Acquired Hypothalamic Obesity

Rhythm PHARMACEUTICALS

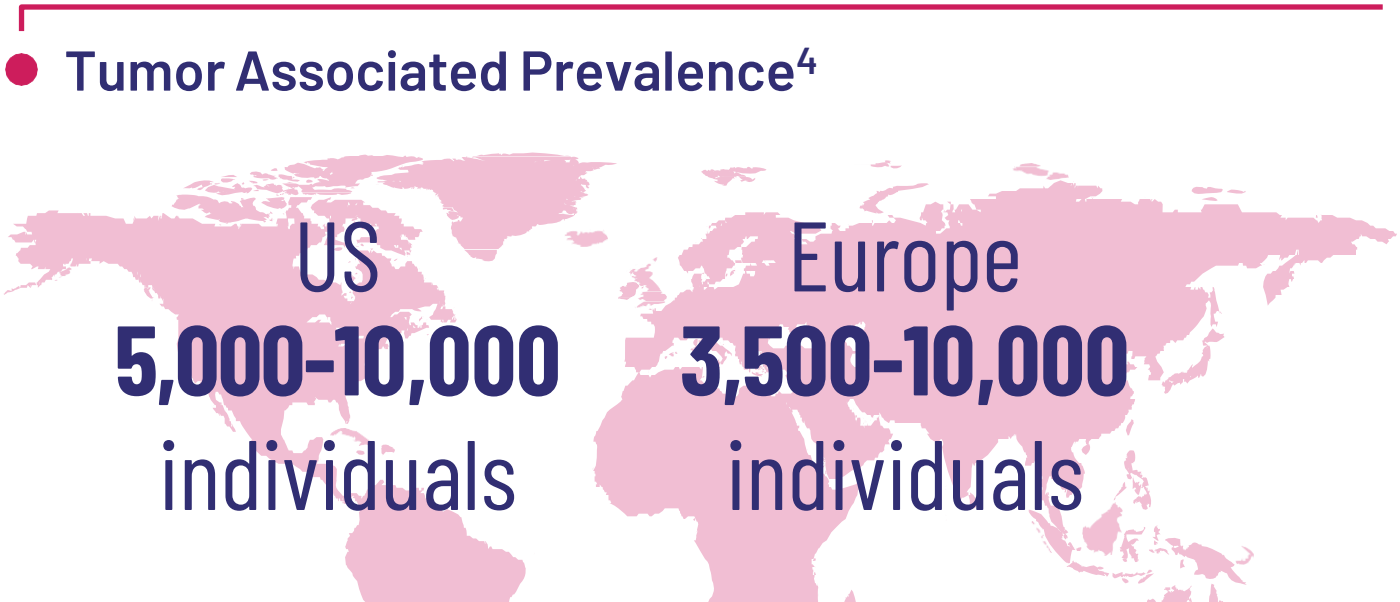


What is Acquired Hypothalamic Obesity?

Acquired hypothalamic obesity (HO) is defined as weight gain following hypothalamic-pituitary injury, which can occur both in children and adults.

Causes of injury can include, but are not limited to, benign or malignant hypothalamic-pituitary tumors and their treatments, traumatic brain injury, stroke, and autoimmune, vascular, inflammatory or neoplastic conditions.[1-3]

Tumor Associated Prevalence[4]



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Recognizing the Signs: Linking Hypothalamic Injury, Dysfunction, and Acquired HO



Injury to the hypothalamic-pituitary region[3]
commonly results in



Hypothalamic dysfunction[21]
which may result in one or more of the following

Hypopituitarism/ hypothalamic-pituitary hormonal deficiency[21]

Weight gain known as acquired HO[21]

Suspect acquired HO in patients with[1,3,11-14]:



History of hypothalamic injury which may result from hypothalamic-pituitary tumors and/or their treatment, traumatic brain injury, hypothalamic inflammation or stroke



Evidence of hypothalamic dysfunction, particularly hypopituitarism
Other manifestations may include but are not limited to decreased physical activity, behavioral dysfunction, fatigue, sleep disturbances, temperature dysregulation



Weight gain which may be accompanied by hyperphagia or increased hunger



Within the first 3 months post-injury, early, mild, and transient weight gain is common due to titration of hormone and/or steroid therapy[19].

Once these therapies are stabilized, sustained weight gain is indicative of acquired HO.

