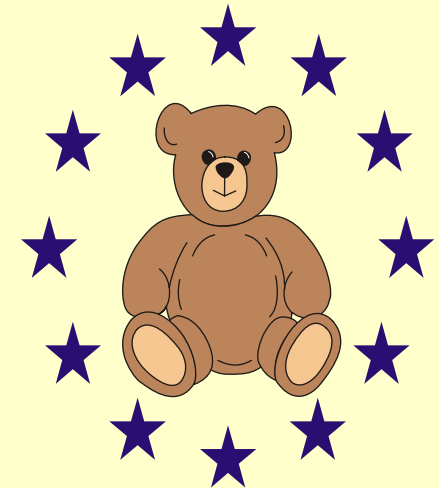


IGF-1 AXIS AND AMINO ACID SERUM CONCENTRATIONS IN INFANTS WITH VARIOUS PROTEIN INTAKE

DATA FROM CHOP STUDY

P. Socha, D Gruszfeld, B Koletzko,
V Grote, R von Kries, R Cachera,
H Demmelmair, D. Brasseur, M.
Giovannini, R C Monasterolo, J
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*European
Childhood
Obesity
Project*





IGF-1 axis

- stimulatory role of IGF-1 in adipogenesis in vitro and in primary adipocyte cultures of pig, rat and rabbit.
 - Smith PJ et al. J Biol Chem 1988; Hausman GJ et al. J Anim Sci 1989; Deslex S et al. Exp Cell Res 1987
- correlations between IGF-1 serum concentrations in 5-years old children and anthropometric values: fat-free mass and fat mass as well as with weight gain (between 0-2 years)
 - Ong K, et al. J Clin Endocrinol Metab 2002
- In primary cell cultures from normal prepubertal children IGF-I enhanced differentiation of both subcutaneous and visceral fat cells.
 - Grohmann M, et al. J Lipid Res 2005

- At 9 mo of age IGF-1 significantly correlates with protein intake ($R=0,3$), but not at the age of 10y
 - Hoppe C, et al. Am J Clin Nutr 2004
- IGF-1 mediates positive correlation between protein intake in early infancy and body growth?



Excess of protein in formula feed infant

- higher concentrations of many plasma amino acids from 4 to 6 months of age than in breast fed infants

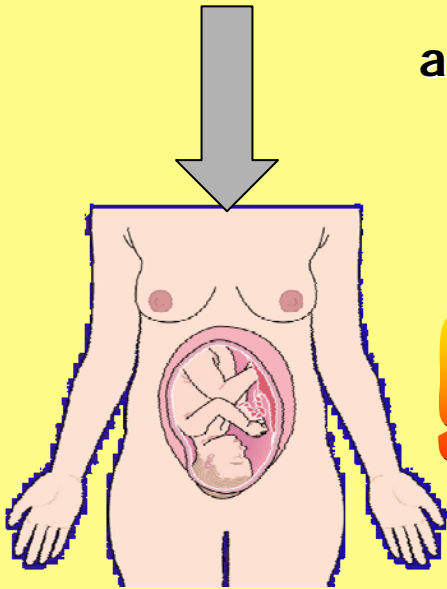
– Axxelsson I et al. Acta Paediatr Scand 1988

Nutrition

Short term

long-term

diet



Fetus and infant feeding



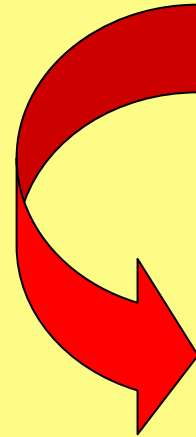
gens



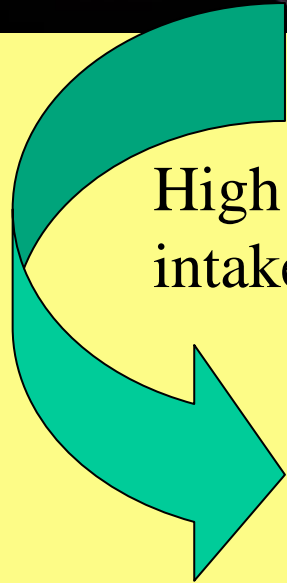
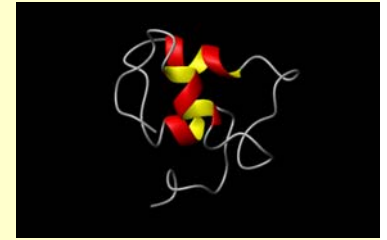
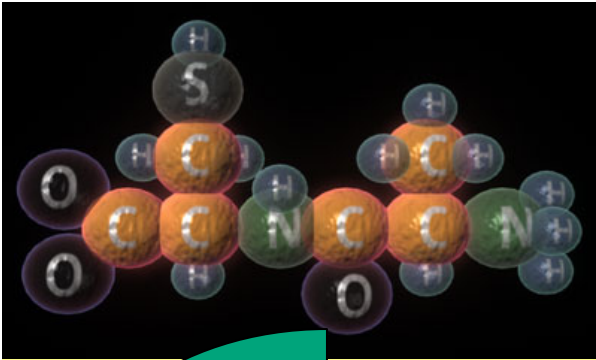
Infections and other environmental factors

Metabolic programming
carbohydrates, lipids,
protein, hormones, receptors
gens

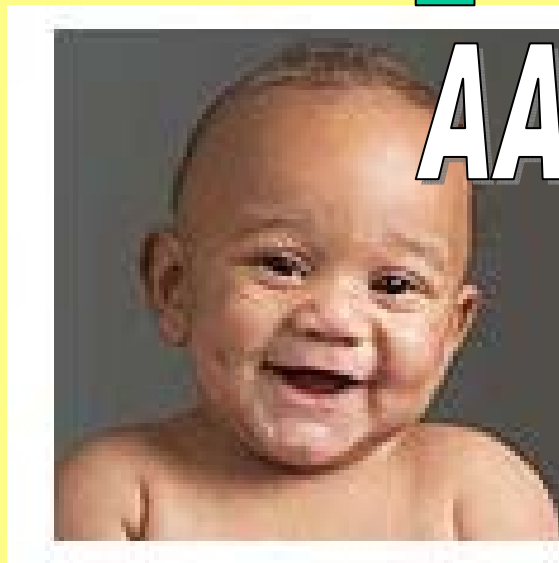
Diabetes
Obesity
Hipertension
Heart disease
Aging



