

Biology: Why complex disease requires combination treatments

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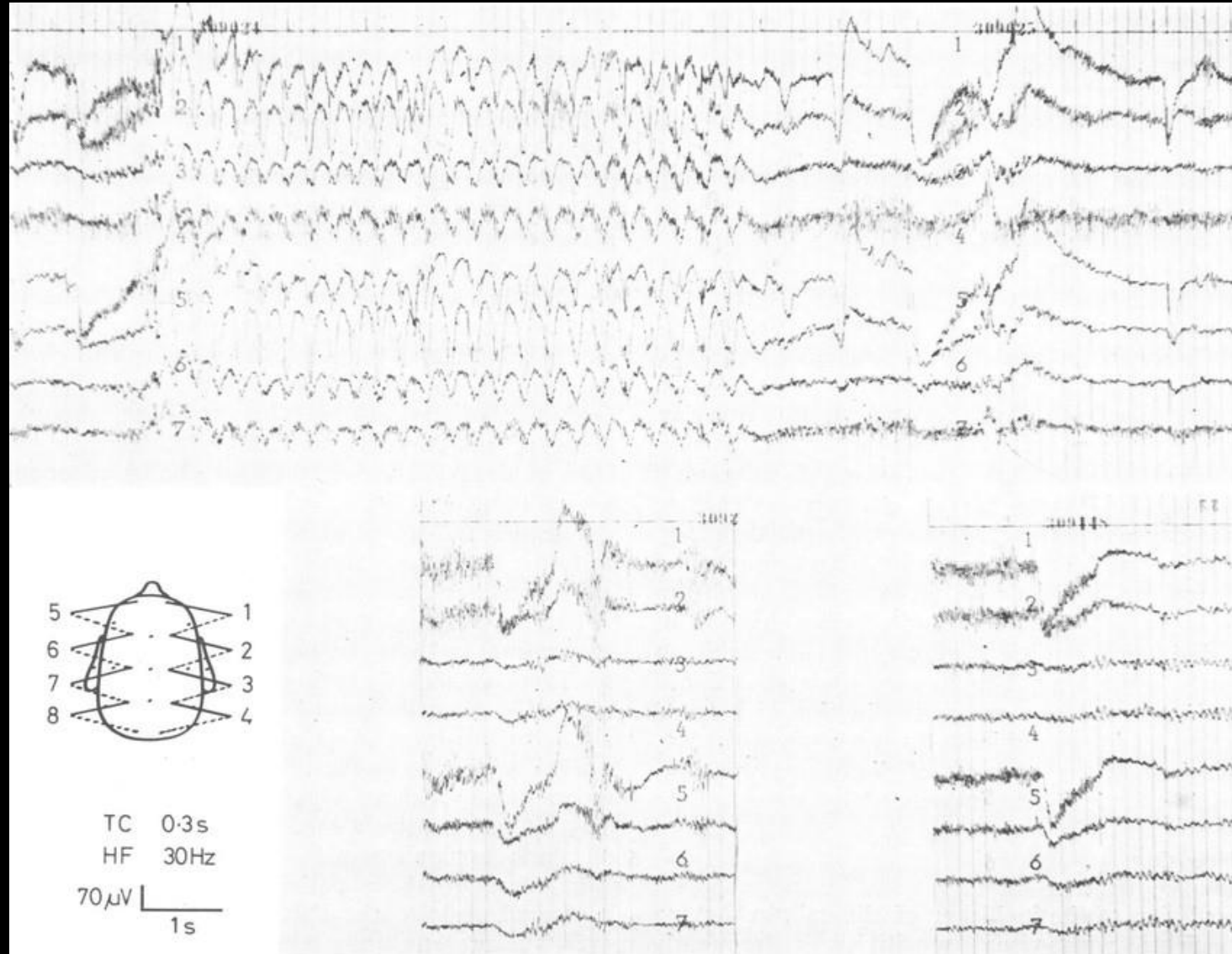
**Imperial College
London**

Epilepsy in 1400

St. Geminianus exorcising the daughter of the Byzantine emperor Jovian



Epilepsy in 1900

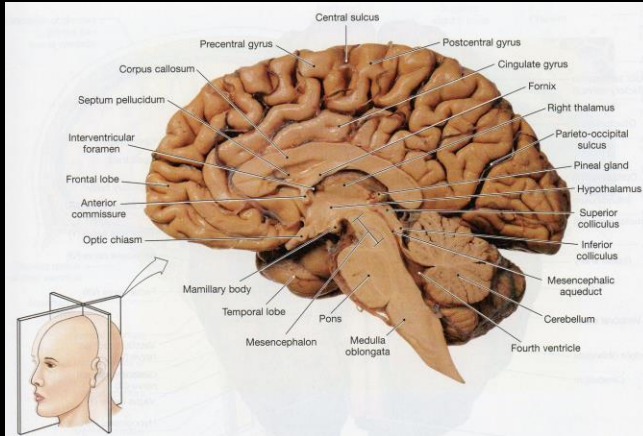


Epilepsy in 2026



Typical perception of Disease

Organ



Mechanism



Manifestation



Traditional perception of Obesity

Mechanism (Behaviour)



