MISSED CONNECTIONS: THE ROLE OF FAULTY WIRING IN ANOREXIA NERVOSA

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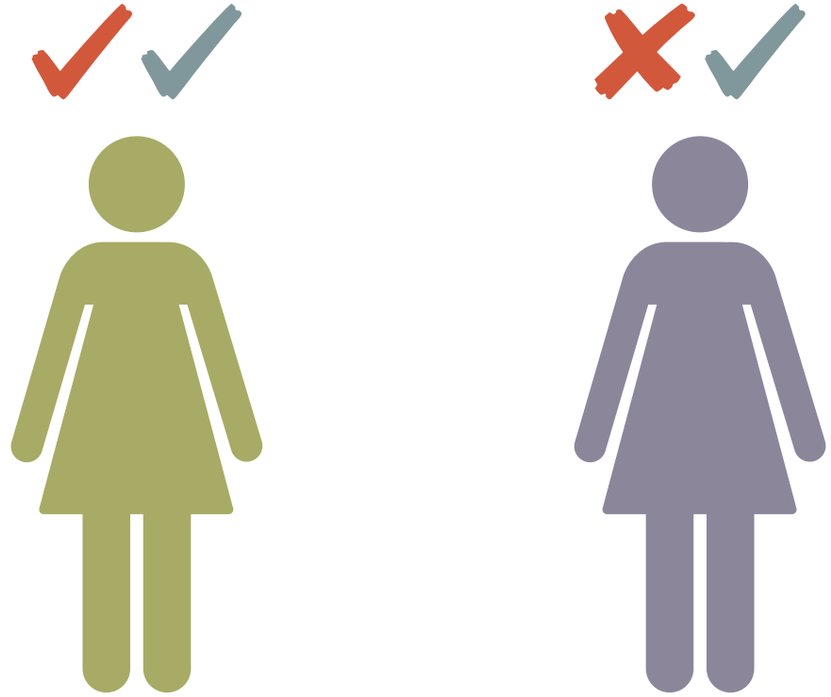
KEY POINTS

- **Variations in brain structure** have been reported in women with Anorexia Nervosa (AN).
- Some of these variations are **state-dependent**.
- Others are **trait-based**.

reversible consequences of **malnutrition**

irreversible consequences of **malnutrition**

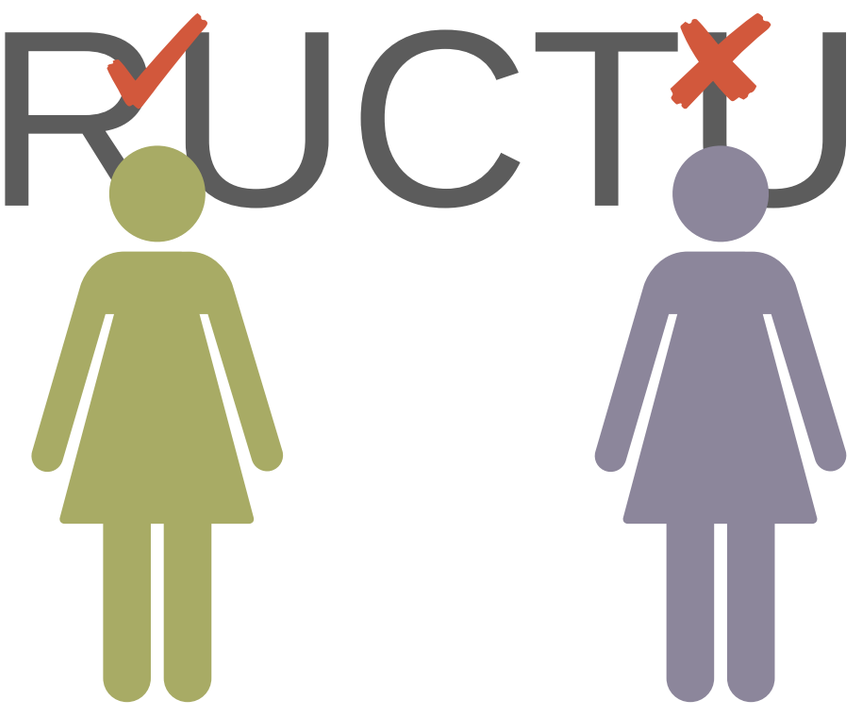
neurodevelopmental differences associated with disease vulnerability



current AN
BMI < 18.5 kg/m²

past AN
BMI > 18.5 kg/m²

STATE-DEPENDENT CHANGES IN BRAIN STRUCTURE



current AN
BMI < 18.5 kg/m²

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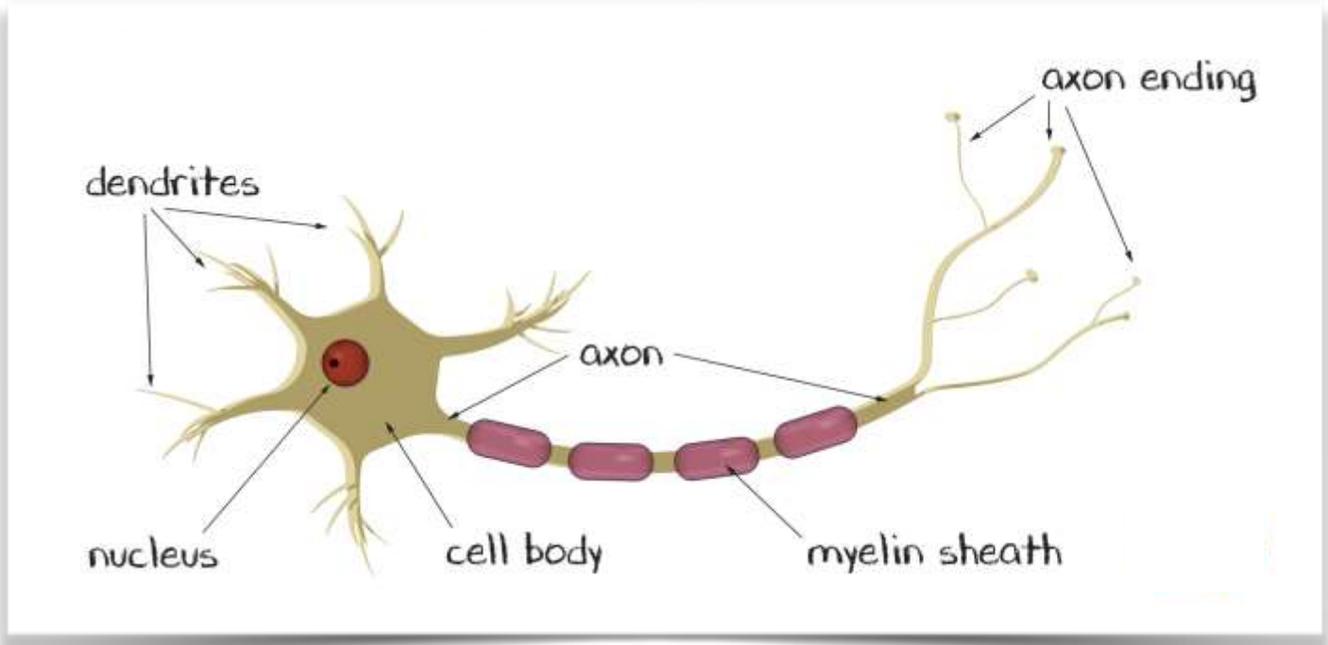
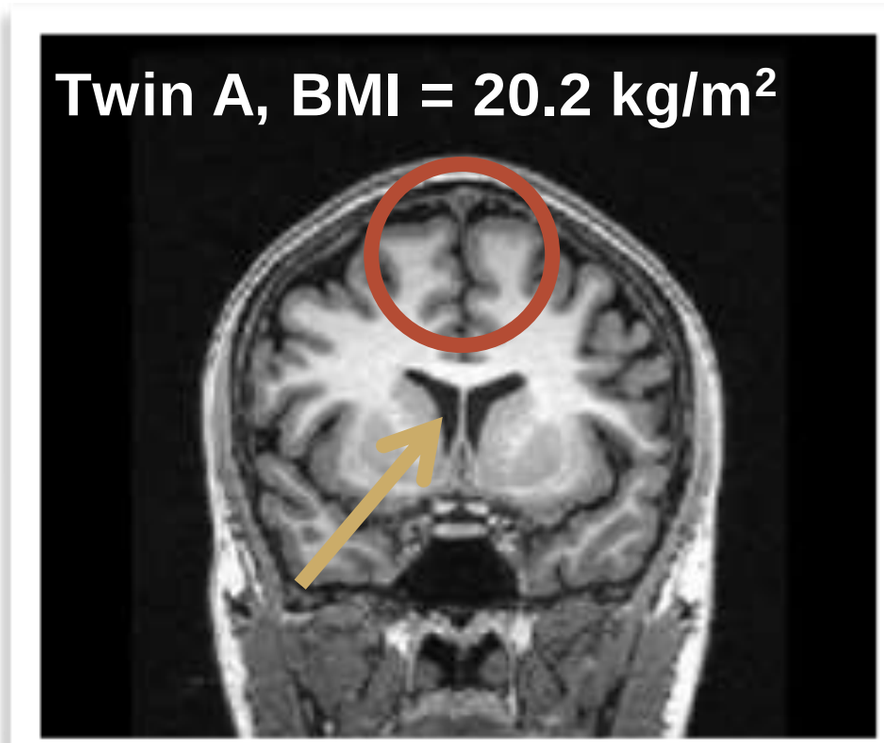
WHAT IS IMPACTED?