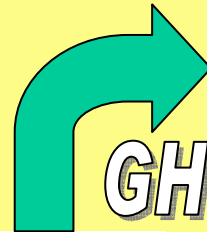
AA, IGF, insulin



High protein
intake

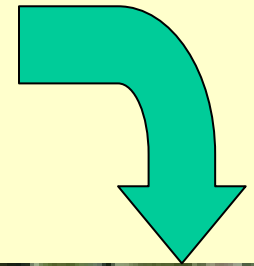


AA



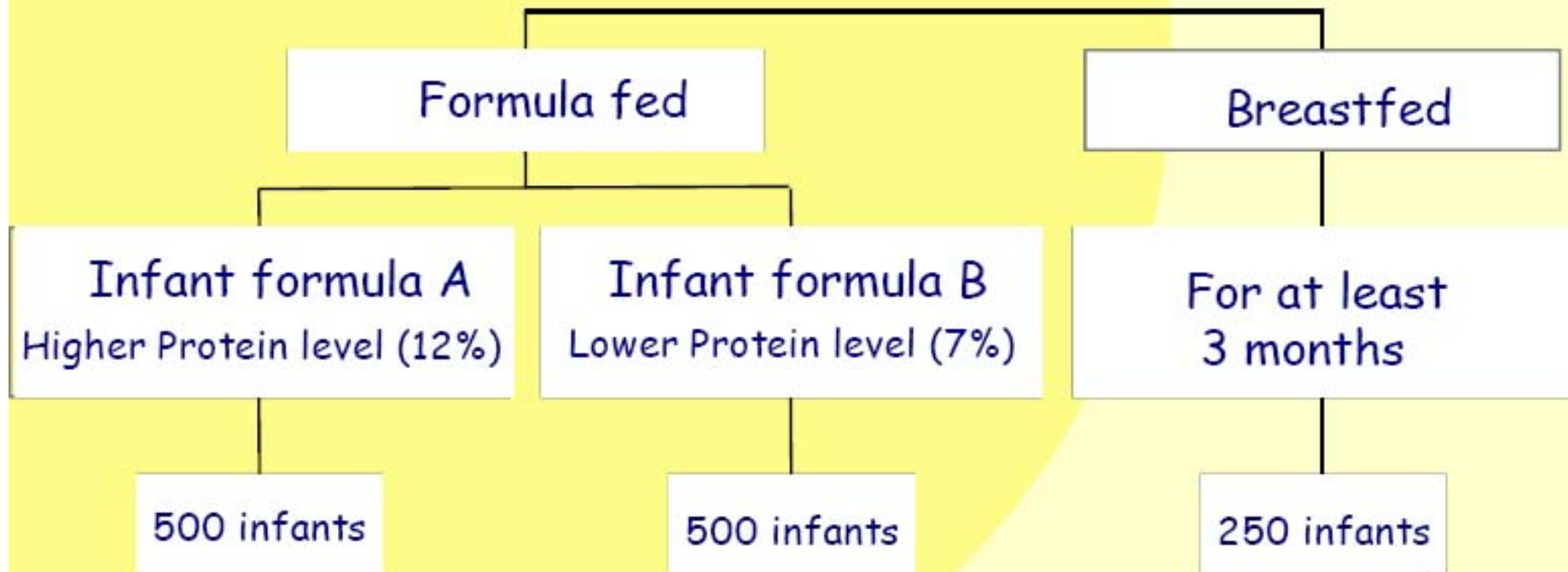
insulin

IGF-1



adipocytes

Study plan: 3 experimental groups



Subjects with at least one urine/blood parameter

- **children from 4 countries: (Germany, Spain, Belgium, Poland)**
- **where local ethics committees approved urine and blood sampling**
- **Time of blood and urinesampling: 6 m-ths**

Country	Low-protein	High-protein
GE	65	68
BE	43	38
PL	80	79
ES	117	116
Total	305	301