Acquired HO is caused by impairment of the MC4R pathway, a key hormonal pathway that regulates energy balance[10-13]

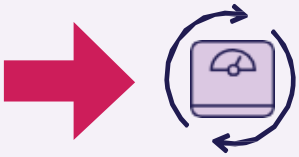


Hyperphagia or increased hunger

and/or



Decreased energy expenditure



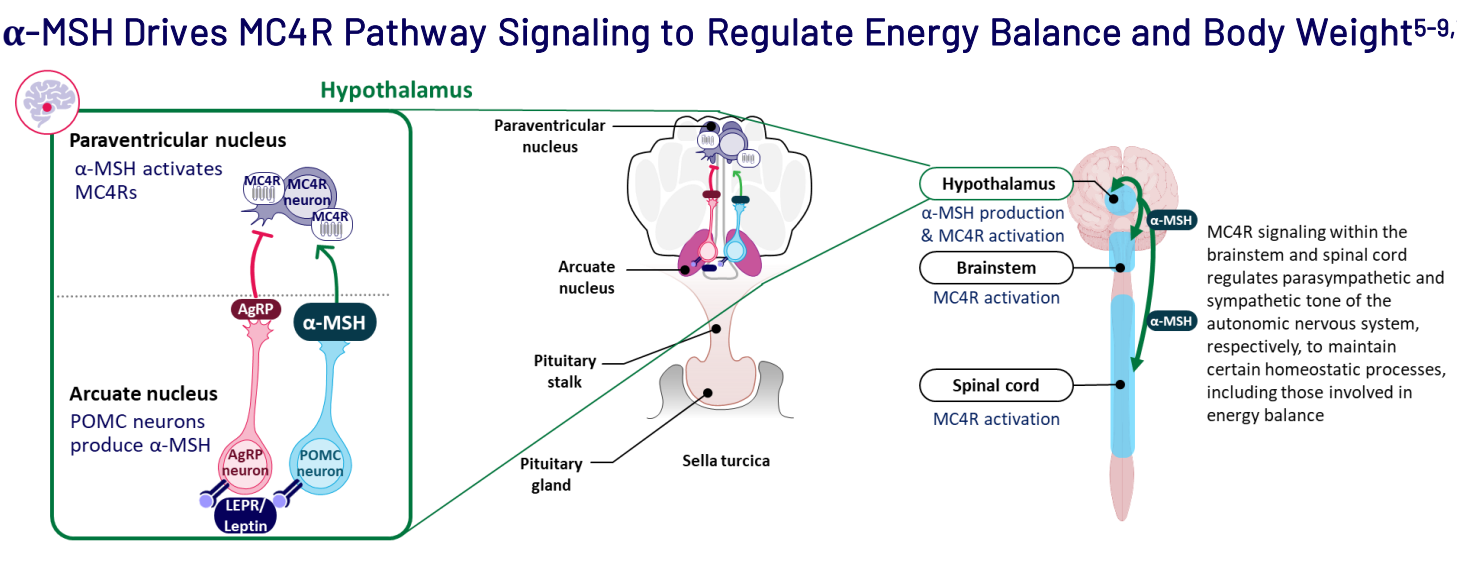
Weight gain

- may be accelerated and/or sustained
- can occur despite caloric restriction and/or increased physical activity

The MC4R Pathway in Focus: A Deeper Look into Satiety and Energy Balance[5-9]