Manifestation





Robert Plomin



Identical twins

differences all environmental

Non-identical twins

have both genetic and
environmental differences

Over 5,000 same-sex twin pairs

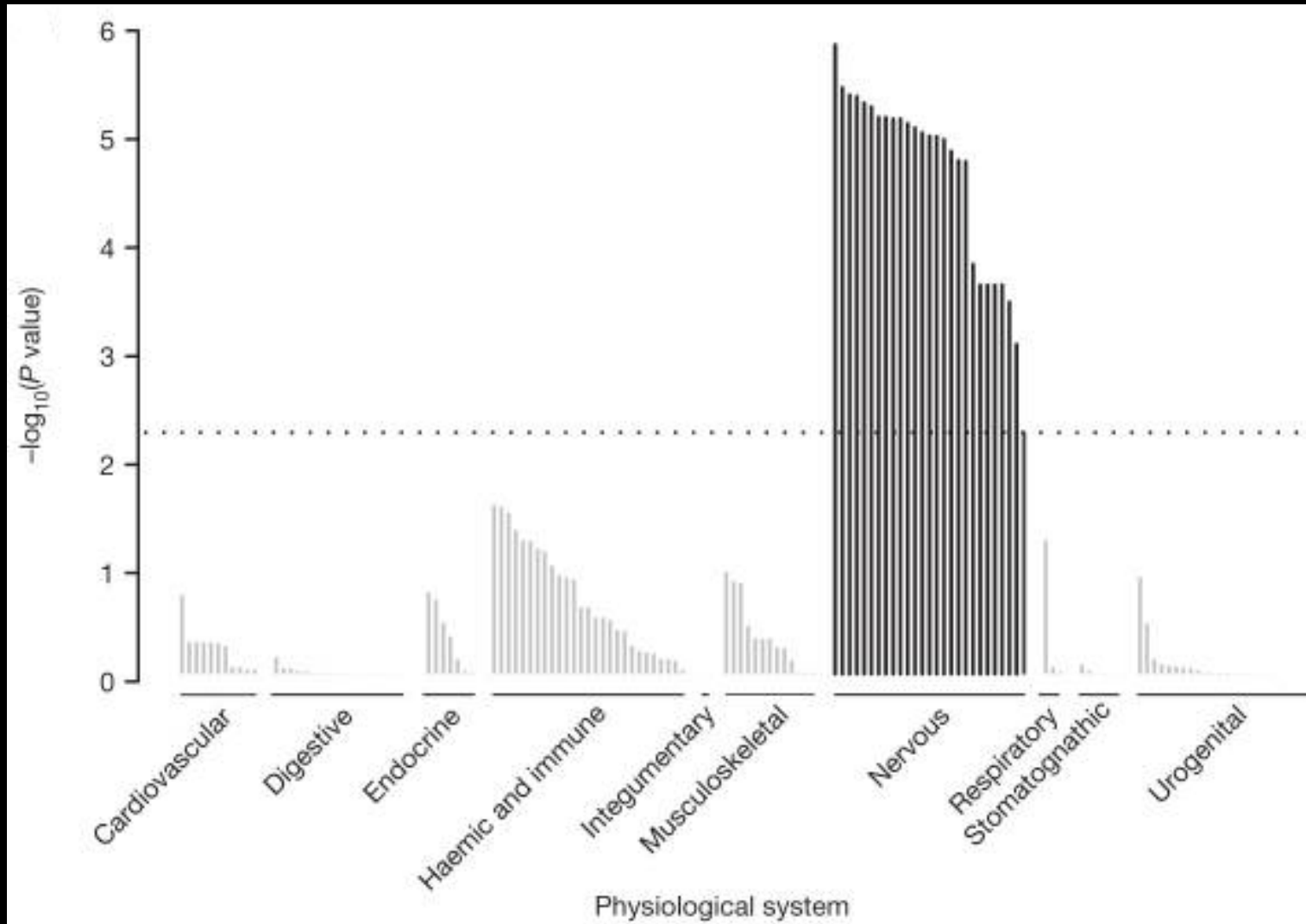
Heritability:

BMI 77%

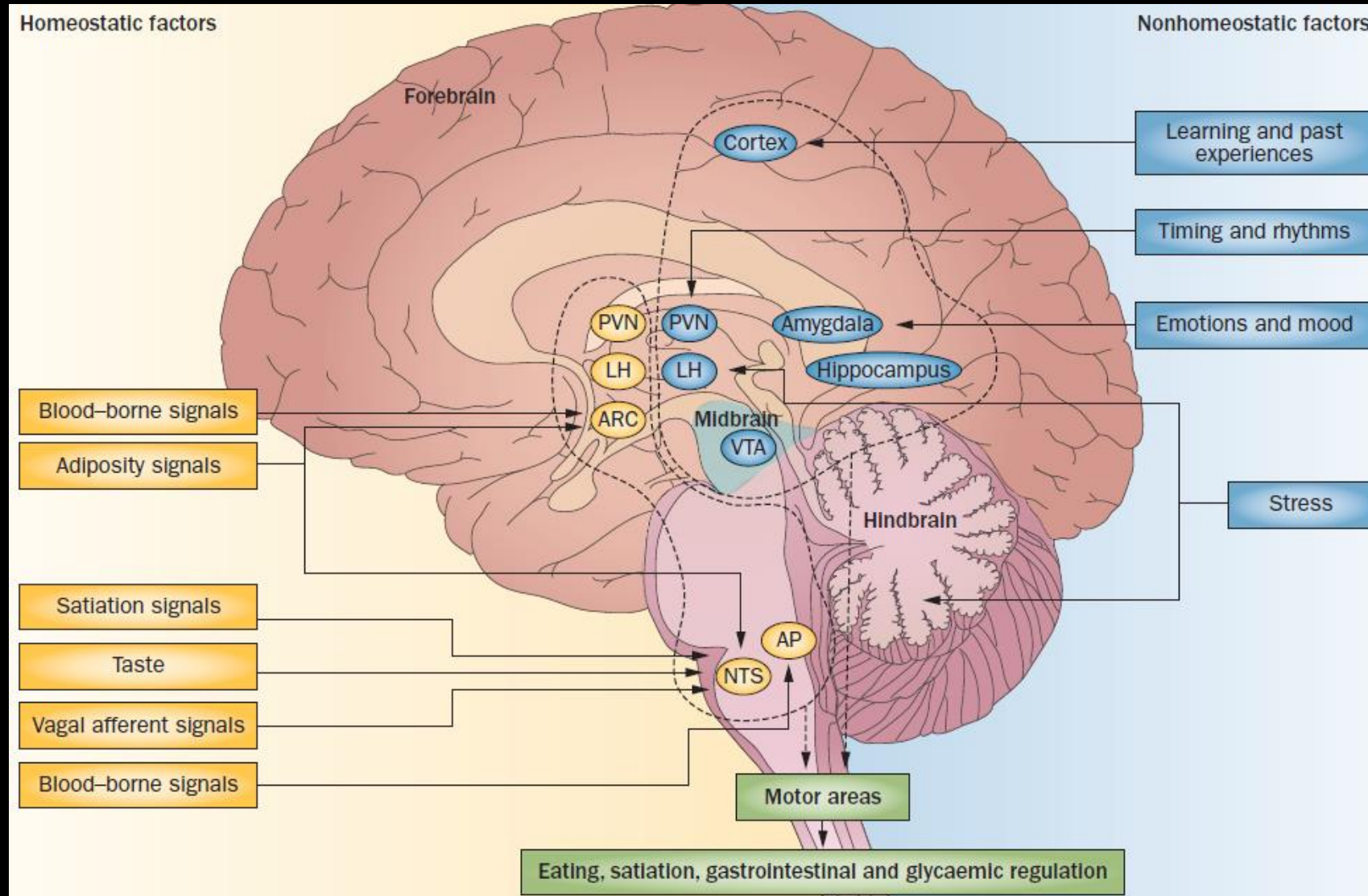
Waist circ. 77%



Where do most risky genes work?