vs 203 breast fed infants

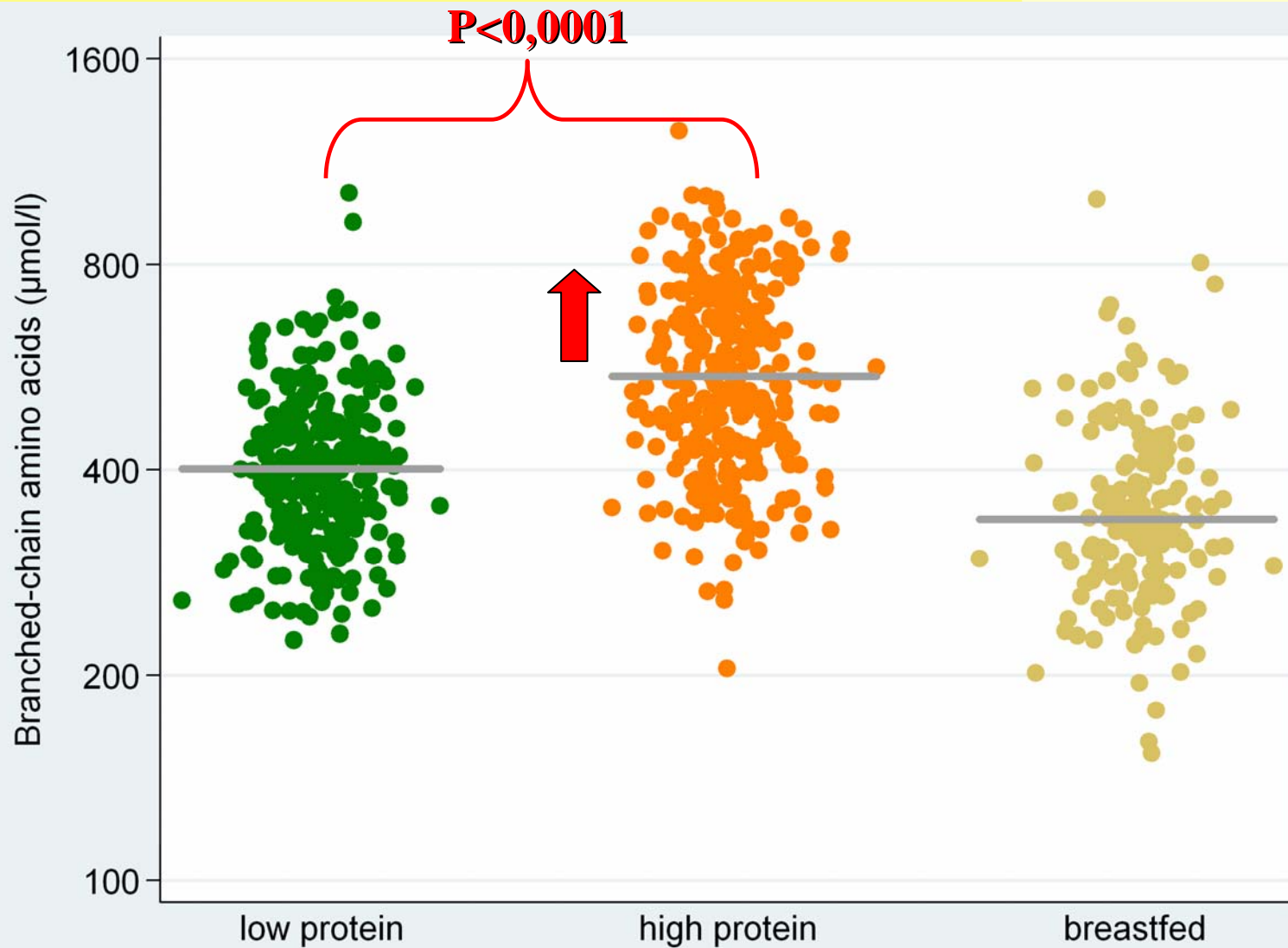
Population characteristic

	Low-protein Mean (SD)	High-protein Mean (SD)	Breast fed Mean (SD)
Females	51,5%	48,5%	55,8%
Birthweight (g)	3273.1 (329.3)	3279.9 (343.3)	3340.4 (369.0)
Maternal age (years)	29.1 (5.0)	29.4 (5.2)	30.7 (4.6)

