Decreased energy expenditure is an under-recognized driver of weight gain in acquired HO

- Patients with injury to the hypothalamus may have **a unique form of obesity known as acquired hypothalamic obesity (HO)**, a chronic and progressive condition that can be challenging to manage[1-4]
- **Acquired HO is characterized by weight gain following injury from hypothalamic-pituitary tumors, their treatment, or other injuries to the hypothalamus[3]**

The MC4R pathway **is a key signaling pathway in the hypothalamus** that regulates satiety, hunger, and energy expenditure to **maintain energy balance** and control body weight.[5-8]

Impairment of the MC4R pathway due to **hypothalamic injury can lead to energy imbalance and weight gain.**[1,2,6,9]

Increased hunger or hyperphagia

- **Reduced satiety** can cause persistent feelings of hunger or hyperphagia that may lead to increased caloric intake[10,11]
- **Not all patients with acquired HO show signs of increased hunger.** Hyperphagia is present in ~70% of cases, but levels of hunger and increased caloric intake can vary between patients. The experience of hyperphagia and difficulty in managing this symptom can vary dramatically[12,13]

Varying severity, not always present

Decreased energy expenditure

- **Decreased energy expenditure** contributes to progressive weight gain even in the absence of hyperphagia or increased caloric intake[5,6,14,15]
- **Resting energy expenditure (REE)** in patients with acquired HO* was found to be ~1/3 lower than expected in a recent study[16]

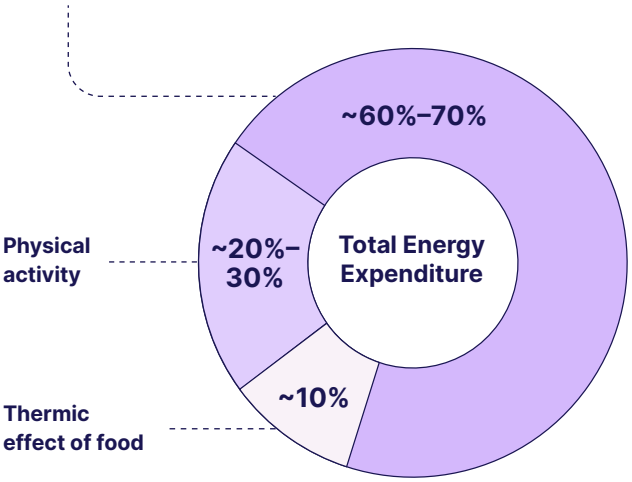
Commonly present

*The study included 12 patients with severe hypothalamic dysfunction.[16]

Decreased energy expenditure adds a unique challenge to managing acquired HO

Resting energy expenditure (REE) is defined as the energy required to maintain basic physiological functions and body temperature while at rest.[17]

REE accounts for the majority of the body's total daily energy expenditure[17-19]



Decreased REE due to MC4R pathway impairment has a significant impact on weight gain in acquired HO[1,5,15]

35%

In a study of patients with acquired HO,* **REE was shown to be lower by as much as 35%** compared to expected values. **This decrease in REE can result in unused energy being stored as fat.**[5,14,16]

- In acquired HO, decreased REE can lead to an energy surplus and weight gain even in the absence of increased caloric intake; therefore, diet alone may be insufficient to reduce weight[5,14,15,20]
- Even substantial increases in physical activity may be insufficient to offset the resulting energy surplus[16,21]
- Bariatric surgery and some pharmacologic interventions may temporarily reduce weight, but long-term efficacy is limited[1,14,22]

*The study included 12 patients with severe hypothalamic dysfunction.[16]

Early identification and education can make a difference.

Identifying and discussing the cause of weight gain in cases of hypothalamic injury can help patients better understand and manage the unique dynamics of their disease.

Rhythm InTune
Support made personal

Connect patients and family members with educational support.

Rhythm Patient Education Managers† are trained to provide one-on-one educational support for people with acquired HO and their family members.

†Patient Education Managers are employees of Rhythm Pharmaceuticals and do not provide medical care or advice. We encourage patients to always speak to their healthcare providers regarding their medical care.

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