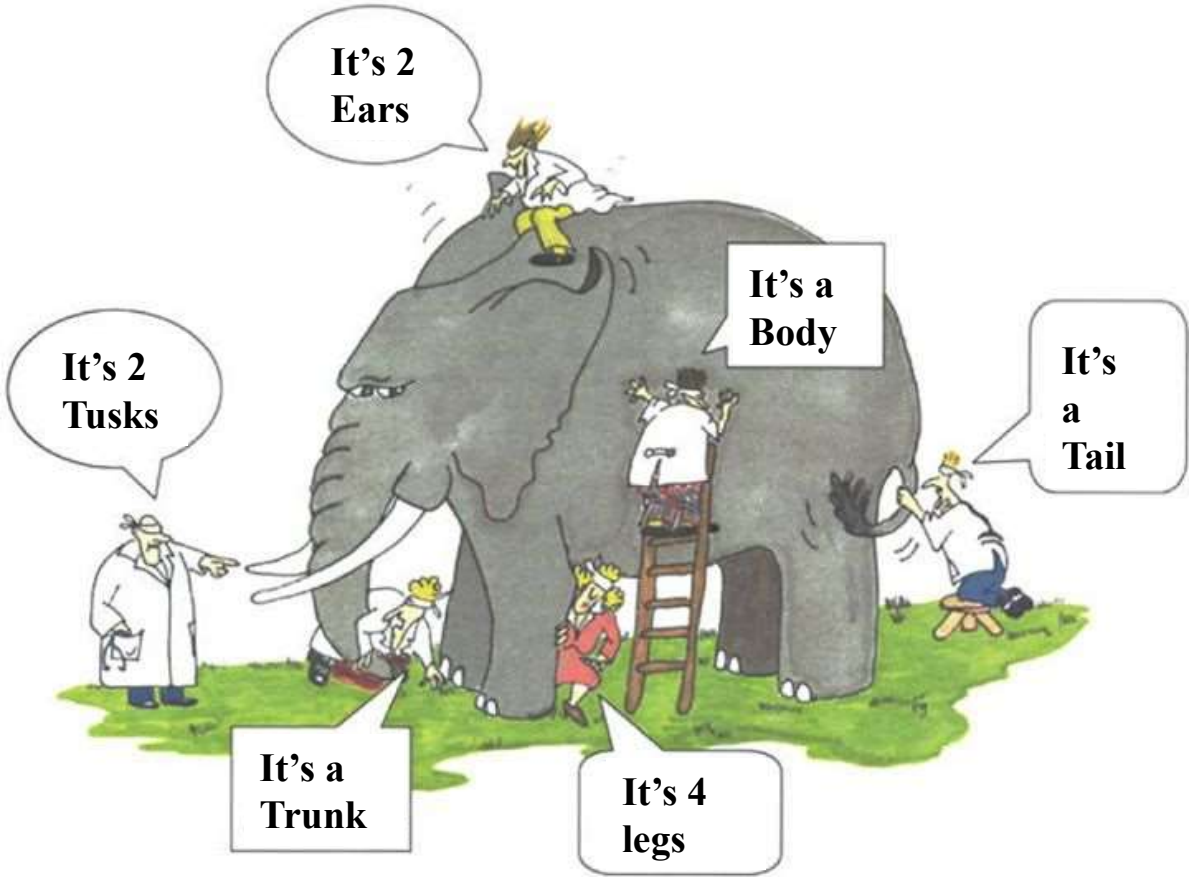
Rising Neuropsychiatric Phenomena

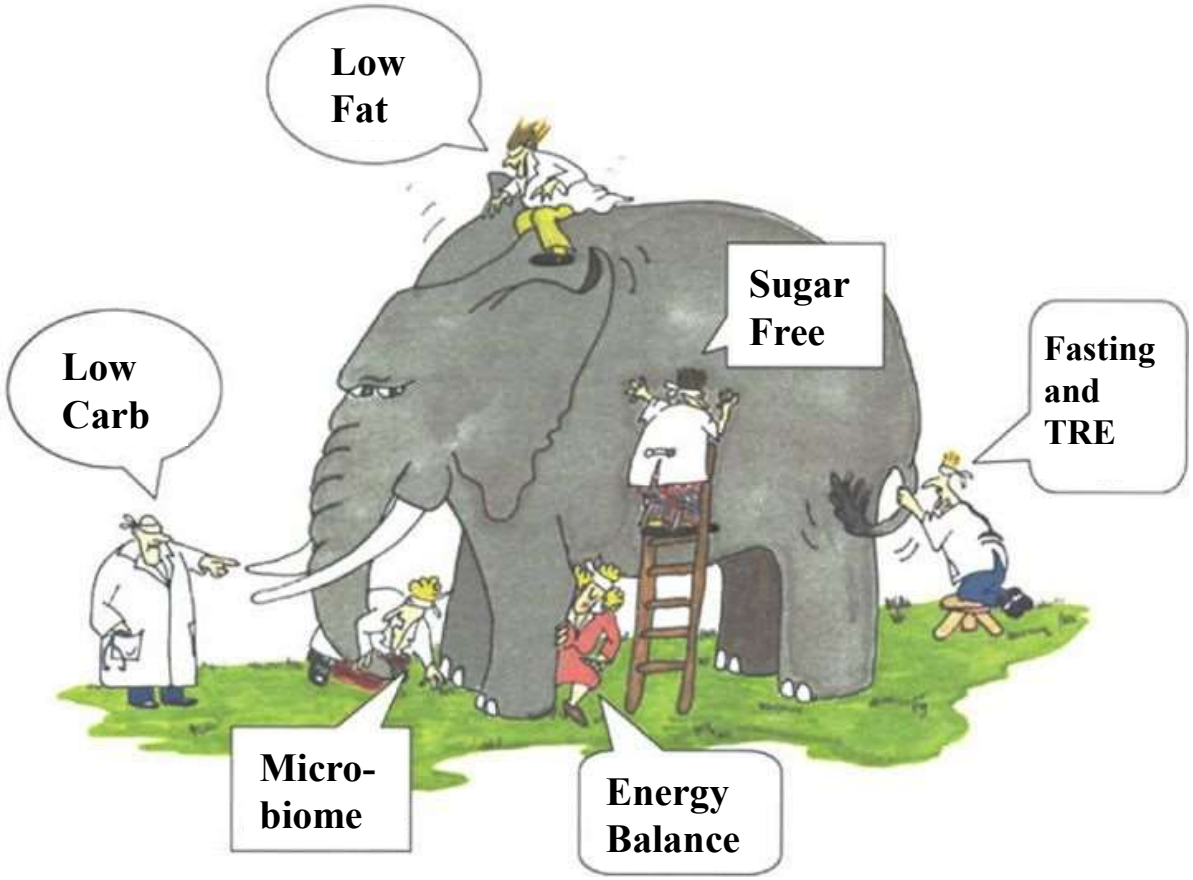
- Female > Male, Teens/early 20's
- Non-Epileptic Attack Disorder
- Tics / Tourette's
- Strongly coexisting with Anxiety, Depression, Attention issues