Biochemical/hormonal parameters studied

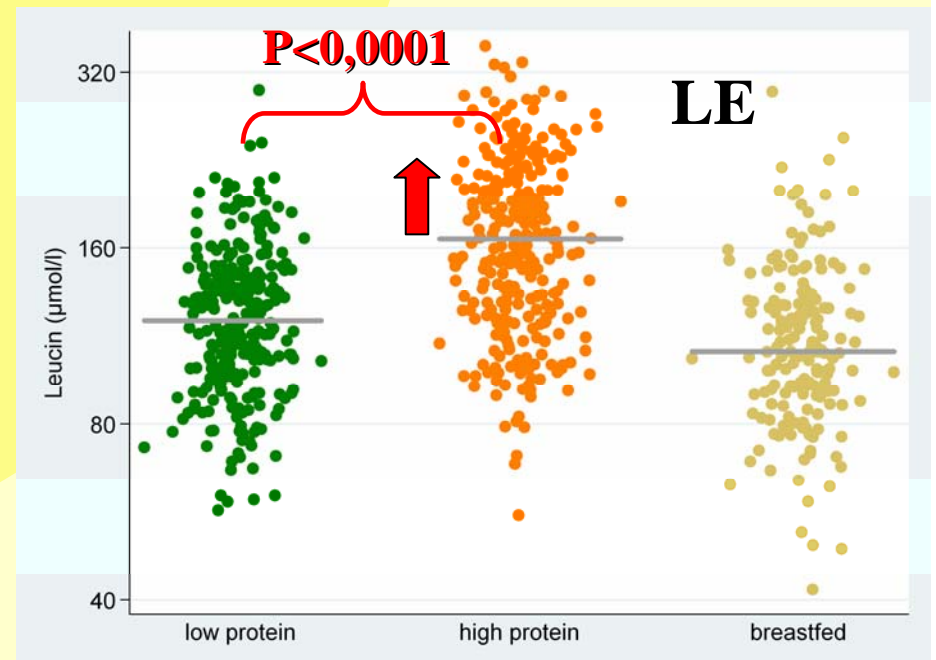
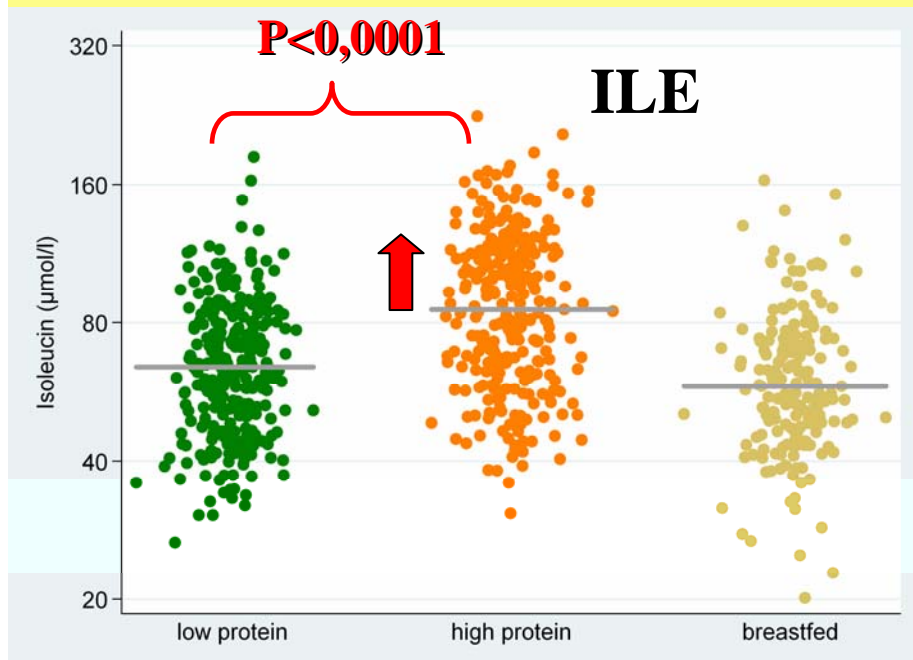
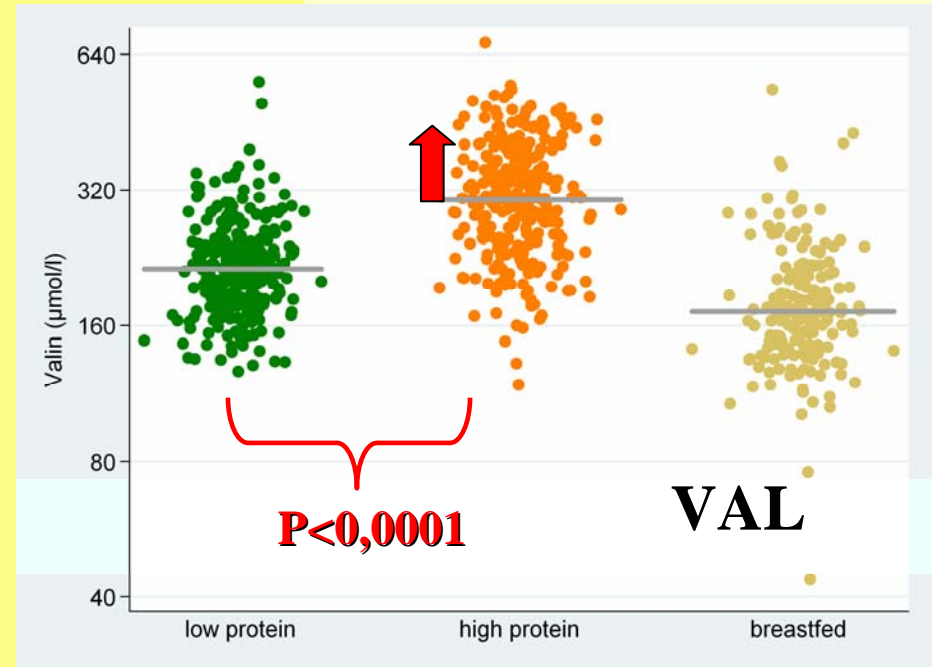
- Serum: IGF-1 total and free, IGF-BP2, IGF-BP3
 - measured by RIA
- Urine: C-peptide of insulin/creatinine
 - measured by RIA
- Serum: Amino acids
 - measured by HPLC