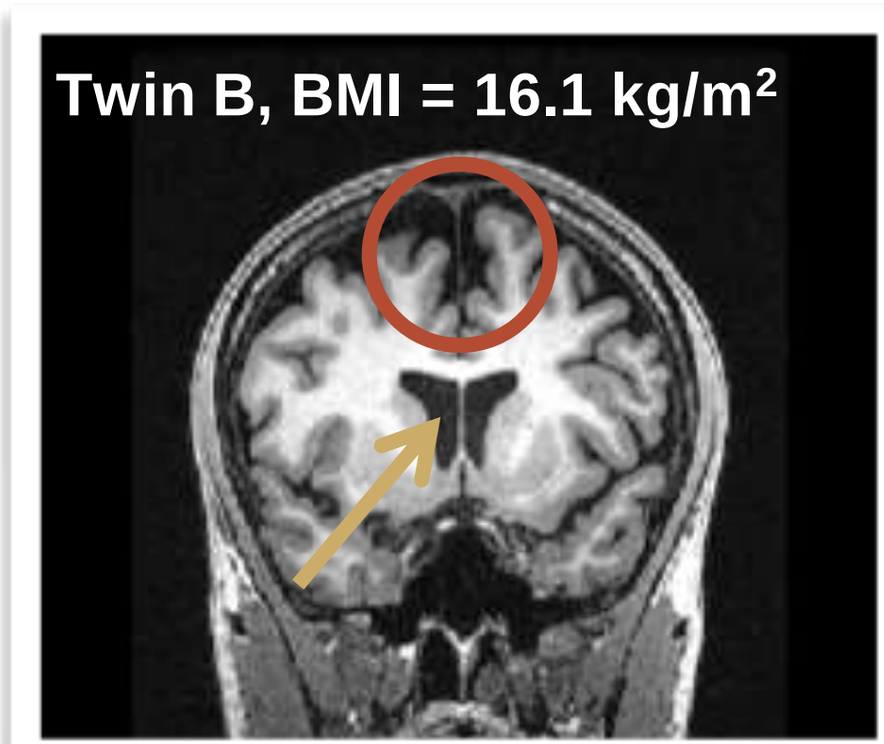
- **Neurons**, the functional units of the brain.
- Neurons cluster on the surface of the brain (e.g. **cortex**) and deep within the brain (e.g. **subcortical nuclei**).
- Collectively, these clusters constitute **grey matter**.



HOW IS IT IMPACTED?

- **Neurons** change size; their cell bodies **shrink** and their axons/dendrites **retract** and **lose branches**.
- The relative proportion of **grey matter decreases**, and the vacant space is filled with cerebrospinal fluid.





WHY DOES IT HAPPEN?

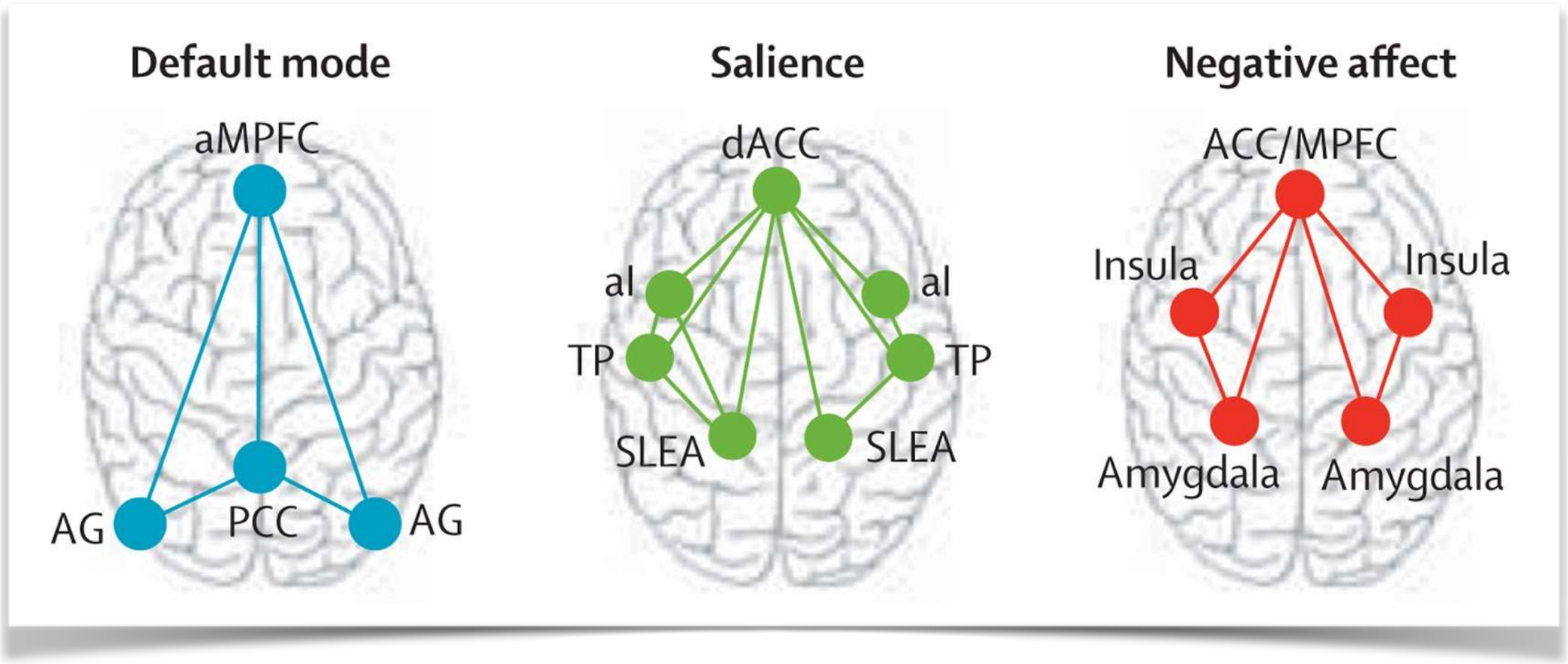
- Change in neuron size is attributed to **excess cortisol** production.
- Change in neuron size facilitates **energy conservation**; smaller neurons require fewer resources, leaving more available for critical functions such as breathing.