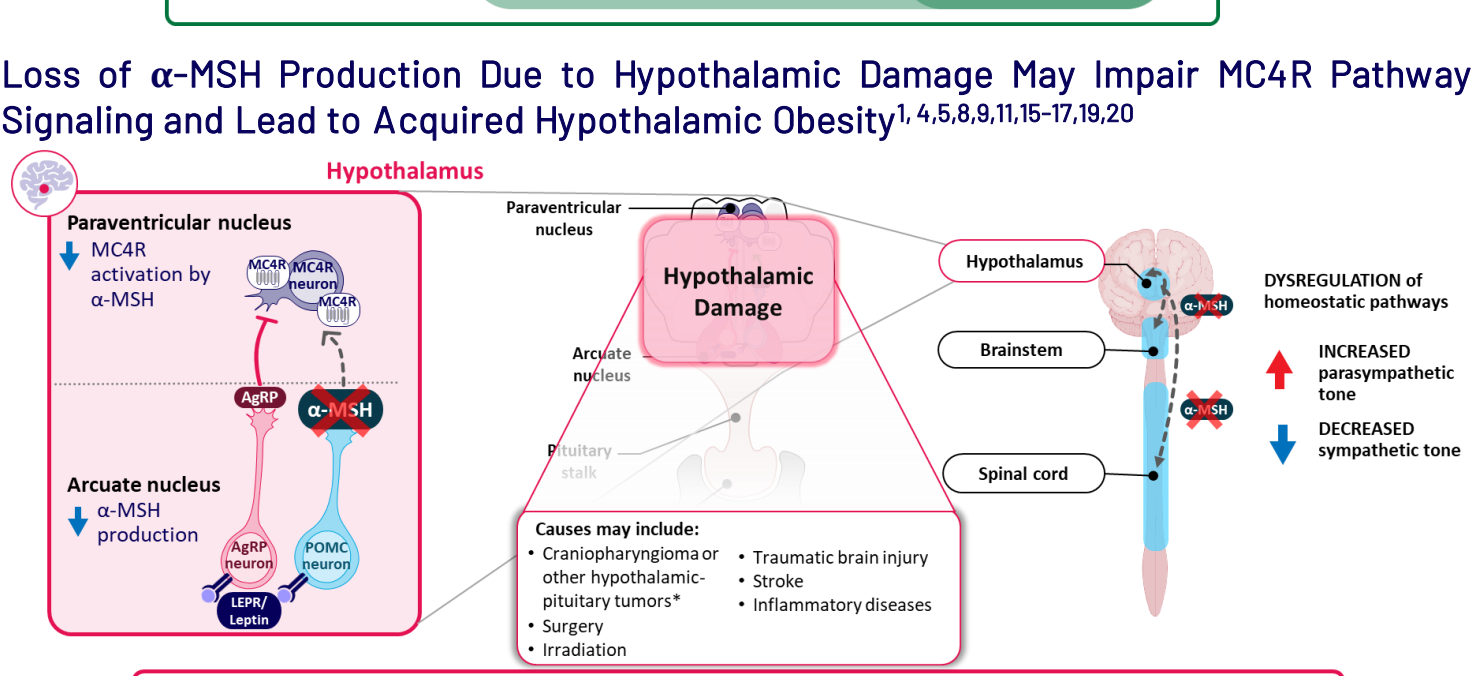
a-MSH, a key hormone naturally produced in the hypothalamus, activates MC4Rs in multiple locations, including the hypothalamus, brainstem, and spinal cord, to drive MC4R pathway signaling.[10-14] Hypothalamic damage may decrease a-MSH production, which impairs MC4R pathway signaling, and can result in accelerated and sustained weight gain due to decreased energy expenditure and hyperphagia.[1,15,16]

α-MSH Drives MC4R Pathway Signaling to Regulate Energy Balance and Body Weight[5-9,17,18]



α-MSH activation of MC4R regulates: • Hunger & food intake • Energy expenditure → **Body weight**

Loss of α-MSH Production Due to Hypothalamic Damage May Impair MC4R Pathway Signaling and Lead to Acquired Hypothalamic Obesity[1,4,5,8,9,11,15-17,19,20]



Decreased α-MSH activation of MC4R may result in: • Increased hunger/hyperphagia • Reduced energy expenditure → **Accelerated and sustained weight gain**

*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.

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Medical Record Codes to Help Identify Patients with Acquired HO

Review Medical History

☑ 1. Hypothalamic Injury

C75.2, D35.3, D44.4	Neoplasms of the craniopharyngeal duct (craniopharyngioma)
C75.1, D35.2, D44.3	Neoplasms of the pituitary gland
C71.7, C71.9	Malignant neoplasm of brain, brain stem
D33.0, D33.1, D33.2, D33.3, D33.4, D33.7, D33.9	Benign neoplasm of brain, cranial, spinal cord, CNS
D43.0, D43.2, D48.9	Neoplasm of uncertain behavior of brain
C72.30, C72.31, C72.32	Malignant neoplasm of optic nerve
S0636XA, S069X9A	Severe TBI
D76.3	Histiocytosis syndromes

☑ 2. Hypothalamic Dysfunction

E23.3	Hypothalamic dysfunction
E23.0, E23.1, E89.3	Hypopituitarism/Panhypopituitarism
E03.8, E03.9	Hypothyroidism
E23.6, E23.7	Pituitary gland disorders
E27.1, E27.3, E27.40, E27.49	Adrenal insufficiency
E34.50	Androgen insensitivity syndrome
E34.321	Insulin-like Growth Factor 1 (IGF-1) deficiency
E23.2	Arginine Vasopressin Disorders (AVD)/ Diabetes insipidus

☑ 3. Weight Gain after injury

R63.5	Abnormal weight gain
E66.1	Drug-induced obesity
E66.01, E66.09, E66.2, E66.9	Obesity

Facilitating Patient Care Coordination

☑ Document your findings in the patient's medical record to help facilitate continuity of care. Thorough documentation is important for patients with acquired HO as they are at risk for experiencing fragmented care.

☑ Communicate the diagnosis and implications of acquired HO to the patient

Diagnosis is based on the independent medical judgment of the healthcare professional.

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