AA
low- and high-protein group
(& breastfed infants)

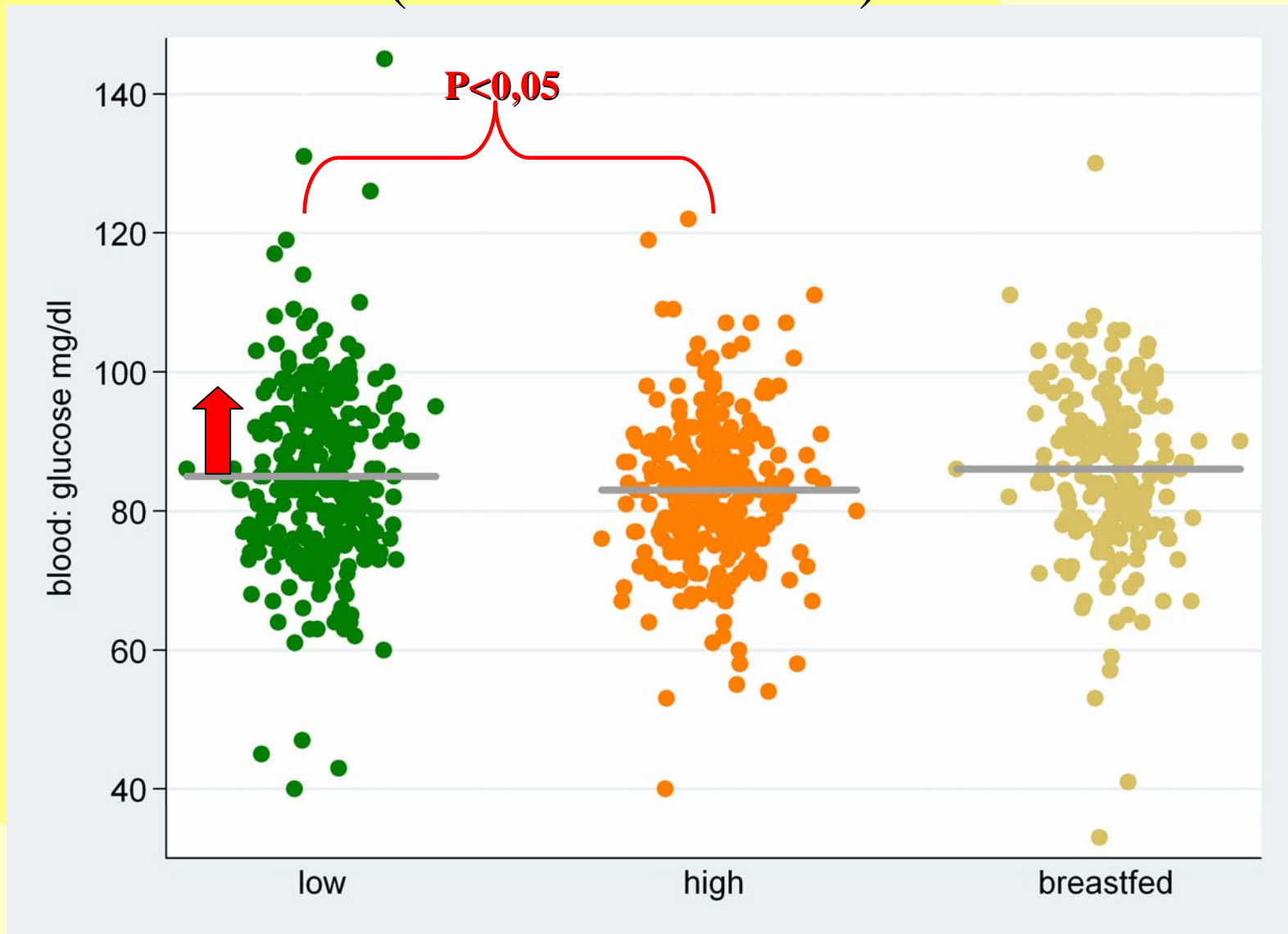


BCAA

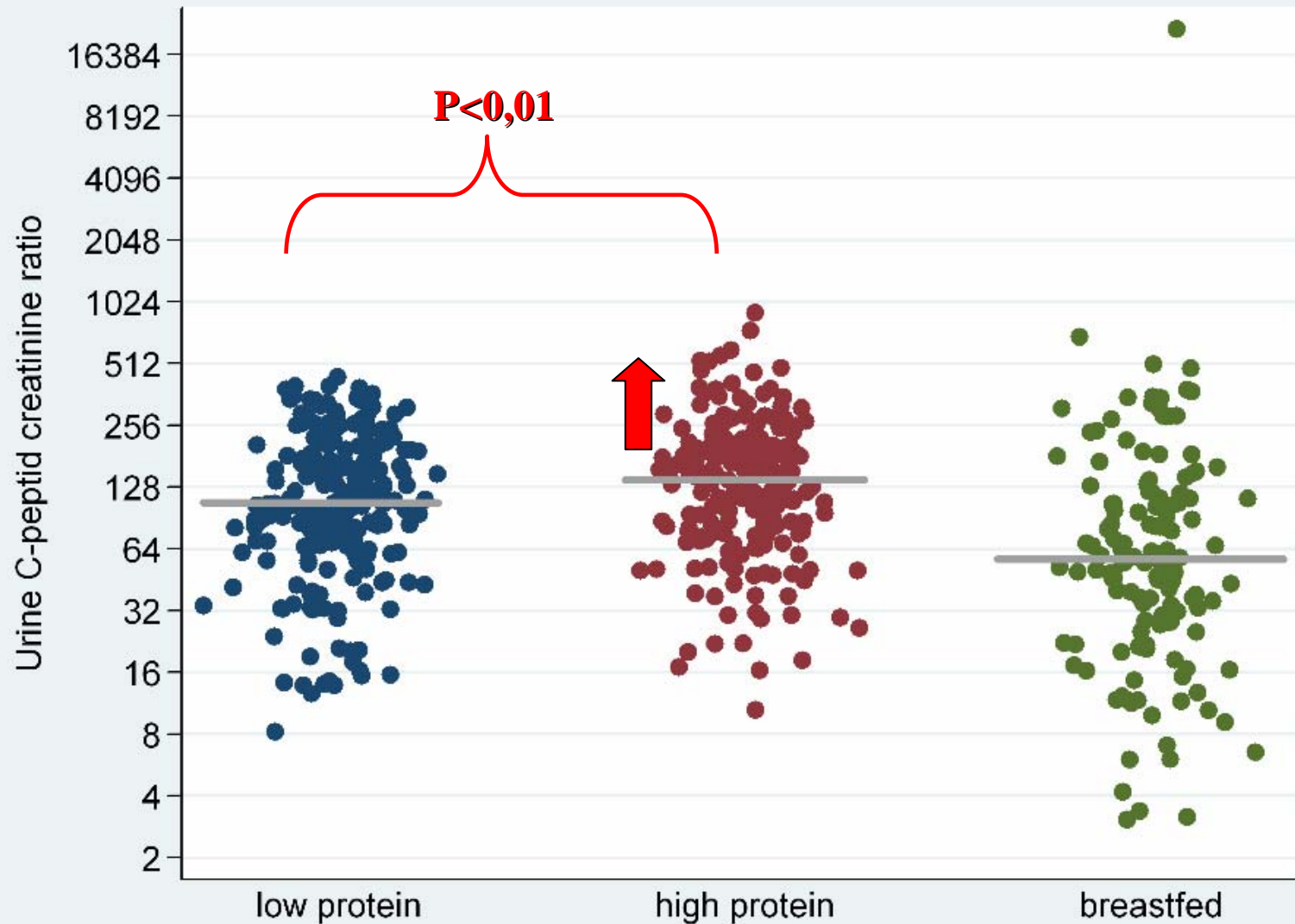
Low-protein vs. High-protein group



Serum glucose low- and high-protein group (& breastfed infants)