anhedonia
lack of motivation
fatigue
difficulty concentrating
anxiety
depression
mood instability

immune suppression
metabolic suppression
fluid retention
fat retention
arterial plaque formation
insulin resistance
nerve damage

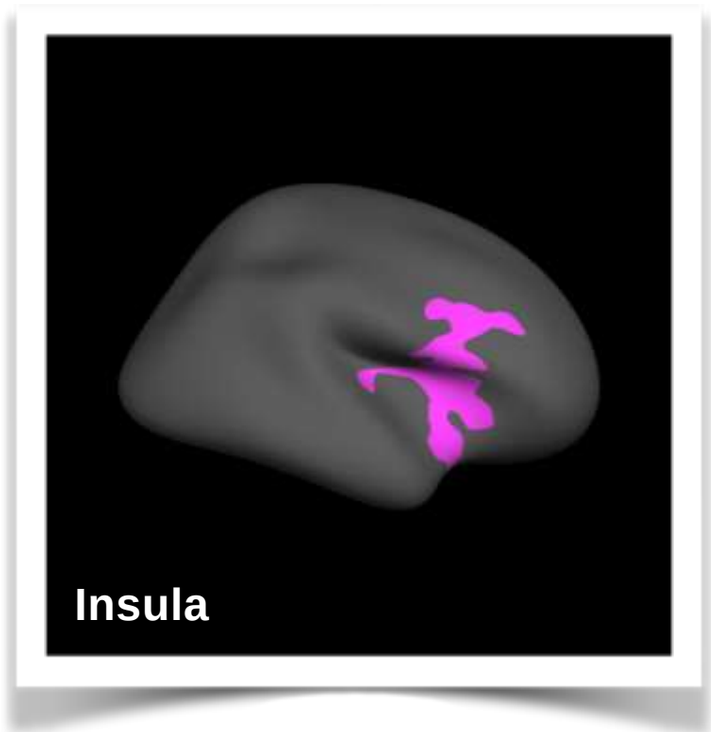
WHAT ARE ITS CONSEQUENCES?

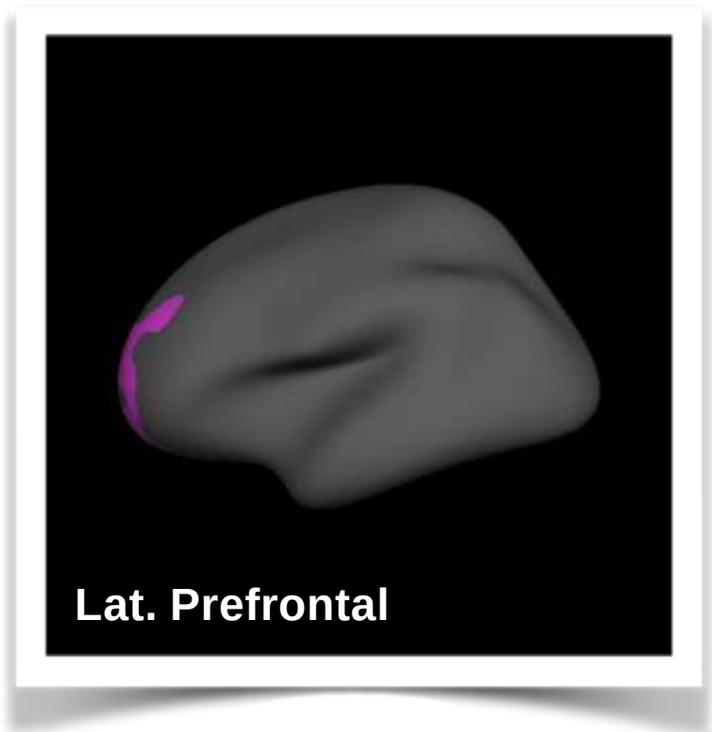
- Changes to neurons can **disrupt information flow within neural networks**.
- Perturbations in network function can **produce pathological thoughts, feelings, and behaviors**.

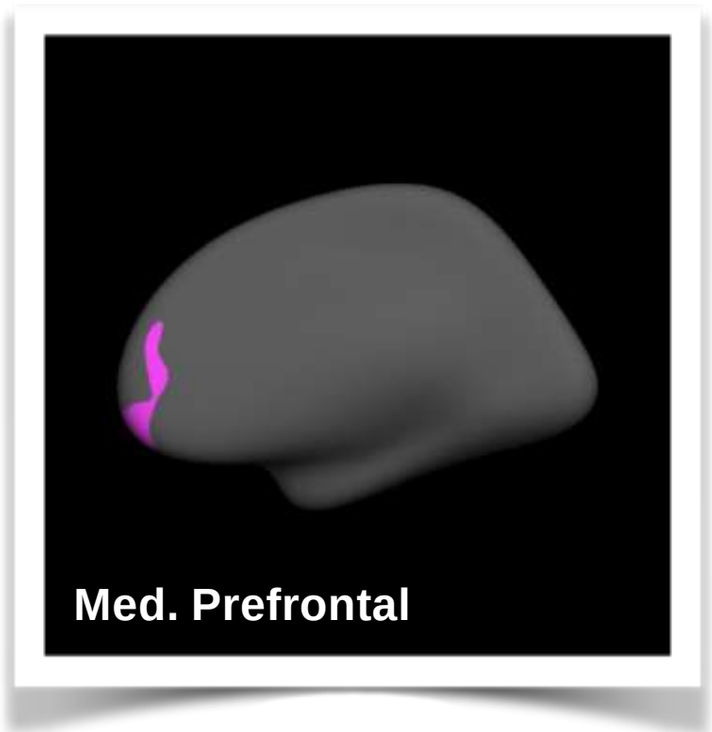


WHERE ARE THESE GREATEST?