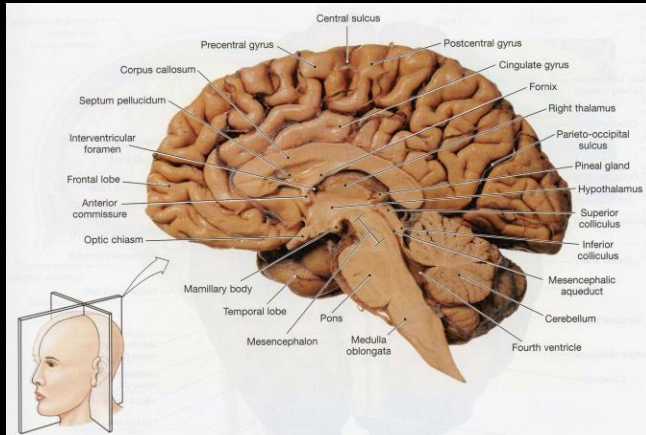


Brain control of body weight regulation



Modern perception of obesity

Organ



Mechanism



Manifestation



Breast cancer

BREAST CANCER IS NOT ONE DISEASE

Understanding subtypes helps guide treatment



**HORMONE
RECEPTOR-
POSITIVE**

ER and/or
positive



**HER2-
POSITIVE**

too much
HER2 protein



**TRIPLE-
NEGATIVE**

not ER, PR or
HER2 positive