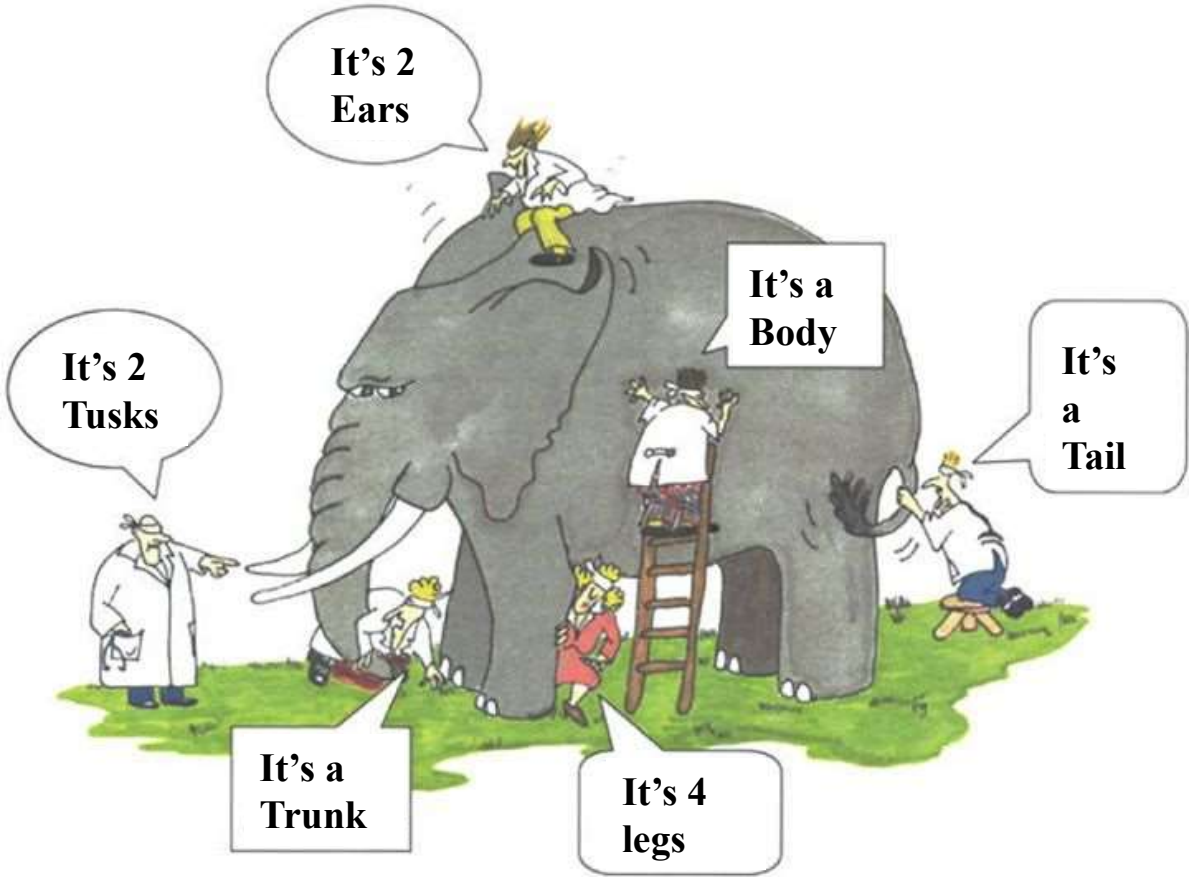
Causes of Acquired Metabolic Dysfunction

- Environmental
  - >90% Dietary
  - Sleep and Exercise also contribute

- **Nutritional Modulation is key**
  - Food is very emotional, and conducive to tribalism
  - Easy to fall into the trap of Ideological thinking/Dogmatism when considering diet