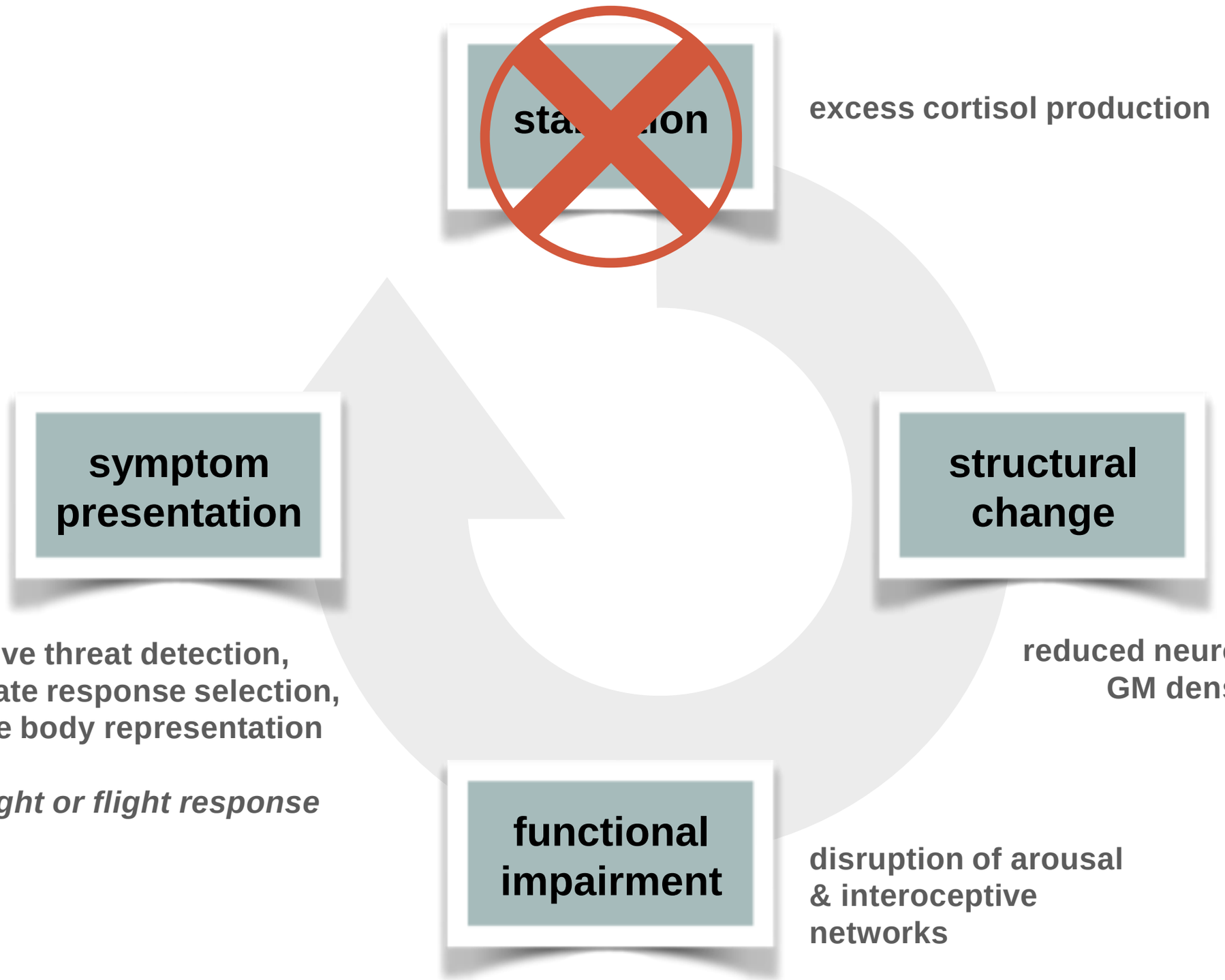
- Structural changes occur throughout the brain; however, they are most prominent in the **insula and prefrontal cortex**.
- These regions constitute **key components of arousal/attention and interoceptive networks**.