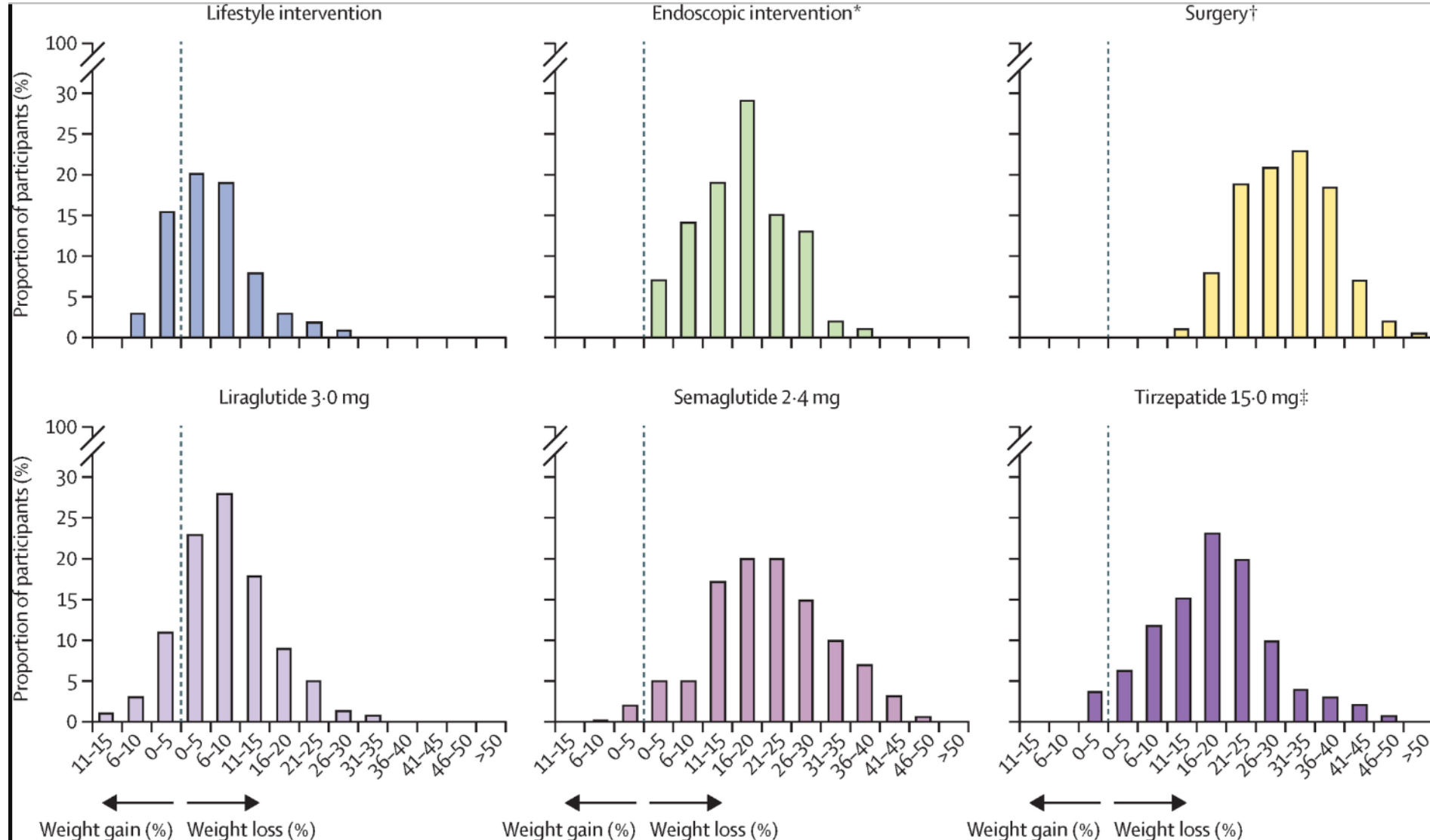


**RARE
SUBTYPES**

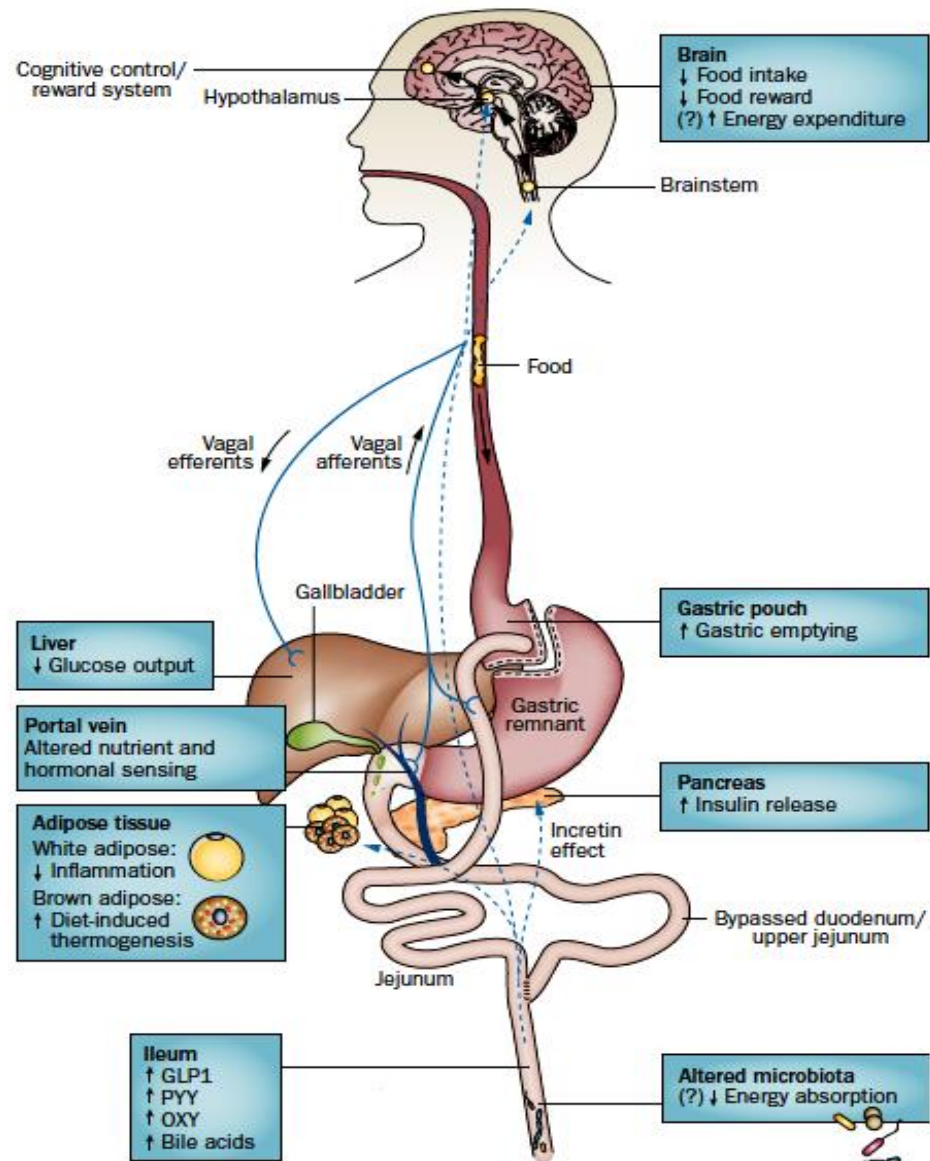
less common
types

SUBTYPE GUIDES TREATMENT

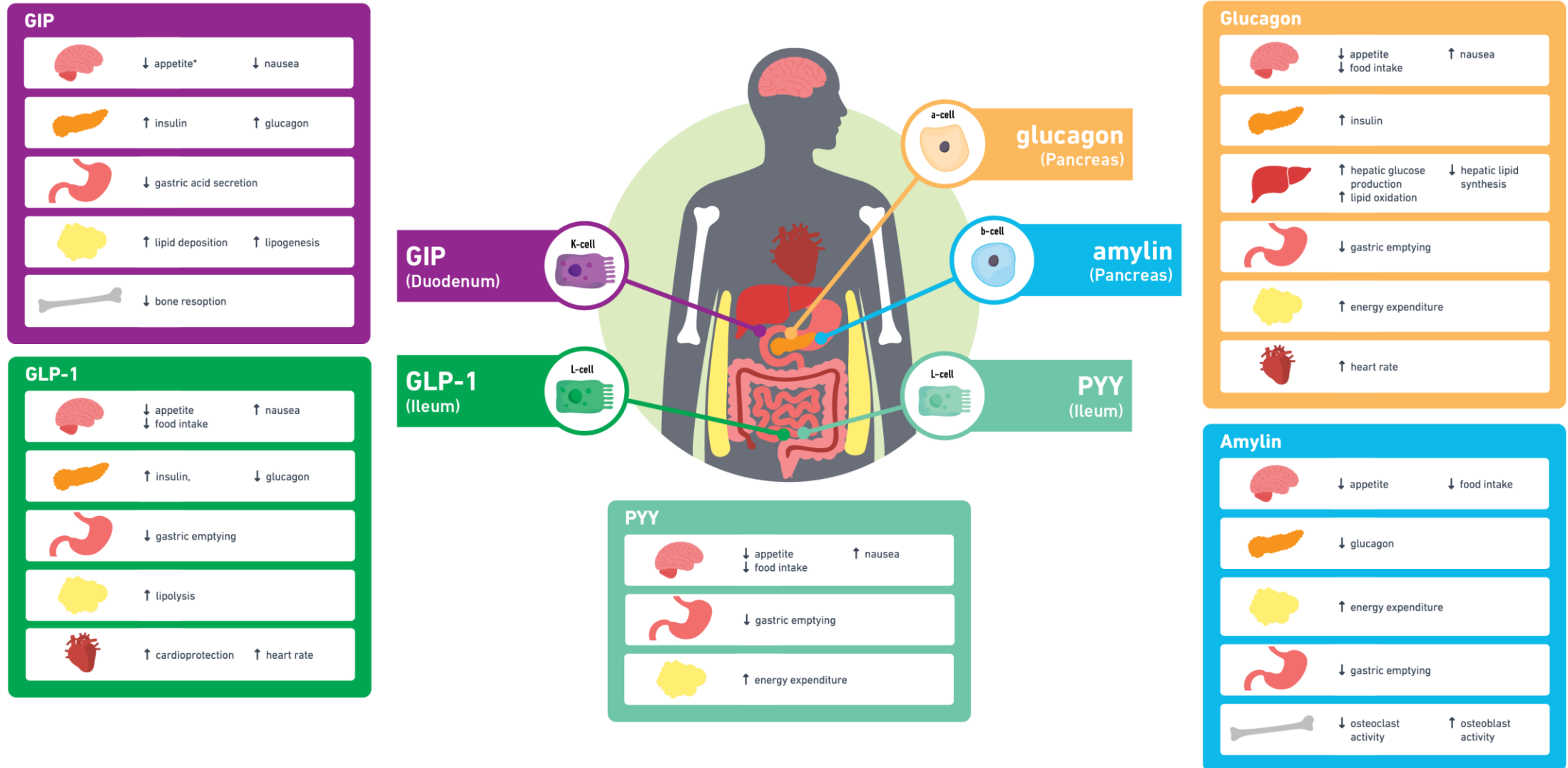