It's 2 Ears
It's a Body
It's a Tail
It's 2 Tusks
It's a Trunk
It's 4 legs


Low
Fat
Sugar
Free
Low
Carb
Fasting
and
TRE
Micro-
biome
Energy
Balance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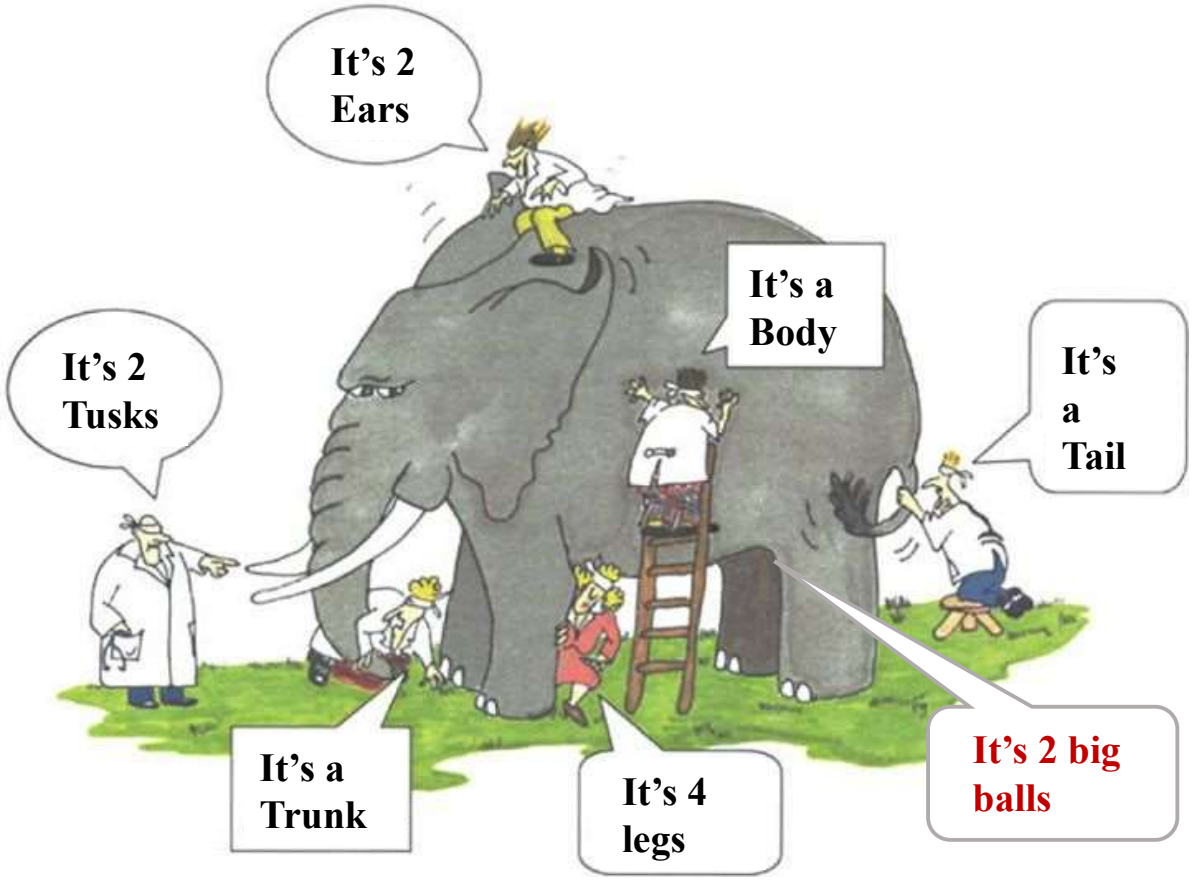
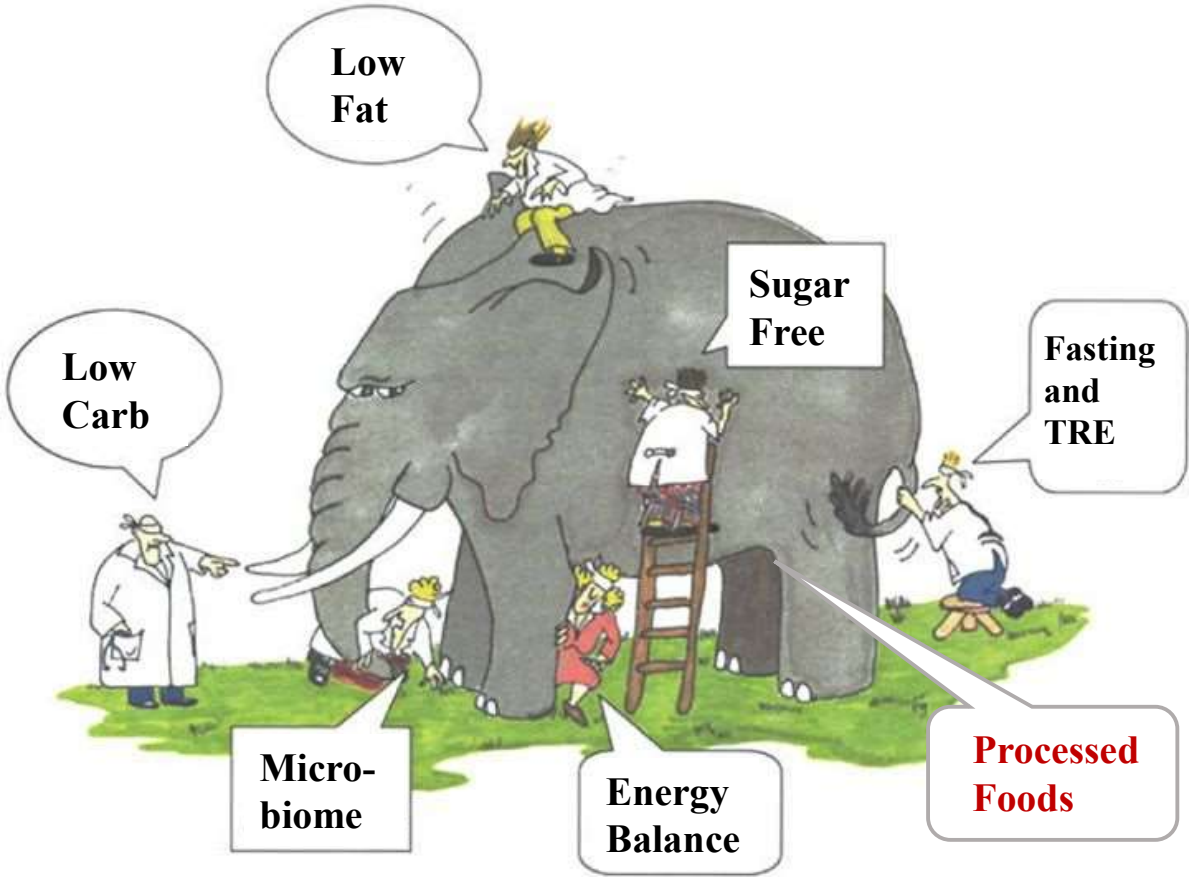