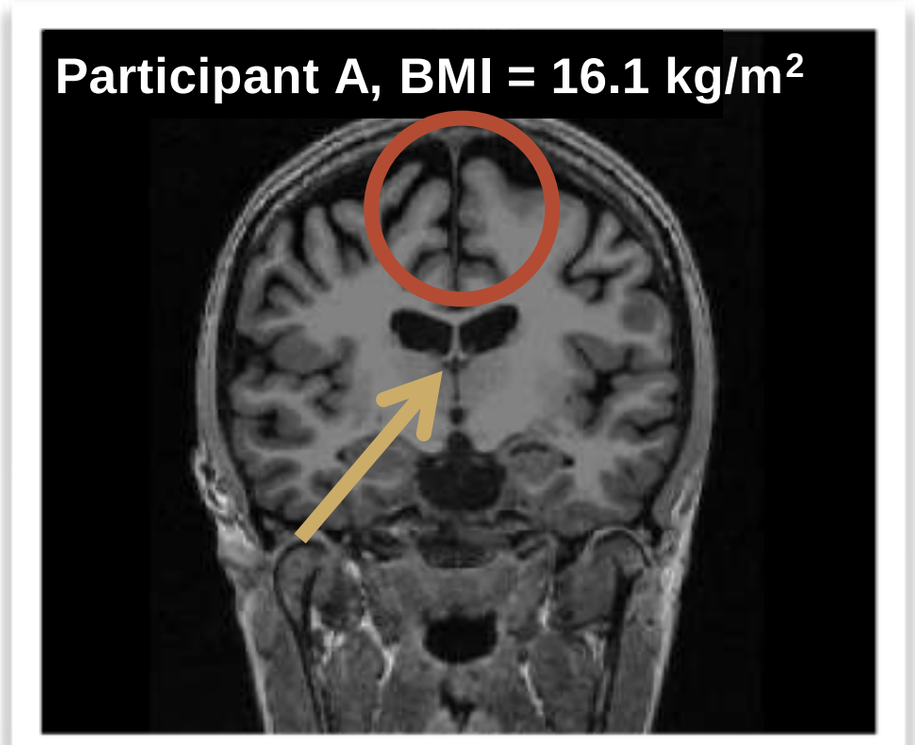


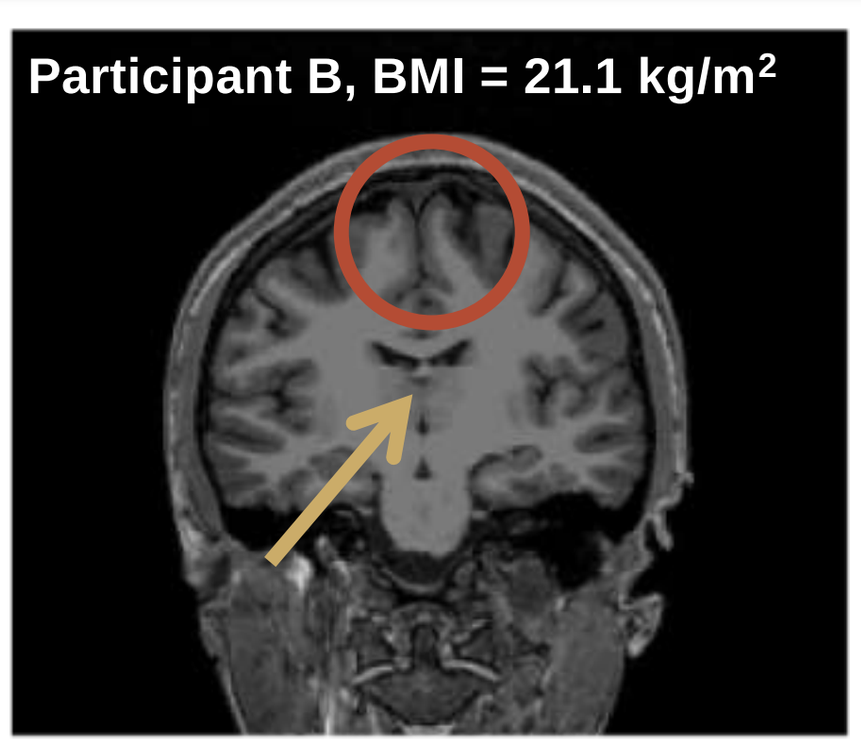
REVIEW


stabilization
excess cortisol production
structural change
reduced neuron size & GM density
functional impairment
disruption of arousal & interoceptive networks
symptom presentation
excessive threat detection, inappropriate response selection, inaccurate body representation
mimics fight or flight response

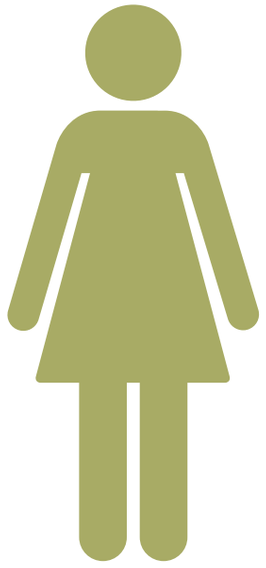
WHEN CAN IT BE REVERSED?

- Within **twelve months** of refeeding.
- This requires **weight maintenance** (BMI ≥ 18.5 kg/m^2) and relative **symptom abstinence**.





TRAIT-BASED CHANGES IN BRAIN STRUCTURE



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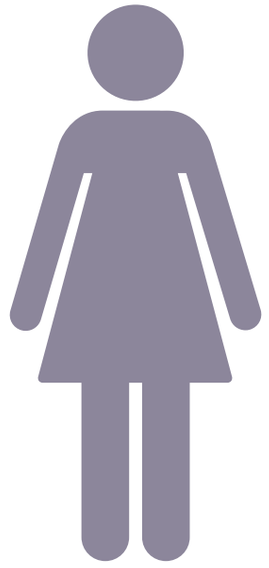
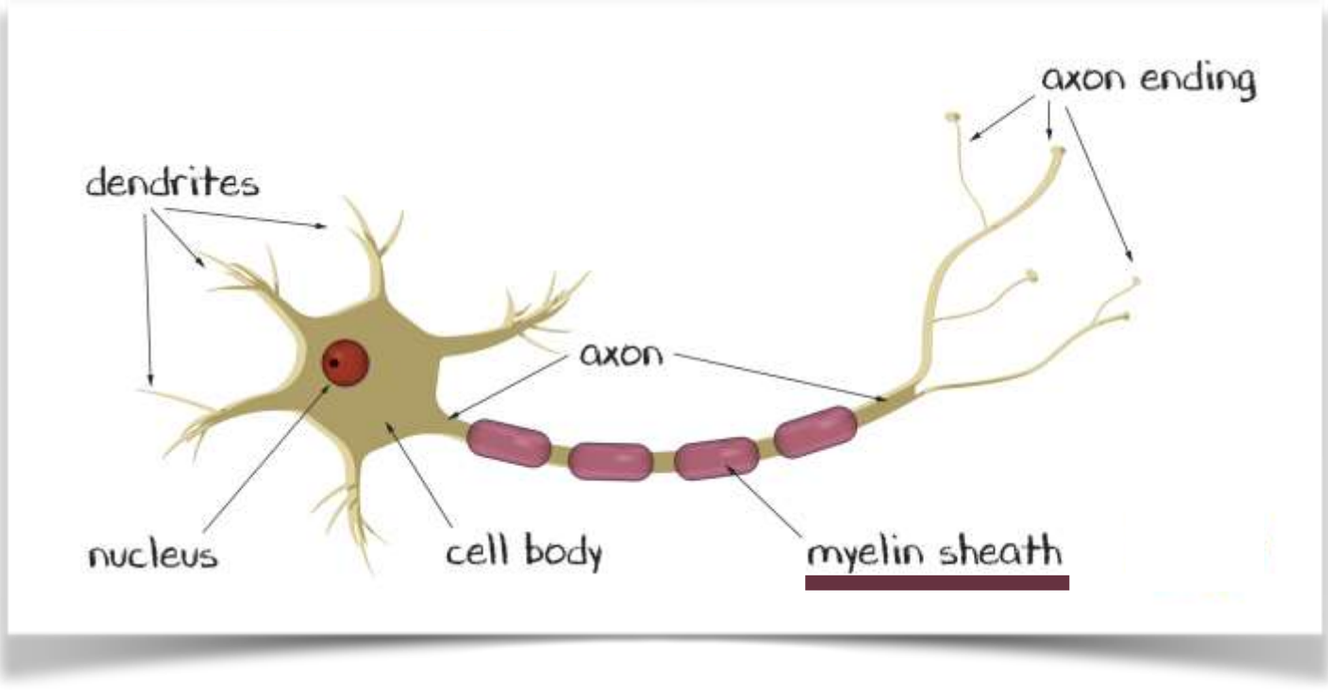
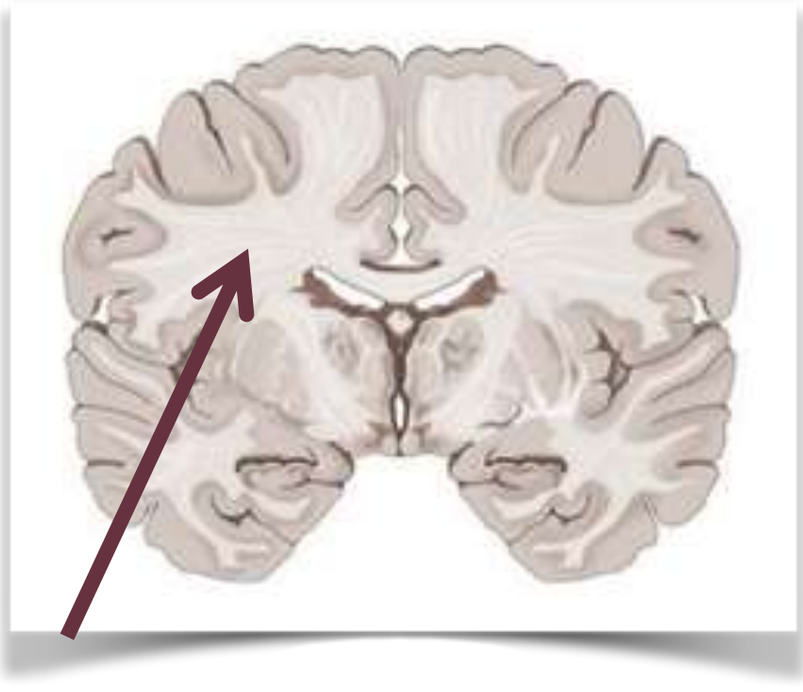


past AN
BMI > 18.5 kg/m²

WHAT IS IMPACTED?