Heterogeneity of response to treatments



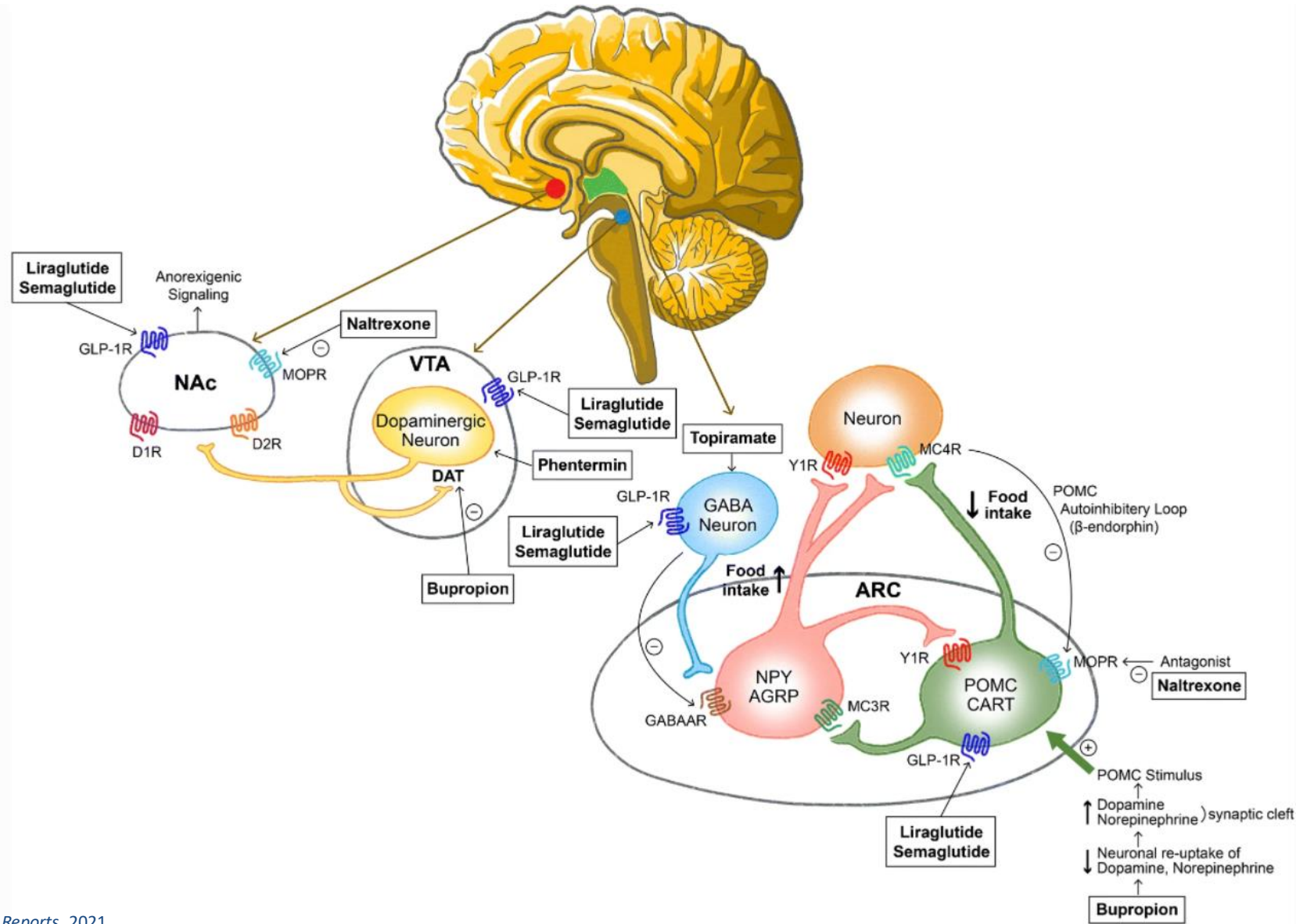
Mechanisms of weight loss after RYGB



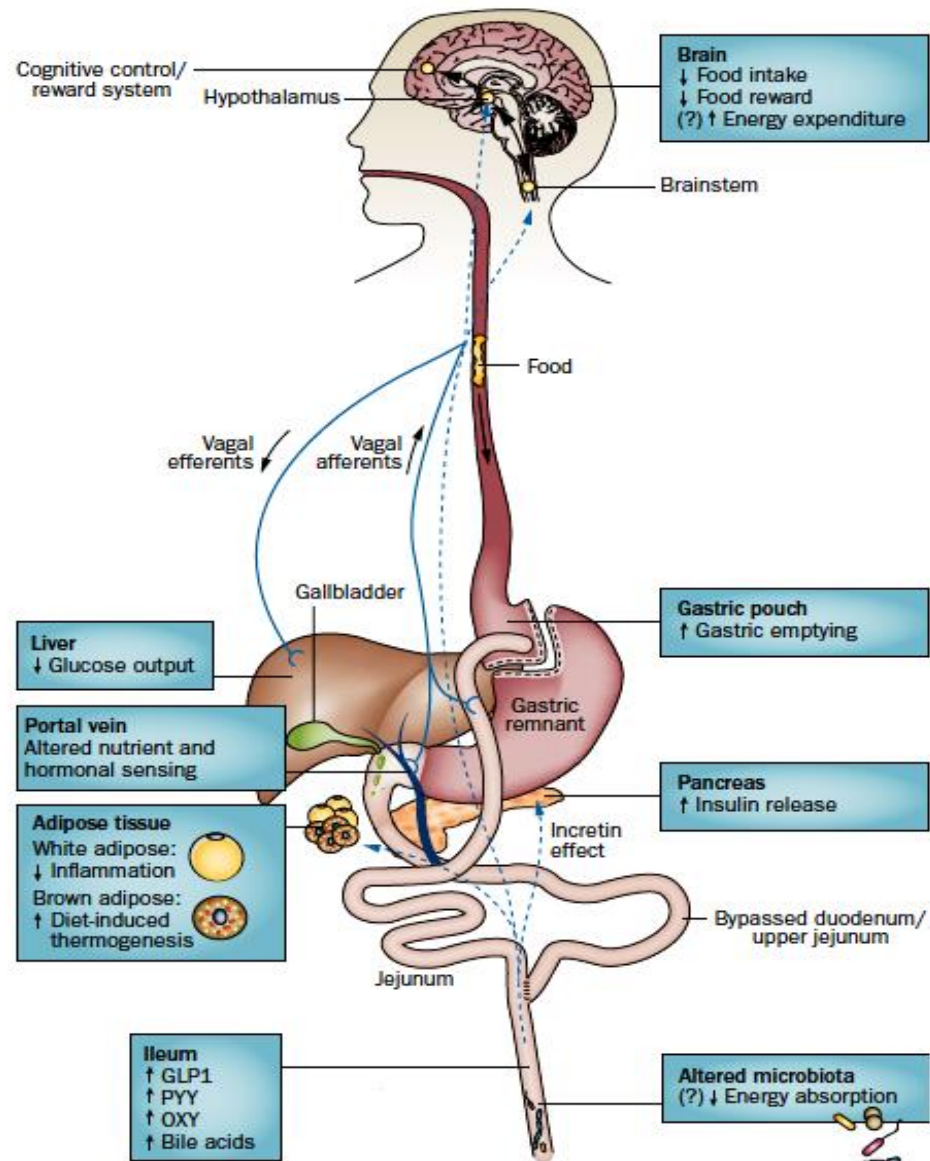
Gut hormones used in the pipeline obesity treatments