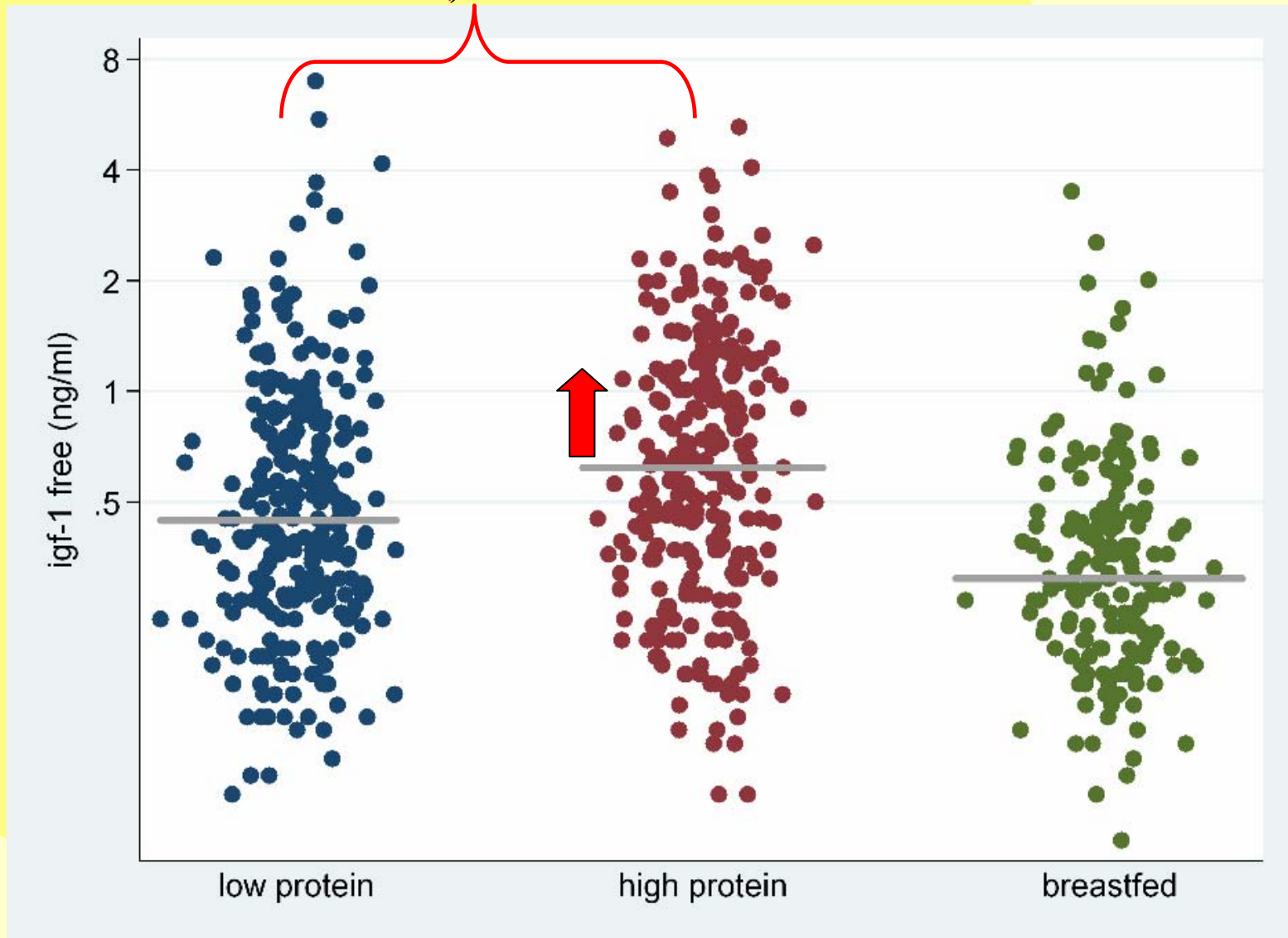


Urine C-peptide/creatinine – 6th m-th low- and high-protein group (& breastfed infants)

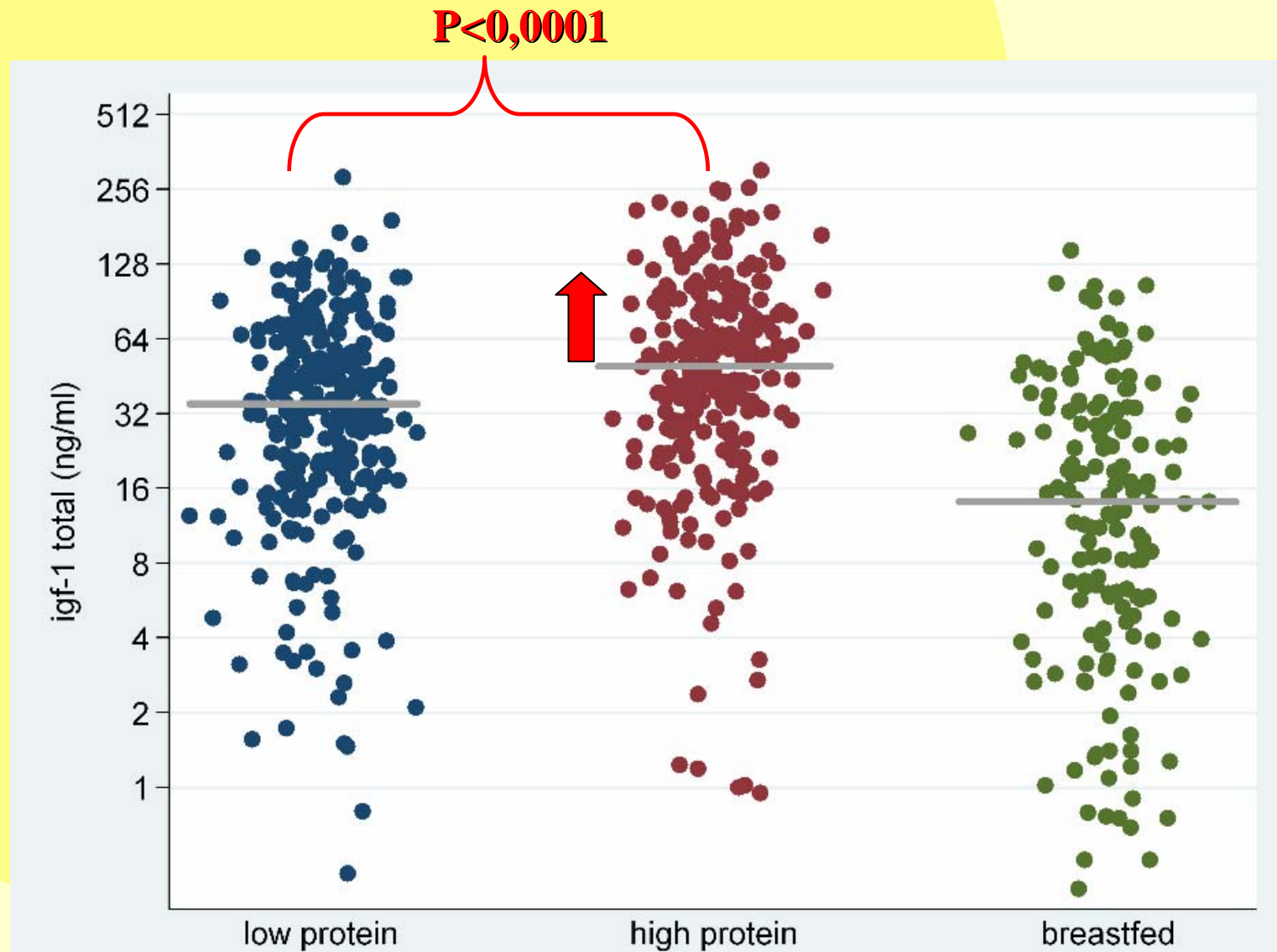


IGF-1 free: low- and high-protein group (& breastfed infants)