It's 2 Ears
It's a Body
It's a Tail
It's 2 Tusks
It's a Trunk
It's 4 legs
It's 2 big balls


Low Fat
Sugar Free
Low Carb
Fasting and TRE
Micro-biome
Energy Balance
Processed Foods

Processed Food

- Strongly associated with significant metabolic dysfunction
  - GIP predominant gut Incretin signalling and resultant Hyperinsulinaemia
  - Lower Leptin, Higher Ghrelin signalling
  - Increased Hypothalamic Melanocortin Pathway Orexogenic Signalling
  - Increased Visceral Fat Deposition (especially in females)
  - Increased Metabolic (non-alcoholic) liver disease
  - Omega 6:3 ratio >20:1 – pro-inflammatory
- Associated with **Anxiety, Depression, Attention issues**

Rising Neuropsychiatric Phenomena

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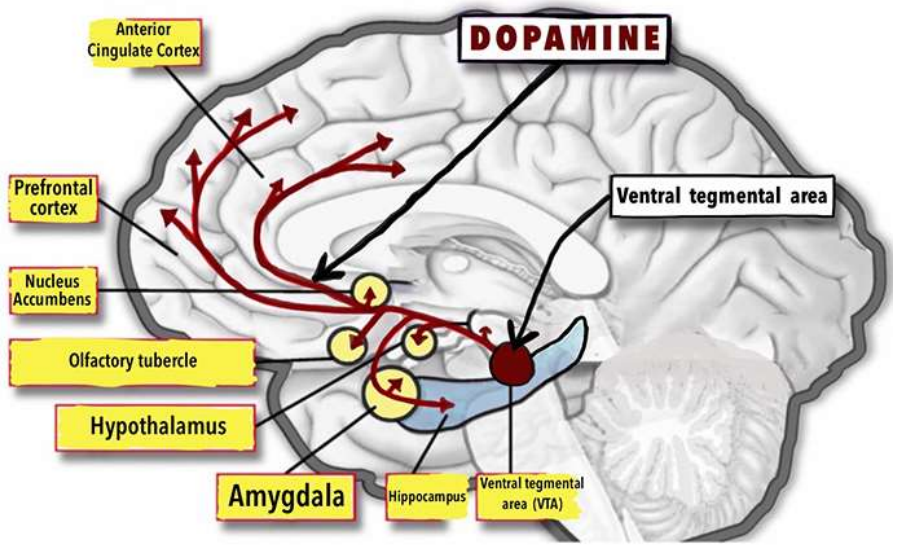
But, there is more going on…