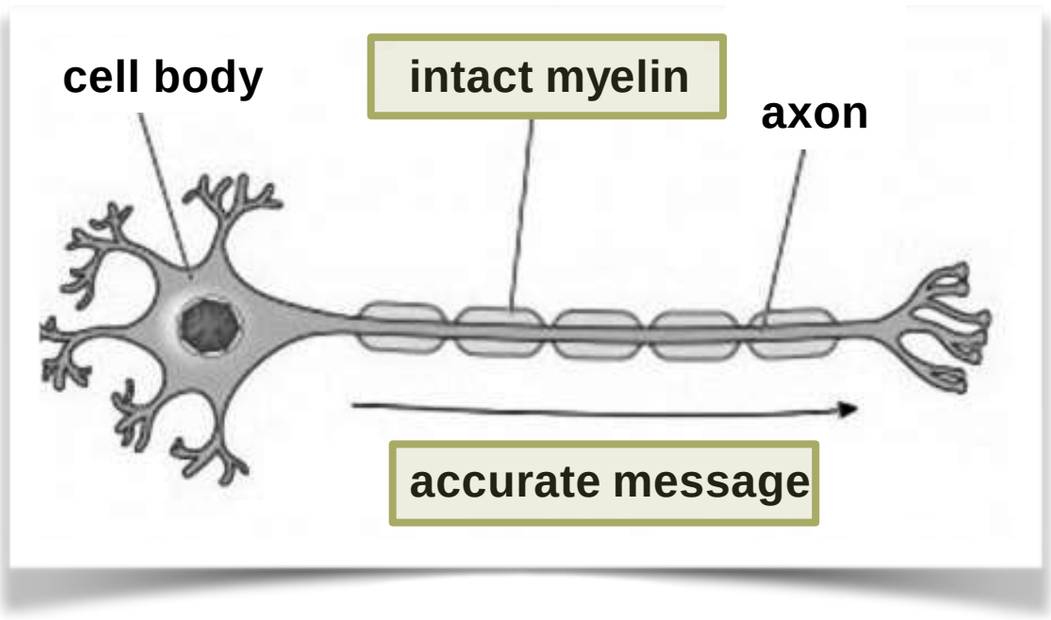
- **Neurons and glia**, the support cells of the brain.
- Glial cells encircle axons (e.g. **myelin sheathing**). In doing so, they protect individual neurons and facilitate network-wide communication.
- Collectively, bundles of myelinated axons constitute **white matter**.

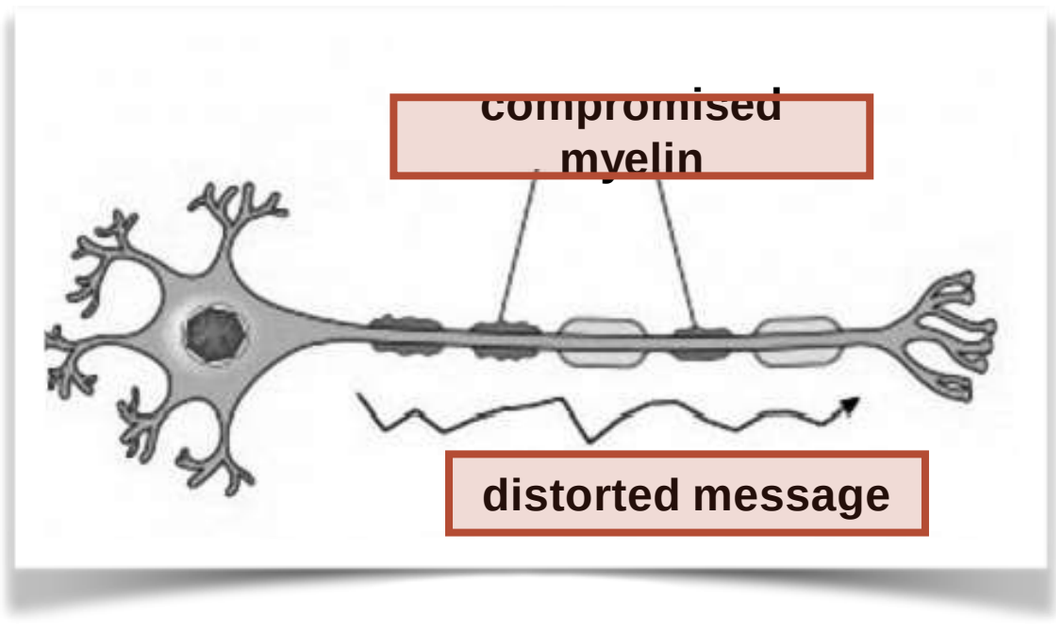




HOW IS IT IMPACTED?

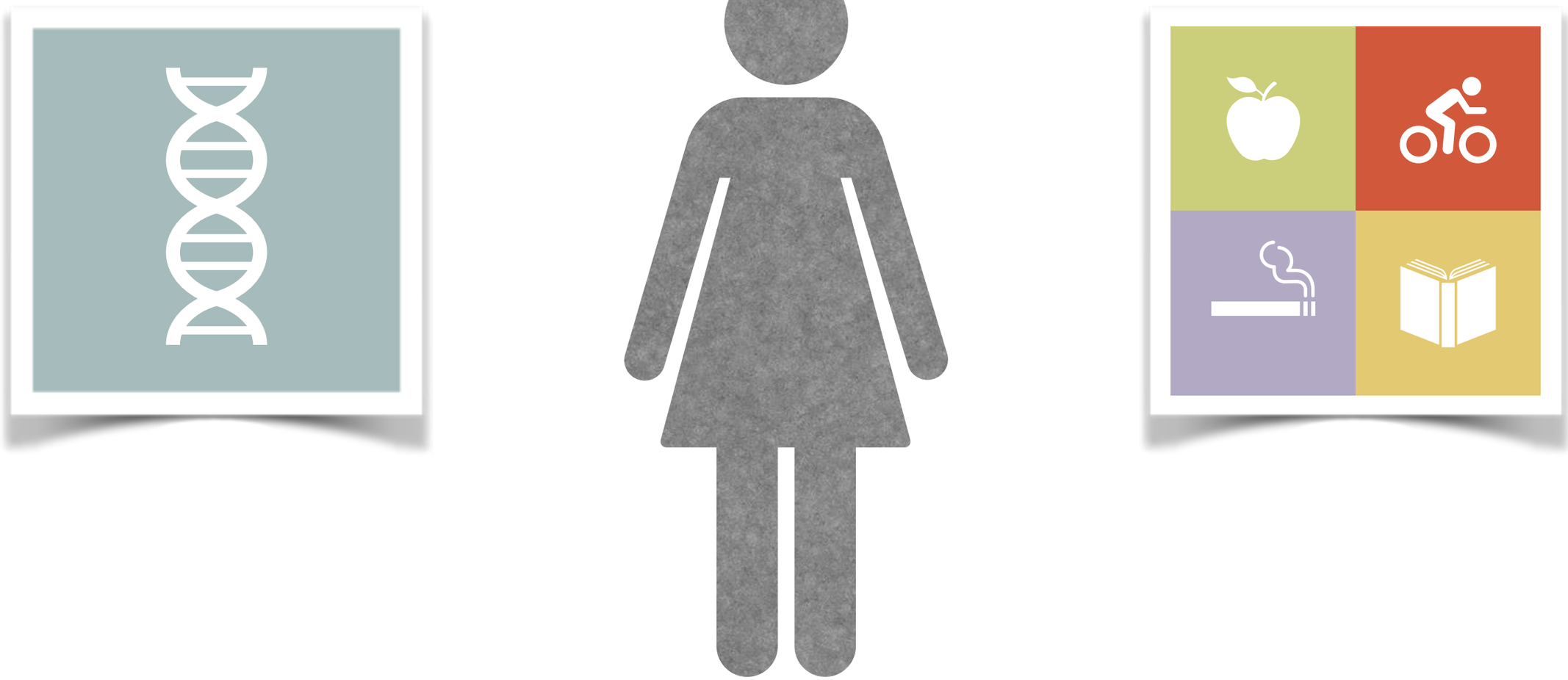
- **Improper assembly or excessive pruning of glial cells** prevents adequate myelination.
- Inadequate myelination **compromises axon integrity** and **disrupts information flow along white matter tracts**.





