P1-75

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Ghrelin and brain-derived neurotrophic factor in children with Prader-Willi syndrome

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Background

Prader-Willi syndrome (PWS) is a complex multisystem genetic disorder, arising from lack of expression of paternally inherited imprinted genes on chromosome 15q11-q13. Hyperphagia represents one of the most serious symptoms of the PWS, leading to develop premature mortality.

Objective

To compare orexigenic (ghrelin) and anorexigenic factor (brain derived neurotrophic factor (BDNF)) concentration in non-GH-treated obese patients with genetically confirmed PWS with age, sex and BMI-matched obese controls (OC) and lean controls (LC).

Subjects and Methods:

Fasting and postprandial levels of plasma ghrelin and serum BDNF during mixed meal testing (370 kcal: 20% protein, 50% carbohydrate and 30% fat) were evaluated in obese children with PWS in comparison with OC and LC. All patients were prepubertal (Tanner1). Data are reported as medians (interquartile range), Manne-Whitney test was used for between-group.

Results:

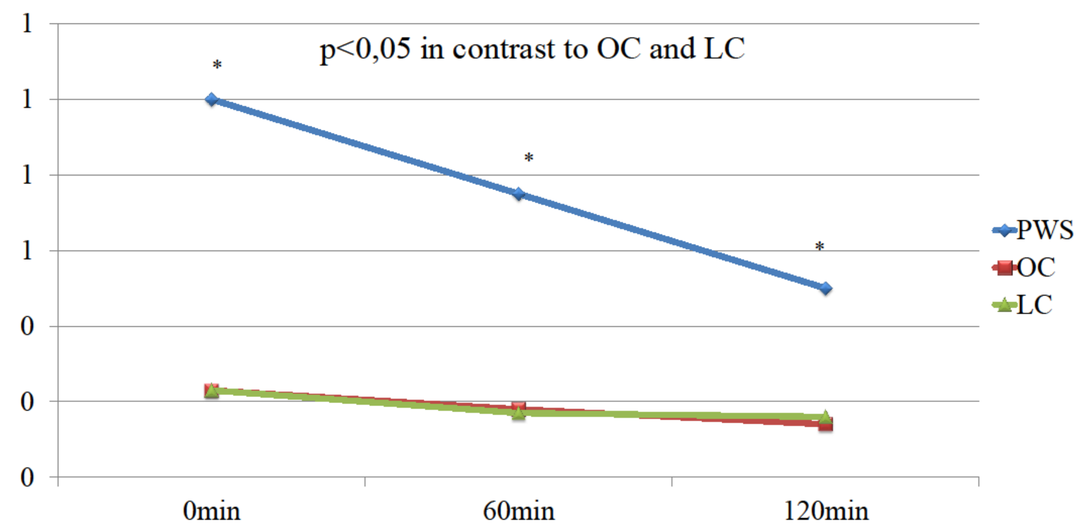
Characteristics of groups are shown in Table 1 and Table 2. Groups with *different superscripts* are significantly different (*p<0.05)* from each other *(*- in comparison with OC, **- relative to LC)*.

Hyperghrelinemia (fasting and postprandial) was observed in 17 patients with PWS in contrast with 15 OC and 10 LC (Table 1, Pic.1). The fasting glucose, insulin level and HOMA-IR were lower in these PWS patients compared with OC, suggesting that PWS children are more insulin sensitive than OC (Table 1).

Table 1 – Measurements of ghrelin in PWS, OC and LC

Characteristics	PWS (n=17)	OC (n=15)	LC (n=10)
Age (years)	9,9 [6,5÷13,9]	9,8 [6,5÷12,0]	9,7 [7,05÷10,7]
Males/females	6/11	4/11	4/6
Tanner stage	1	1	1
SDS BMI	3,6 [2,99÷4,57]**	3,3 [2,76-3,62]**	0,75[-0,69÷1,27]*
Ghrelin (ng/ml)	*1,0 [0,5÷1,0]*,***	*0,23 [0,13÷0,3]*	*0,23 [0,1÷0,45]*
Insulin 0 min (U/l)	*7,8 [4,2÷14,1]**	*15,0 [10,0÷24,7]*	5,4 [2,7÷9,59]*
Glucose 0 min (mmol/l)	*4,2 [3,9÷4,5]**	*4,9 [4,1÷5,2]*	*4,0 [3,73÷5,2]*
HOMA-IR	*1,5 [1,04÷2,64]**	*2,85 [2,47÷4,15]*	*1,1 [0,43÷2,3]*