P<0,0001

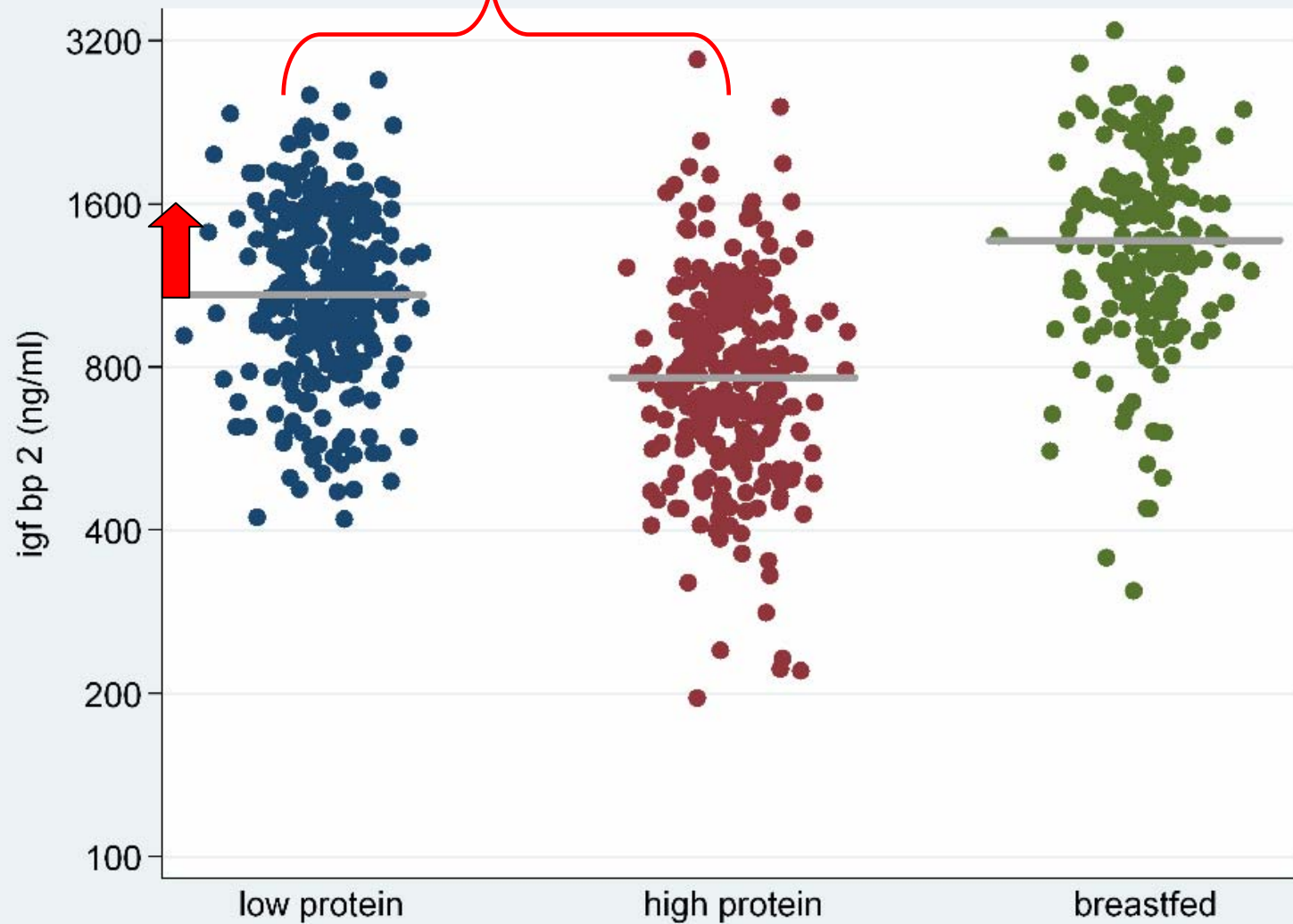


IGF-1 total: low- and high-protein group (& breastfed infants)

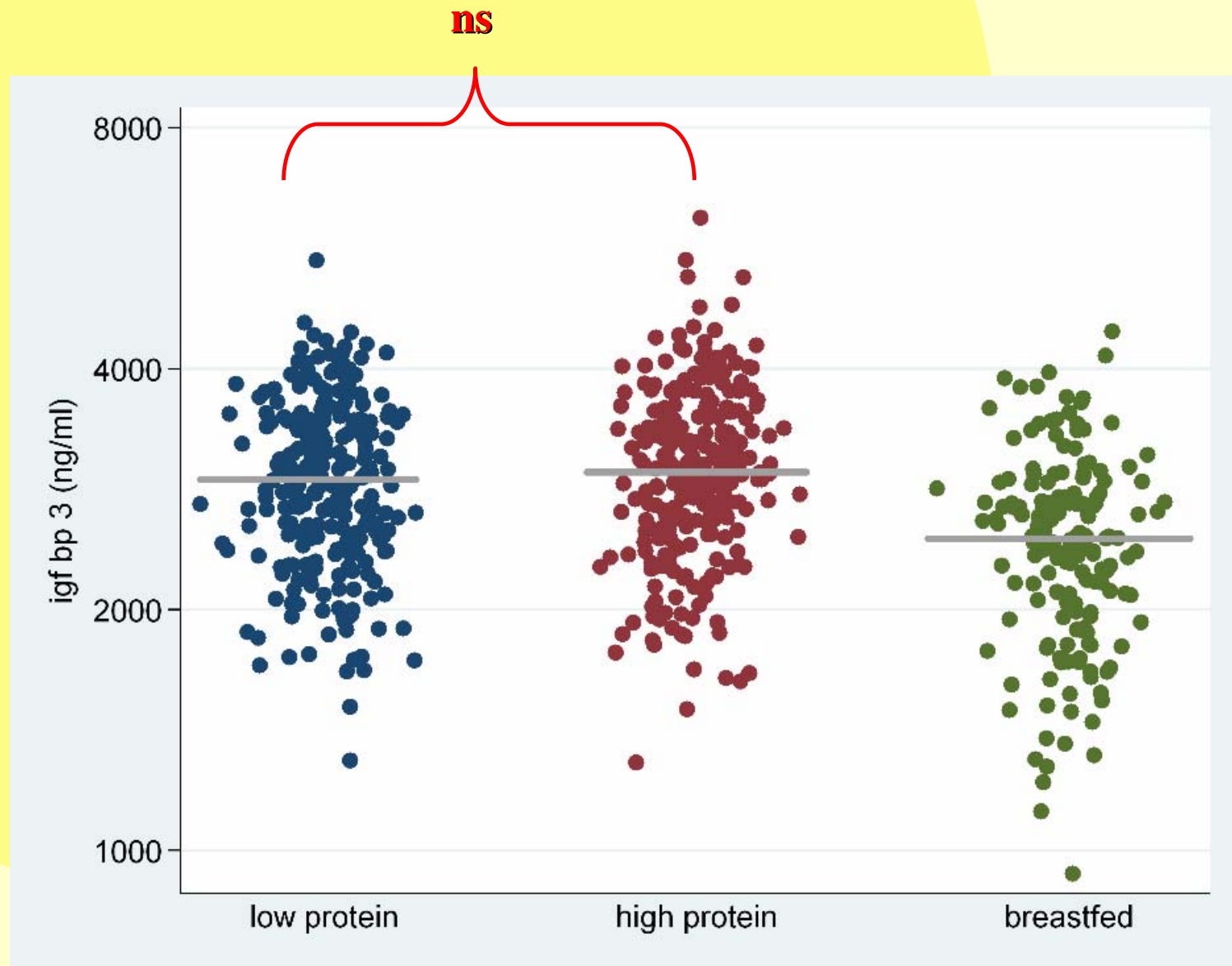


IGF-BP2: low- and high-protein group (& breastfed infants)

