INTRODUCTION

PHP1A and PseudoPHP are caused respectively by maternal and paternal mutations involving the GNAS exons that encode the alpha-subunit of the stimulatory G protein. Common to different forms of PHP1B is a loss-of-methylation (LOM) at one or several maternal GNAS exons, which likely reduces Gsa expression in certain tissues. In most autosomal dominant PHP1B variants, LOM is restricted to exon A/B and usually patients carry deletions affecting imprinting control elements; in contrast, sporadic PHP1B patients (sporPHP1B) display broad LOM at GNAS, yet lack deletions in the vicinity of this complex locus. PseudoPHP and, albeit to a less extent, PHP1A patients present with foetal and postnatal growth retardation, while PHP1B patients show with considerable overgrowth at birth.

Figure 1: schematic representation of the GNAS locus

OBJECTIVE AND METHODS

Compare the final heights (patients >18yrs) and BMIs of 121 female (F) and 81 male (M) patients affected either by PHP1A (n=72), PseudoPHP (n=26), AD-PHP1B (n=33), or sporPHP1B (n=71).

Figure 3: BMIs in AD-PHP1B and sporPHP1B patients

CONCLUSIONS

As previously described, patients with mutations in the coding sequence of GNAS have much reduced adult heights. Obesity was encountered only in PHP1A, not in PseudoPHP. Despite being born macrosomic, patients with LOM at the GNAS locus attained a normal final height and a normal BMI, suggesting a particular important role of GNAS in the regulation of foetal growth.

REFERENCES