Pic.1 Fasting and postprandial ghrelin levels (ng/ml) in PWS, OC and LC during mixed meal test

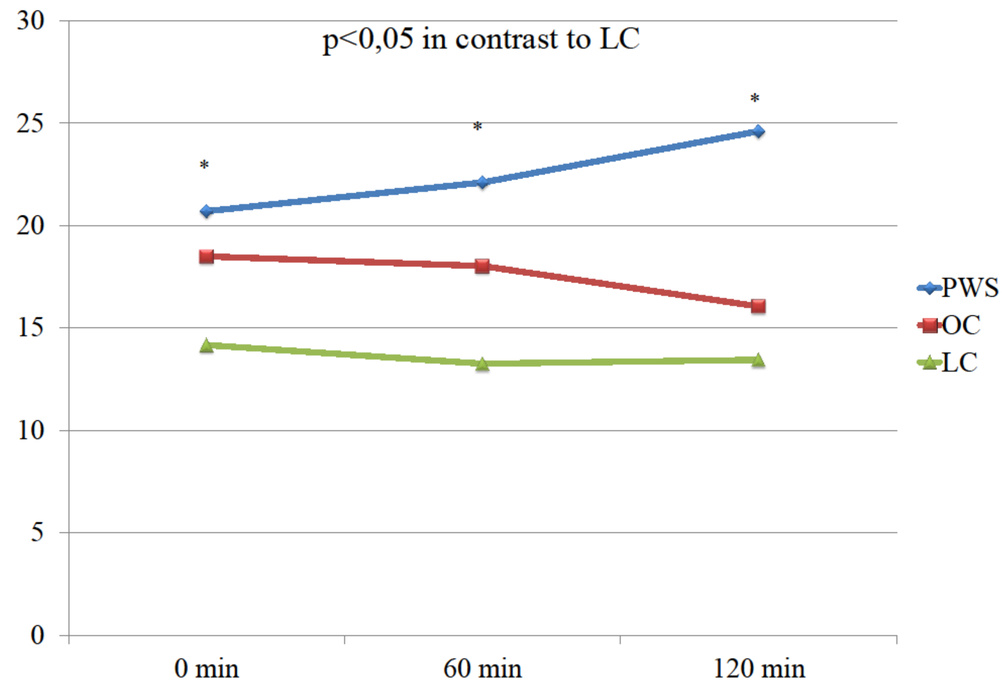


There were no significant differences in basal and postprandial BDNF levels on 60 and 120 min between 29 PWS children and 17 OC. However, there was a trend, though nonsignificant, toward the increasing BDNF concentration after the meal in PWS patients on 120 min (24,62[15,68÷27,75] vs 16,05[12,29÷22,42] ng/ml, p=0,07). The concentration of BDNF was significantly higher in PWS compared with 14 LC (p<0,05).

Table 2 – Measurements of BDNF in PWS, OC and LC

Characteristics	PWS (n=29)	OC (n=27)	LC (n=14)
Age (years)	10,3 [6,5÷11,6]	9,0 [6,0÷12,0]	8,9 [5,3÷10,5]
Males/females	20/9	16/11	12/2
Tanner stage	1	1	1
SDS BMI	3,25 [2,98÷4,53]**	3,35 [2,83-3,91]	0,52 [-0,79÷1,35]
BDNF (ng/ml)	*20,72 [15,77÷24,8]***	18,49 [12,99÷24,45]	*14,16 [10,87÷19,34]*
Platelet count per mm^3	285,5[249,0÷ 341,0]	285,0 [267,0 ÷ 324,0]	291,0 [250,0 ÷ 307,0]

Pic.2 Fasting and postprandial BDNF levels (ng/ml) in PWS, OC and LC during mixed meal test



Conclusion:

Fasting and postprandial ghrelin levels were significantly higher in PWS subjects compared to obese and lean controls. The level of BDNF pre- and postprandial secretion was significantly higher in PWS patients in contrast to LC, there was a light tendency toward the increasing BDNF concentration after the meal in PWS patients in contrast to OC, suggesting possible resistance to the actions of BDNF to its receptor or a different role of BDNF in the pathogenesis of food intake response in PWS patients. Further research is necessary to clarify the role of BDNF in weight reduction, energy expenditure, and appetite control in PWS.

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