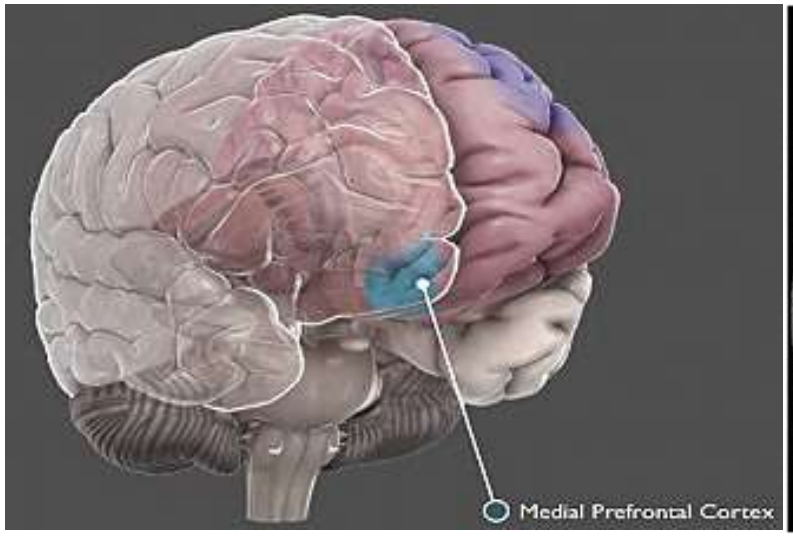
Brain Dopaminergic Reward Networks

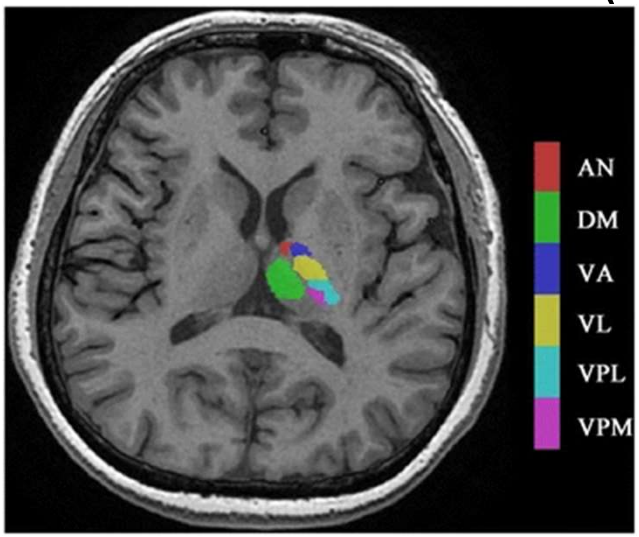
- **Mesolimbic dopaminergic reward pathways** are related to addiction
- **Ventral Tegmental Area (VTA)** is central
- Anterior Cingulate Cortex (ACC)
- Prefrontal cortex (PFC)
- Nucleus Accumbens (NA)
- Olfactory Tubercle
- Hypothalamus
- Amygdala
- Hippocampus



Brain Dopaminergic Reward Networks

- Recent murine models of reward-motivated behaviour also point to involvement of the **mPFC** and Anterior Thalamic Nuclei (**ATN**)





(Yang et al, Nature Communications, 2022)