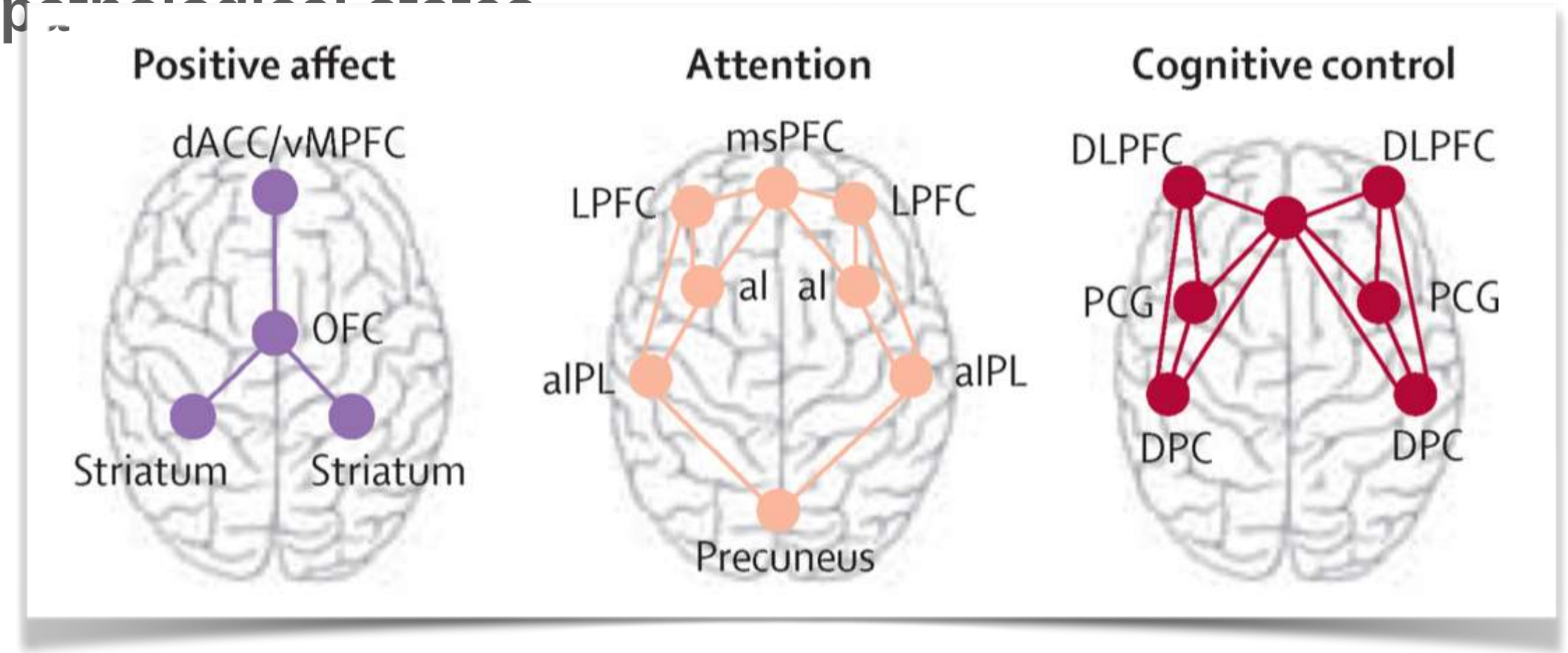
WHY DOES IT HAPPEN?

- Patterns of myelination are influenced by **genetics and environmental exposure**.
- Our **current study** is aimed at further exploring these mechanisms.



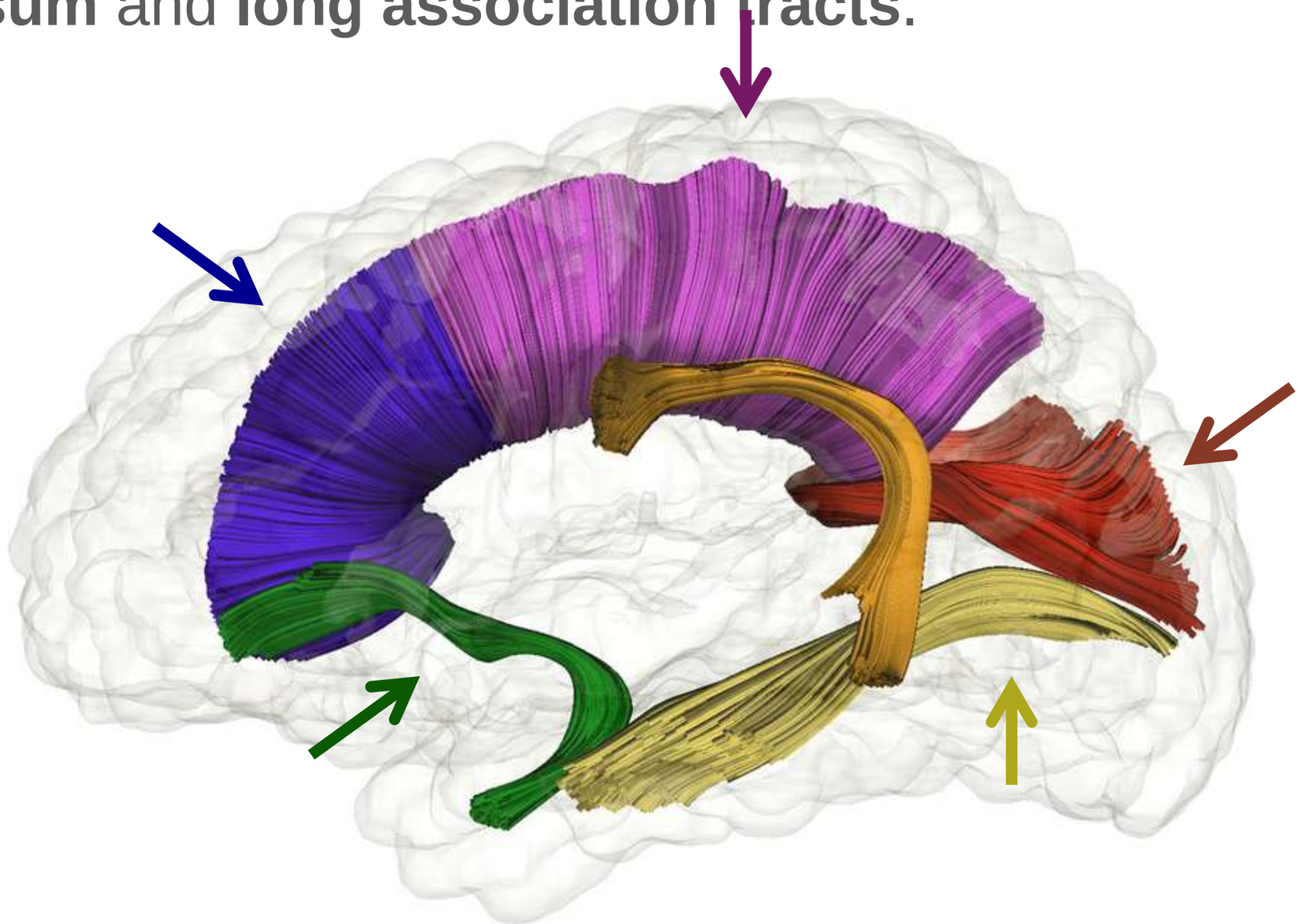
WHAT ARE ITS CONSEQUENCES?

