ASSESSMENT OF HYPERPHAGIA IN PATIENTS WITH MONOGENIC OBESITY

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INTRODUCTION

- Besides an excessive, early-childhood weight gain, hyperphagia is the key symptom in patients with monogenic obesity [1, 2].
- However, the assessment of hyperphagia is still challenging [3].

AIM

Implementation of the hyperphagia questionnaire developed for patients with Prader-Willi-Syndrome (PWS) in patients with monogenic obesity to assess the severity of hyperphagia.

METHODS

- Enrollment of pediatric patients with biallelic pathogenic *leptin receptor* (*LEPR*) variants, heterozygous pathogenic *melanocortin-4 receptor* (*MC4R*) variants and *16p11.2* microdeletion including deletion of *Src homology 2B1* (*SH2B1*)
- Assessment of the 13-item hyperphagia questionnaire from Dykens et al. [4] by their parents, developed and validated to assess hyperphagia in patients with PWS
- Items were summarized in a total hyperphagia score and its subscores hyperphagic behaviour, hyperphagic drive and hyperphagic severity

RESULTS

- Enrollment of 20 children with monogenic obesity (Table 1)
- Significant differences in BMI z-score, body fat ratio, total leptin and bioactive leptin levels between patients with *LEPR* variants and *MC4R* variants or *16p11.2* deletions ($p < 0.05$; Table 1)
- Significantly higher total hyperphagia scores in patients with *LEPR* and *MC4R* variants compared to patients with *16p11.2* deletions ($p < 0.05$, Figure 1)
- Moderate correlation between the age of all patients and the scores total hyperphagia ($r = -0.456$, $p < 0.05$) and hyperphagic behavior ($r = -0.516$, $p < 0.05$)

Table 1: Patients characteristics.

Characteristics	LEPR (n = 8)	MC4R (n = 7)	16p11.2 (n = 5)
Sex (n female)	5	3	4
Intellectual disabilities (n)	2	0	3
Age (years)	7.10 ± 5.74	10.7 ± 6.2	12.3 ± 4.92
BMI (kg/m²)	45.3 ± 15.9	35.1 ± 10.0	35.8 ± 7.0
BMI z-score	4.31 ± 1.82	2.92 ± 0.65*	2.62 ± 0.48*
Fat mass (%)[a]	56.2 ± 4.1**	45.3 ± 3.5**	50.17 ± 3.1
Total leptin (ng/mL)[b]	147.8 ± 114.5**	25.4 ± 16.6**	63.3 ± 11.1
Bioactive leptin (ng/mL)[b]	108.9 ± 60.2**	23.3 ± 15.9**	61.2 ± 16.9

Data are shown as mean ± SD, except for sex and intellectual disabilities, which are presented as absolute values. *significant difference between patients with *LEPR* variants and *MC4R* variants or *16p11.2* deletions ($p < 0.05$). **significant difference between patients with *LEPR* and *MC4R* variants ($p < 0.05$). a) Data were assessed in a subgroup: *LEPR* n = 4, *MC4R* n = 6 and *16p11.2* n = 3. b) Data were assessed in a subgroup: *LEPR* n = 6, *MC4R* n = 6 and *16p11.2* n = 5.

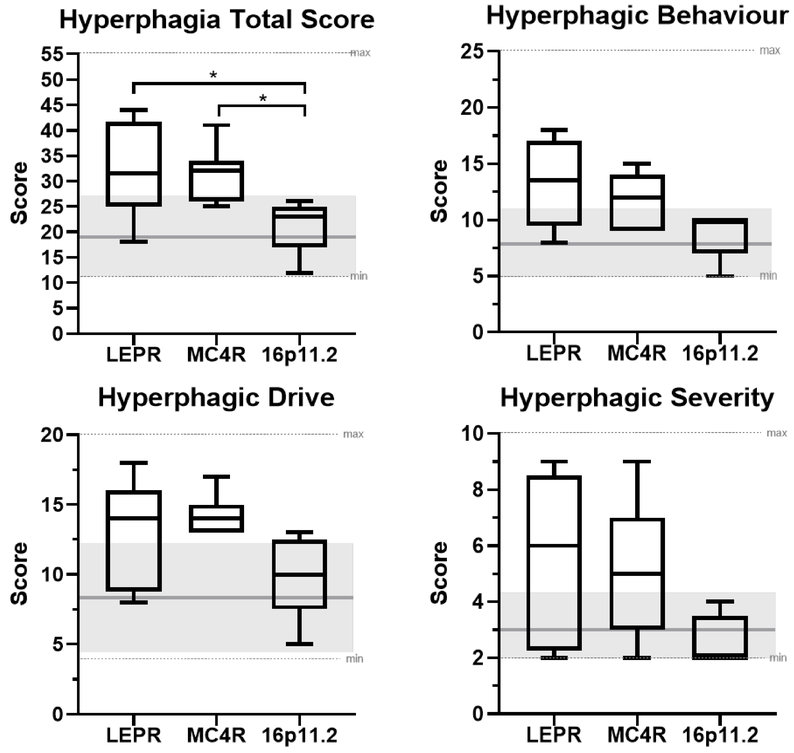

Figure 1: Total hyperphagia score and hyperphagia subscores in patients with *leptin receptor (LEPR)* variants, *melanocortin-4 receptor (MC4R)* variants and *16p11.2* deletions.

Data are presented as median and interquartile range. Significant differences between groups were analysed using Kruskal-Wallis test. Mean values (± SD) for individuals with severe obesity without a genetic cause published by Sherefat-Kazemzadeh et al. [5] are marked by grey line and grey area. Dotted lines indicate the maximum and minimum scores that could be reached.

CONCLUSIONS

- Hyperphagia scores are comparable in patients with *LEPR* and *MC4R* variants
- Patients with *16p11.2* deletions show less severe hyperphagia scores than patients with *LEPR* or *MC4R* variants
- Inverse relationship between age and total hyperphagia score as well as hyperphagic behaviour subscore suggests that the severity of hyperphagia declines with age
- Dykens' hyperphagia questionnaire is a useful tool to assess the severity of hyperphagia in patients with monogenic obesity

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