Rare melanocortin-4 receptor pathway diseases: Clinical features and genetic confirmation

Rare melanocortin-4 receptor (MC4R) pathway diseases can be caused by genetic variants within the pathway, which impair signalling that controls hunger.[1]

Hyperphagia (pathological, insatiable hunger leading to obsessive food-seeking behaviours and abnormal food intake) and **early-onset obesity** are clinical features of a rare MC4R pathway disease.[1] If you see these features in your patients, **they may be living with a rare MC4R pathway disease**.[1]

Hyperphagia[2]

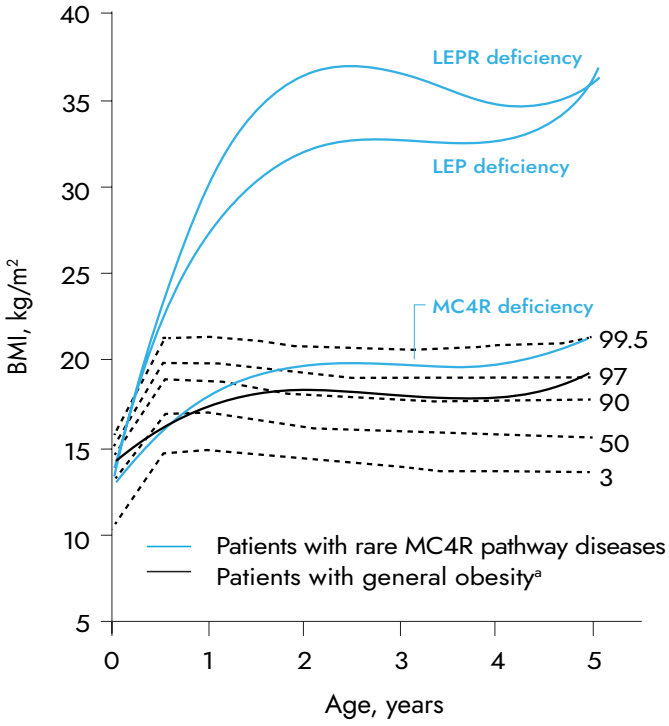
Also known as an abnormally strong sensation of hunger or desire to eat.

Characteristics and behaviours include:

- Heightened and prolonged hunger
- Longer time to reach satiety
- Shorter duration of satiety
- Severe preoccupation with food (hyperphagic drive)
- Obsessive food-seeking behaviours and abnormal food intake
- Distress and functional impairment if denied food

Early-onset obesity[3]

Presence of obesity before age 5, and BMI ≥95th percentile for age and sex.[4]



a) Following inclusion criteria for the control group were defined: BMI at the ages 14, 15, or 16 years >30 kg /m 2, early childhood data on BMI available (at least two values between 0 – 5 years) and exclusion of a mutation in the leptin, leptin receptor, and *MC4R* gene.

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Proactive identification of clinical features, 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.[5]

Access to appropriate tools means genetic variants that cause rare MC4R pathway diseases can be diagnosed early.[5]

The diagnosis pathway[5]

- Patient visits HCP to discuss symptoms
- HCP identifies clinical features
- 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 Path4hcps.com, accessible via the QR code:

References:

1. Loos, RJF and Yeo, GSH. *Nat Rev Gens.* 2022;23:120–133. 2. Heymsfield SB, et al. *Obesity (Silver Spring)*. 2014;22(suppl 1):S1–S17. 3. Kohlsdorf K, et al. *Int J Obes (Lond)*. 2018;42(9):1602–1609. 4. Hampl SE, et al. *Pediatrics.* 2023;151(2):e2022060640. 5. Styne DM, et al. *J Clin Endocrinol Metab.* 2017;102(3):709–757.

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