Acquired Hypothalamic Obesity

Rhythm PHARMACEUTICALS

What is Acquired Hypothalamic Obesity?

An accelerated and sustained weight gain that occurs most frequently after hypothalamic damage (e.g., resulting from craniopharyngioma or other intracranial tumor, traumatic brain injury, stroke, or surgical resection or radiation of brain tumors).[1-3]

Tumor Associated Prevalence[4]

US
5,000–10,000
individuals

Europe
3,500–10,000
individuals

(Rhythm Pharmaceuticals estimate)

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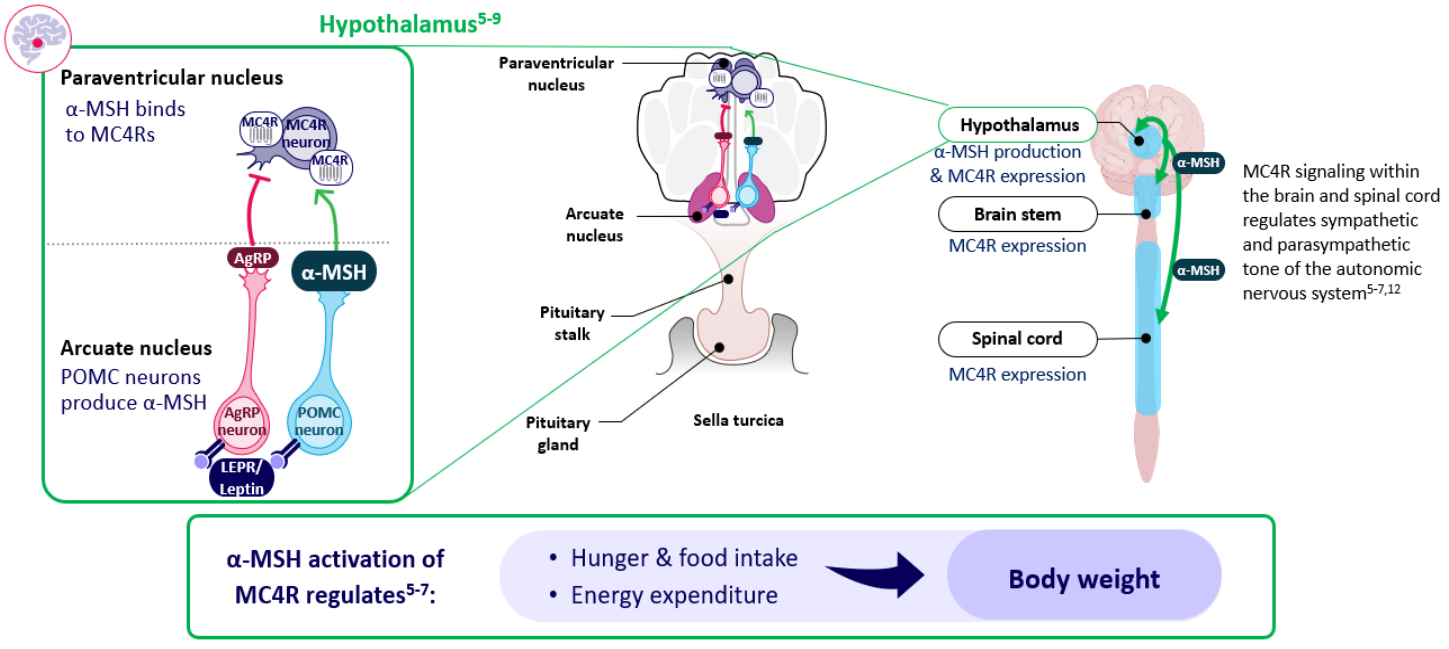
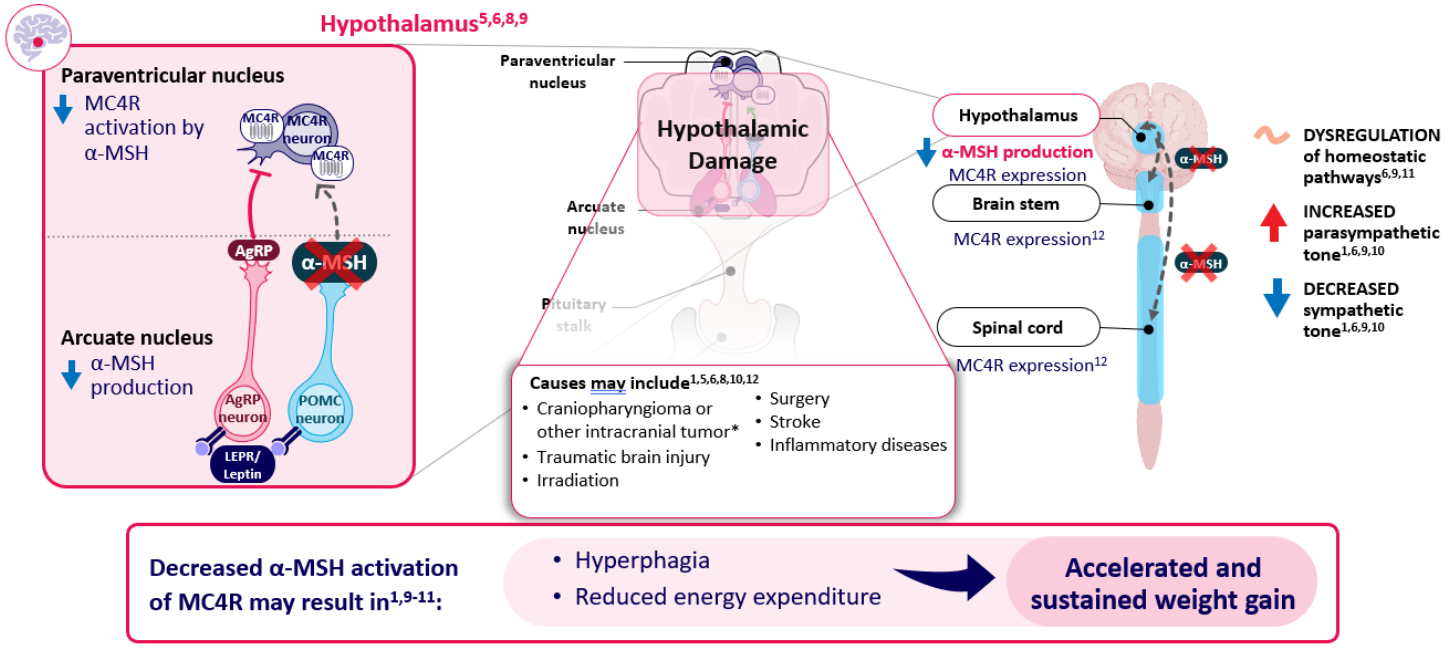
The melanocortin-4 receptor (MC4R) pathway is a critical regulator of satiety and energy balance[5-9]

a-MSH, a key neuropeptide naturally produced in the hypothalamus, activates MC4Rs in multiple locations, including the hypothalamus, brainstem, and spinal cord, to drive MC4R pathway signaling.[5-9] Hypothalamic damage may decrease a-MSH production, which impairs MC4R pathway signaling, and can result in accelerated and sustained weight gain due to decreased energy expenditure and hyperphagia.[1,10,11]

α-MSH Drives MC4R Pathway Signaling to Regulate Energy Balance and Body Weight[5-7]



Loss of α-MSH Production Due to Hypothalamic Damage May Impair MC4R Pathway Signaling and Lead to Acquired Hypothalamic Obesity[1,10,11]



*Suprasellar tumors such as astrocytoma.[1,9]

α-MSH, α–melanocyte-stimulating hormone; AgRP, agouti-related peptide; LEPR, leptin receptor; MC4R, melanocortin-4 receptor; POMC, proopiomelanocortin.

References

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