Need more mechanisms and sites of action



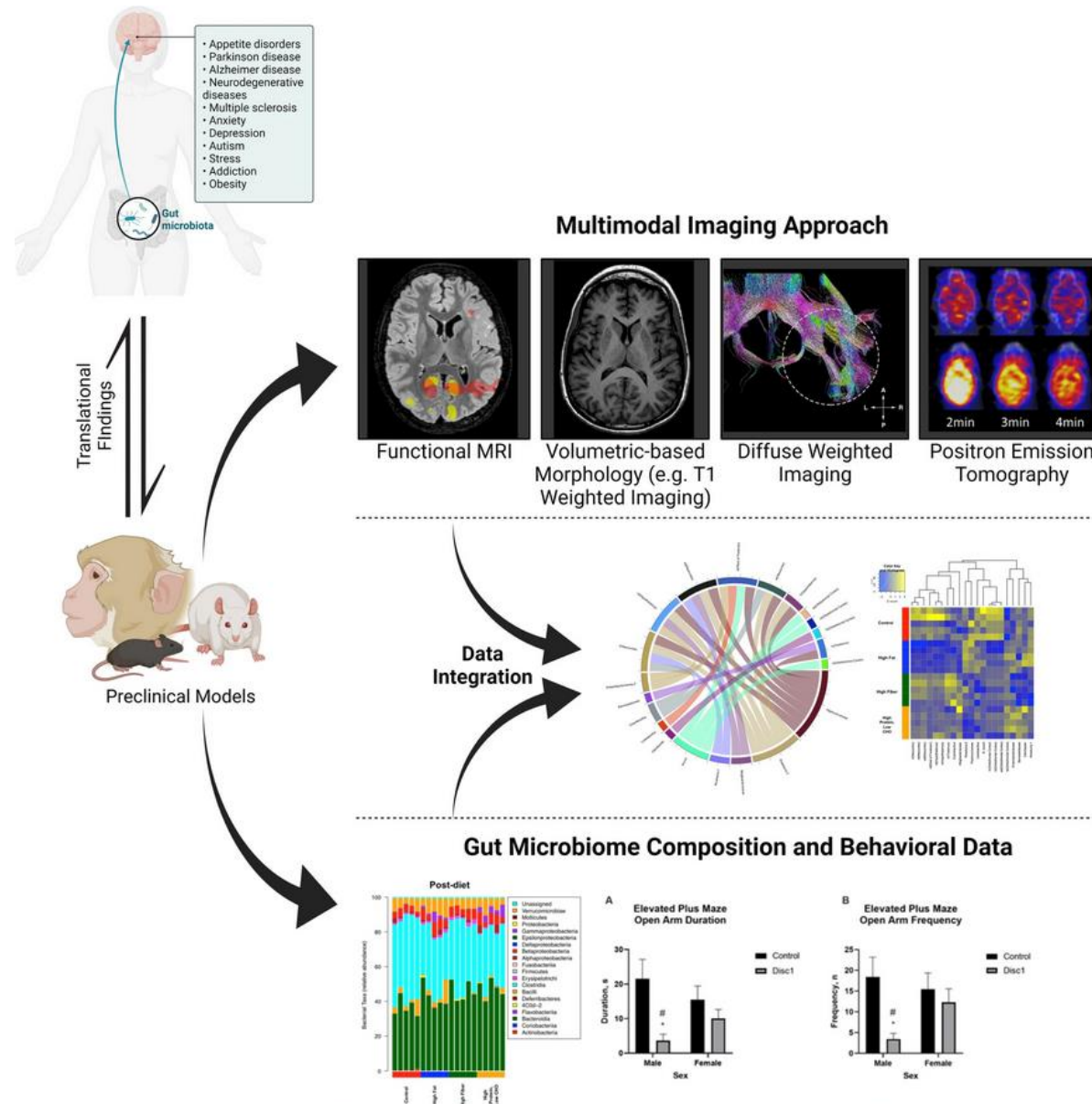
Surgery + medicine



+



Interrogating the complexity - Work in Progress



Montoro et al, *European Radiology* (2022)

Acknowledgements



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