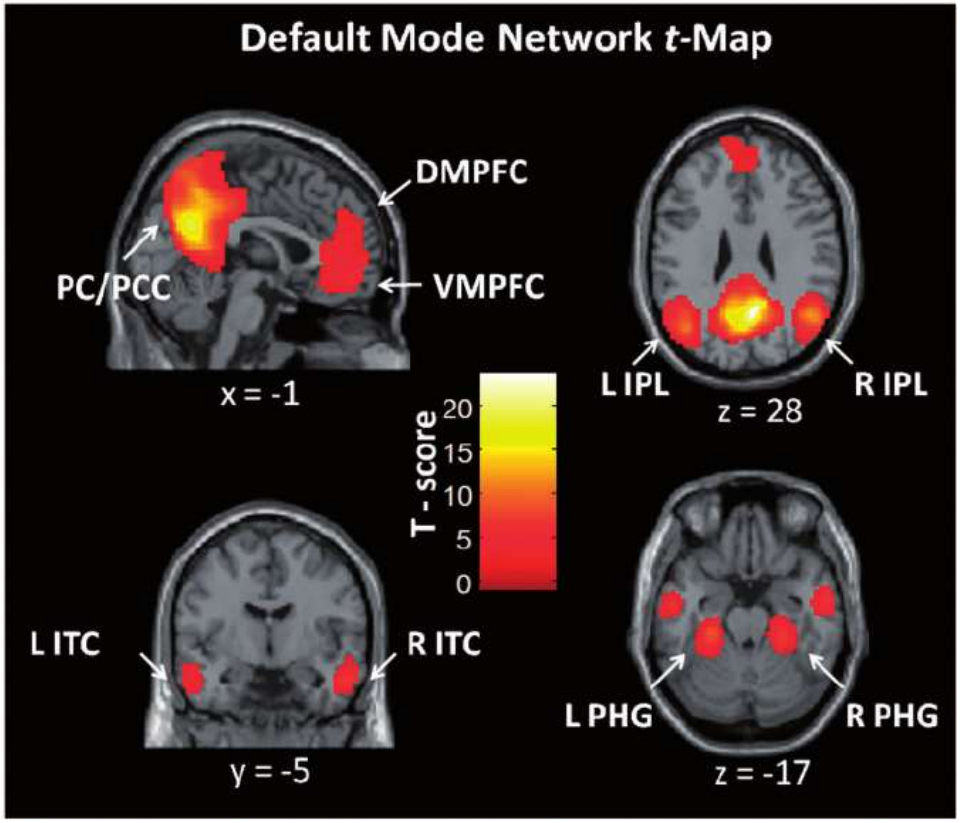
Brain Dopaminergic Reward Networks

- **fMRI brain imaging in humans shown social media videos** -> mainly activated **mPFC** and **ATN**, suggesting very similar reward-motivated behaviour

(Yang et al, Nature Communications 2022)

Default Mode Network

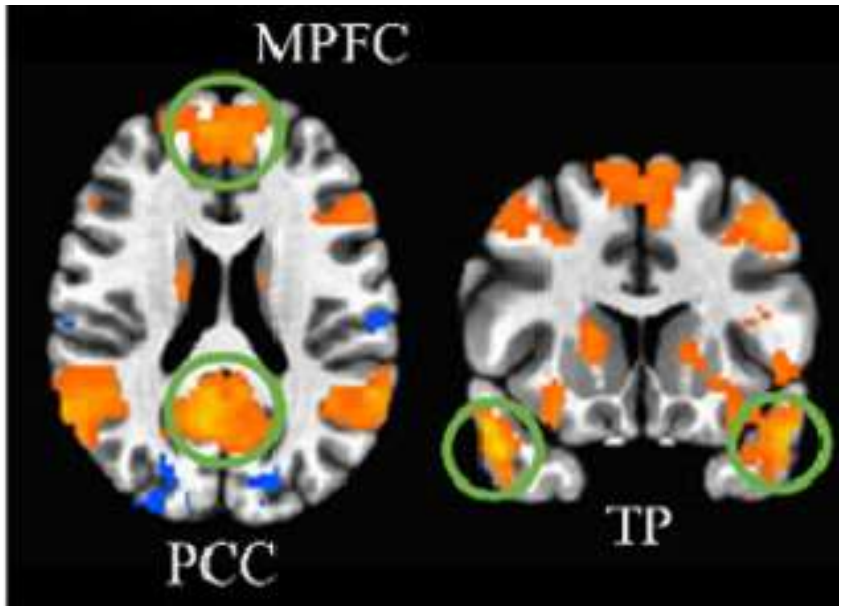
- Medial Pre-frontal Cortex (mPFC)
- Posterior Cingulate Cortex (PCC)
- Angular Gyrus/Inferior Parietal Lobule
- Temporal Poles (infeor-lateral mainly)
- Para-hippocampal Gyrus (PHG)
- Activated mainly when not engaged in active thought, with worry and constant rumination
- It inhibits active cognitive processing and problem-solving
- Linked to Depression/Anxiety