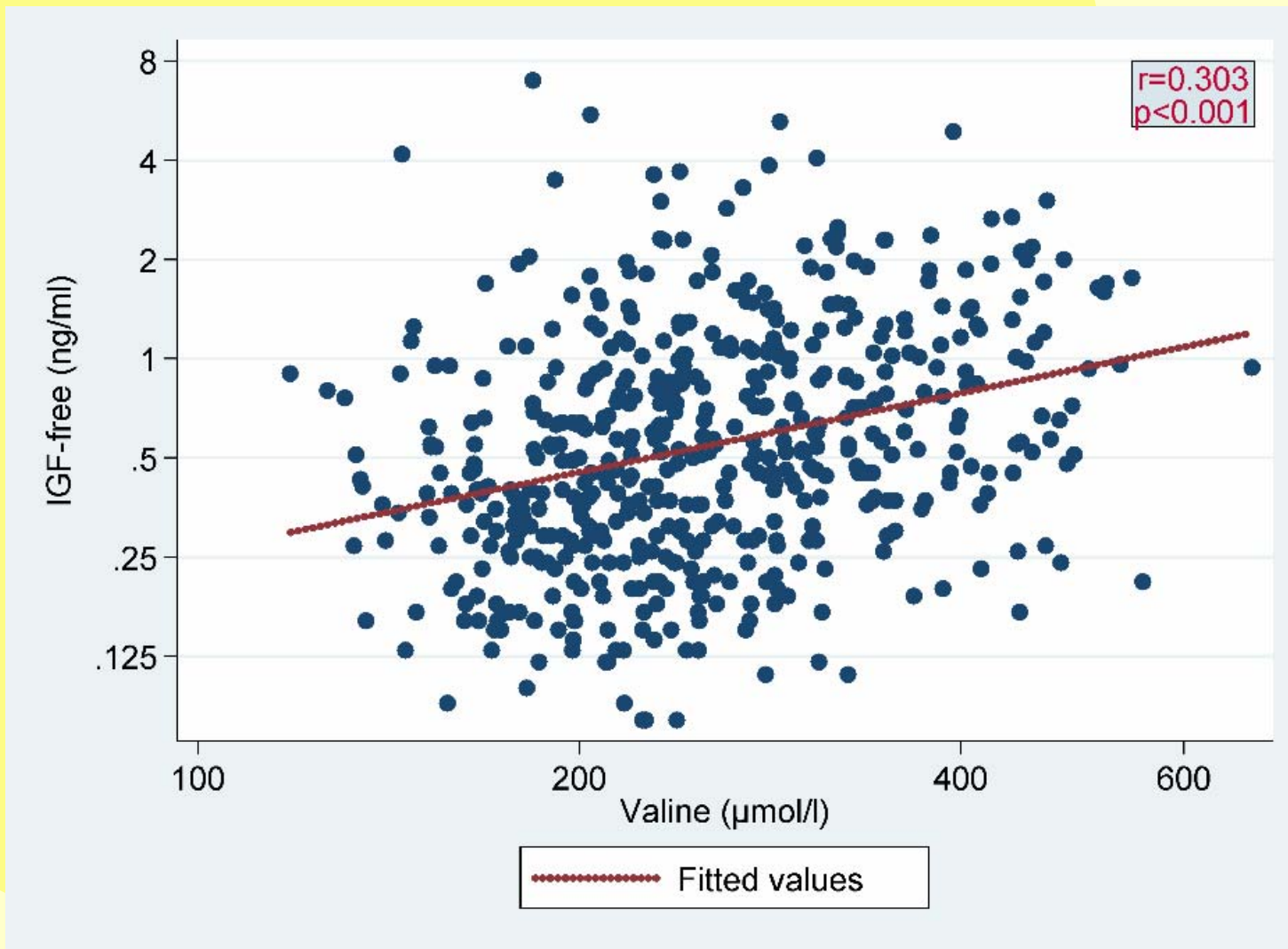
P<0,0001



IGF-BP3: low- and high-protein group (& breastfed infants)



Linear regression: IGF-1-free and serum Valine concentration



Summary

- Increased BCAA concentration with higher protein intake
- Increased C-peptide levels with higher protein intake
- Stimulated IGF-1 axis by higher protein intake



AA and insulin

- Leucine is a stimulator of insulin release.
 - Fajans SS, et al. J Clin Invest 1963
- BCAA are physiological stimulators of insulin secretion
 - Fajans SS, et al J Clin Endocr 1971
- Correlation between plasma valine levels and the urinary C-peptide excretion.
 - Zetterström R, et al Klin Pädiatr, 1985



IGF-1 and obesity

- free IGF-1 increases in obesity that was documented in many studies
 - Frystyk J, et al. Metabolism 1995; Nam SY, et al. Int J Obes 1997; Argente J, et al. J Clin Endocrinol Metab 1997
- IGF-BP-2 decreased in obesity and the results are very consistent
 - Frystyk J, et al. Metabolism 1995; Nam SY, et al Int J Obes 1997; Argente J, et al J Clin Endocrinol Metab 1997
- conflicting results concerning total IGF-1 serum levels - may be explained by different populations studied with different types of adiposity
 - Frystyk J, et al. Metabolism 1995; Nam SY, et al. Int J Obes 1997
 - Argente J, et al. J Clin Endocrinol Metab 1997; Minuto F, et al. J Endocrinol Invest 1988; Skaggs SR, et al. Horm Res 1991
 - Van Vliet G, et al. Acta Endocrinol 1986; Loche S, et al. Clin Endocrinol 1987

Conclusions

- High protein intake is associated with higher BCAA levels, increased insulin secretion and stimulation of IGF-1 axis
- Increased insulin secretion and IGF-1 stimulation may contribute to the increased BMI induced by high protein intake in infancy