- Inadequate myelination can **alter network structure and function**.
- Changes in network structure and function can **produce pathological states**.



WHERE ARE THESE GREATEST?

- Deficits in myelination are most prominent in the **corpus callosum** and **long association tracts**.



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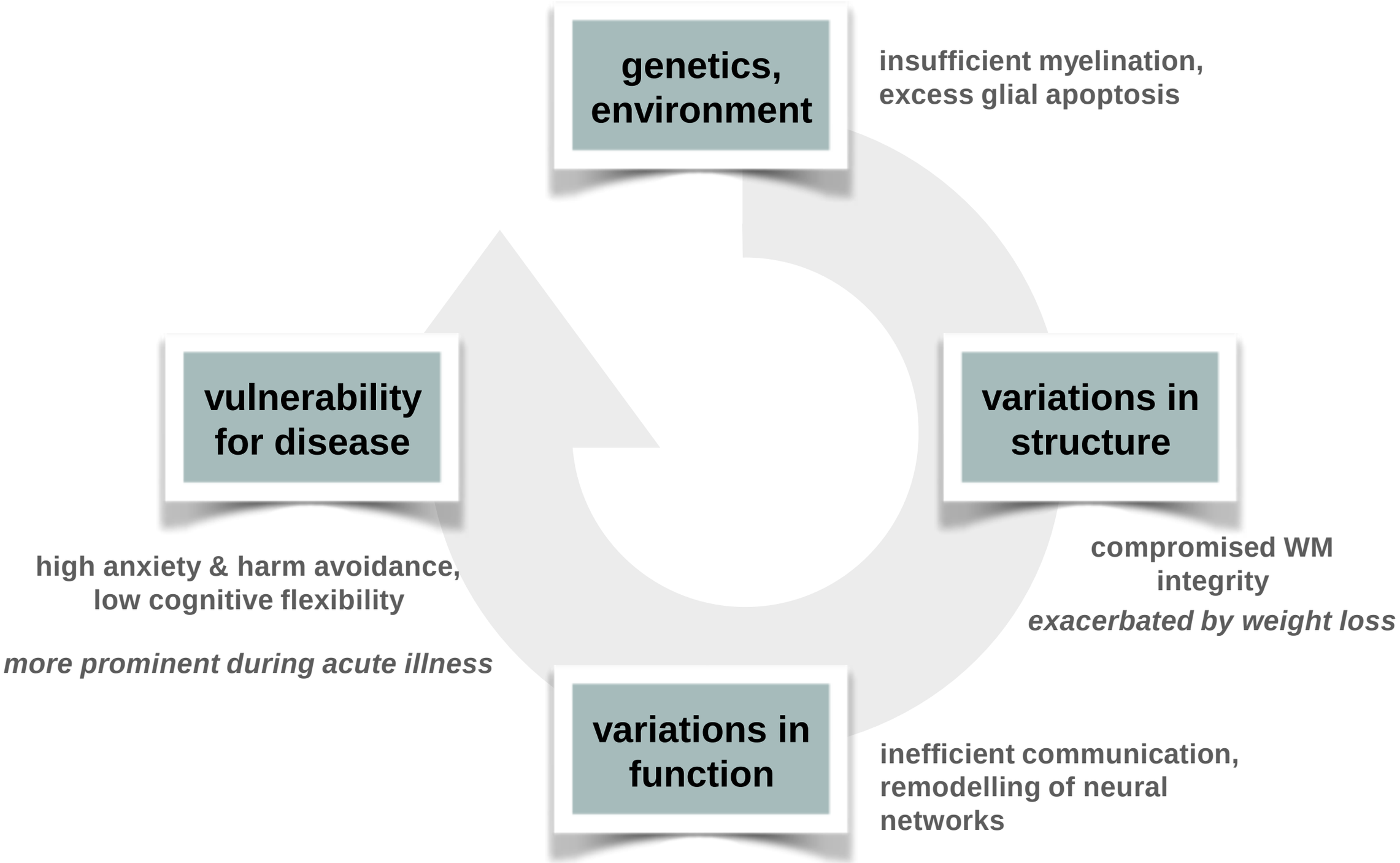
genetics, environment
insufficient myelination, excess glial apoptosis
variations in structure
compromised WM integrity
exacerbated by weight loss
variations in function
inefficient communication, remodelling of neural networks
vulnerability for disease
high anxiety & harm avoidance, low cognitive flexibility
more prominent during acute illness

WHAT CAN BE DONE?

- In isolation, these structural variations **aren't necessarily a bad thing**; in moderation, their functional consequences can be adaptive.
- Ongoing research aimed at **modulating network strength** and **improving network organization and efficiency** could help individuals at risk for AN maintain a more advantageous balance.

CBT

Mindfulness

rTMS

CONCLUSIONS

- **AN is associated with changes in brain structure.**
- **Reduced GM density** reflects cortisol-mediated changes in neuron size that emerge during acute illness, impair body image processing and promote resistance to treatment, and can be reversed with weight restoration and symptom abstinence.
- **Reduced WM integrity** reflects genetically- or environmentally-mediated changes in myelination that emerge early in development, influence personality and confer vulnerability to disease, and can be improved with appropriate treatment.

FINAL THOUGHTS

- **There is hope!** Research is ongoing, and we are learning more everyday.
- **Progress requires participation.**