(Taylor et al, Social Cognitive and Affective Neuroscience, 2013)

Default Mode Network when watching TikTok

- Medial Pre-frontal Cortex (mPFC)
- Posterior Cingulate Cortex (PCC)
- Angular Gyrus/Inferior Parietal Lobule
- Temporal Poles (infeor-lateral mainly)
- Para-hippocampal Gyrus (PHG)
- All areas of the DMN were active when watching personalised TikTok videos
- VTA also active (central to dopaminergic reward pathway)



(208 young adults, Su et al, Neuroimage, 2021)

TikTok's effects on Anxiety/Depression

- >3000 teenagers using TikTok
- Association with TikTok use and **increased Depression and Anxiety**, and **reduced Digit span Attention/Registration/Recall**

(Sha and Dong, Int J Environ Res Public Health, 2021)

Stopping Social Media for 1 week

- Randomised 2 arm study, 154 participants, mean age 29
- **Duration: 1 week**
- Arm 1: Normal use of Social Media (Facebook, Instagram, Twitter, TikTok)
- **Arm 2: Cease all Social Media**
- Controlled for baseline anxiety, depression and well-being, age, sex
- **Reduced Anxiety and Depression, Increased Well-being in Arm 2**

(Lambert et al, Cyberpsychol Behav Soc Netw, 2022, Abstract only)

Processed Food

- Strongly associated with significant metabolic dysfunction
  - GIP predominant gut Incretin signalling and resultant Hyperinsulinaemia
  - Lower Leptin, Higher Ghrelin signalling
  - Increased Hypothalamic Melanocortin Pathway Orexogenic Signalling
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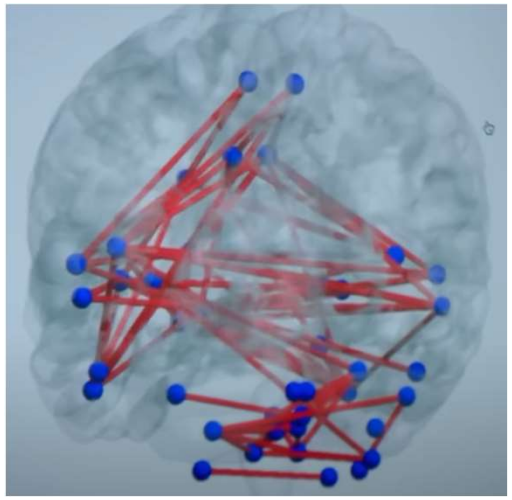
  ?Dopaminergic addiction promoting, and Default Mode Network Stimulating

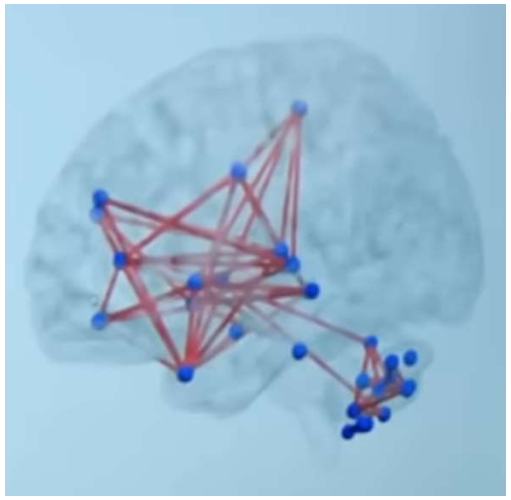
Processed Food

- fMRI of Dr Chris Van Tulleken after 4 weeks on a high Ultra-Processed Food diet in the BBC Documentary “What are we feeding our kids”

Processed Food

- The simplified and unclarified images look very much like the areas associated with the **Mesolimbic reward pathways**, and the **Default Mode Network**





Take Home Points

- **Metabolic Dysfunction** affects every system, including Neurological
- **Nutritional Modulation** is key, but **other factors** also contribute
- Avoid **Single Variable Thinking and Dogmatism**
- Much of the **problem is Societal**, and not just at the Individual level

Get in touch

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Thank you!

Any Questions?