Rare melanocortin-4 receptor (MC4R) pathway diseases: Cardinal symptoms and genetic confirmation

Rare MC4R pathway diseases can be caused by genetic variants within the pathway, which impair signaling that controls hunger[1].

There are **cardinal symptoms** in children that may indicate a rare MC4R pathway disease, which help to differentiate from more common forms of obesity.

Hyperphagia and **early-onset obesity** are the cardinal symptoms of a rare MC4R pathway disease.[2] If you see them in your patients, **they may be living with a rare MC4R pathway disease**.

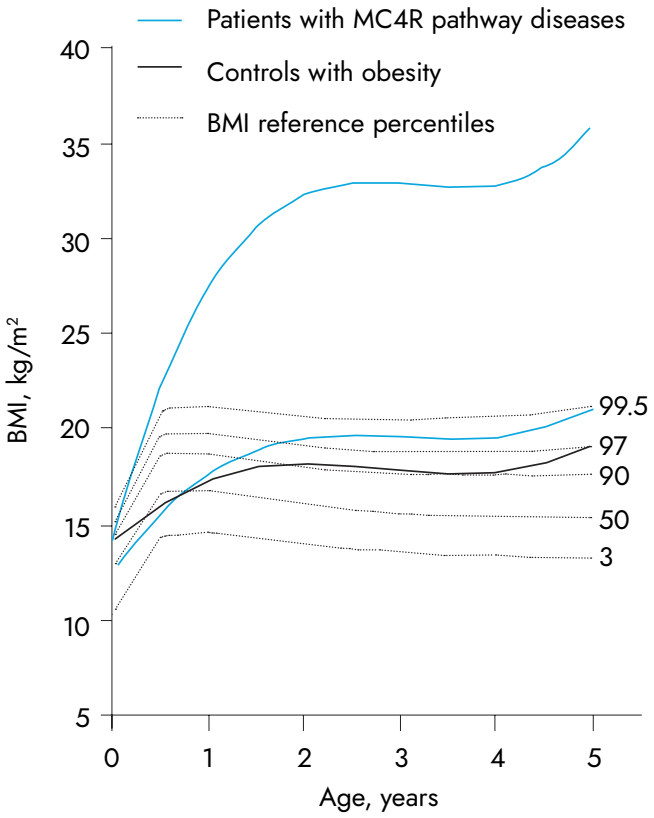
Hyperphagia[3]

Hyperphagia, also known as an abnormally strong sensation of hunger or desire to eat.

Characteristics and behaviours of hyperphagia include:

- **Heightened and prolonged hunger**
- **Longer time to reach satiety**
- **Shorter duraction of satiety**
- **Severe preoccupation with food** (hyperphagic drive)
- **Food-seeking behaviors** (night eating, stealing food, foraging for food in trash)
- **Distress and functional impairment if denied food**

Early-onset obesity[4]



Controls with obesity have a BMI >30kg/m² by age 14 to 16 years and do not have a variant in *LEP*, *LEPR*, or *MC4R*.

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Proactive identification of cardinal symptoms, and appropriate referral for genetic confirmation using correct gene panels can help move children living with a rare MC4R pathway disease, onto their most appropriate care path

Access to appropriate tools means genetic variants that cause rare MC4R pathway diseases, can be diagnosed early

The diagnosis pathway

- Patient visits HCP to discuss symptoms
- HCP identifies cardinal symptoms
- HCP refers patient for genetic testing
- Genetic testing results confirm if the patient has a rare MC4R pathway disease

Through a correct referral, children with genetic variants that cause rare MC4R pathway diseases can be screened, and appropriately cared for

Current genetic screening allows many more rare diseases to be identified – rare MC4R pathway diseases can now be part of this

If you need more information on genetic confirmation or locating expert centres in your country, please visit our website, accessible via the QR code:

References:

1. Yazdi F, et al., et al. PeerJ. 2015;3:e856. 2. Huvenne H, et al. Obes Facts. 2016;9(3):158-173. 3. Heymsfield SB, et al. Obesity (Silver Spring). 2014;22(suppl 1):S1-S17. 4. Kohlsdorf K, et al. Int J Obes (Lond). 2018;42(9):1602-1609.

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