Final heights and BMIs in patients affected with different types of pseudohypoparathyroidism (PHP)

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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**.

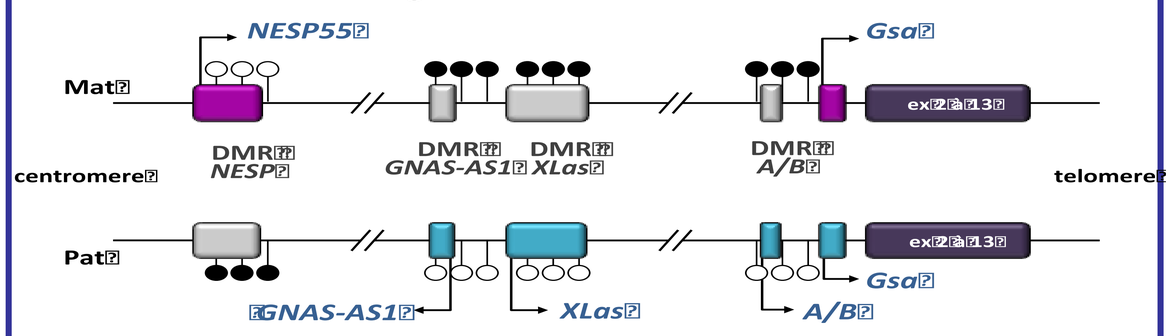


Figure 1: schematic representation of the GNAS locus

OBJECTIVE AND METHODS

Figure 3: BMIs in AD-PHP1B and sporPHP1B patients

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).

RESULTS

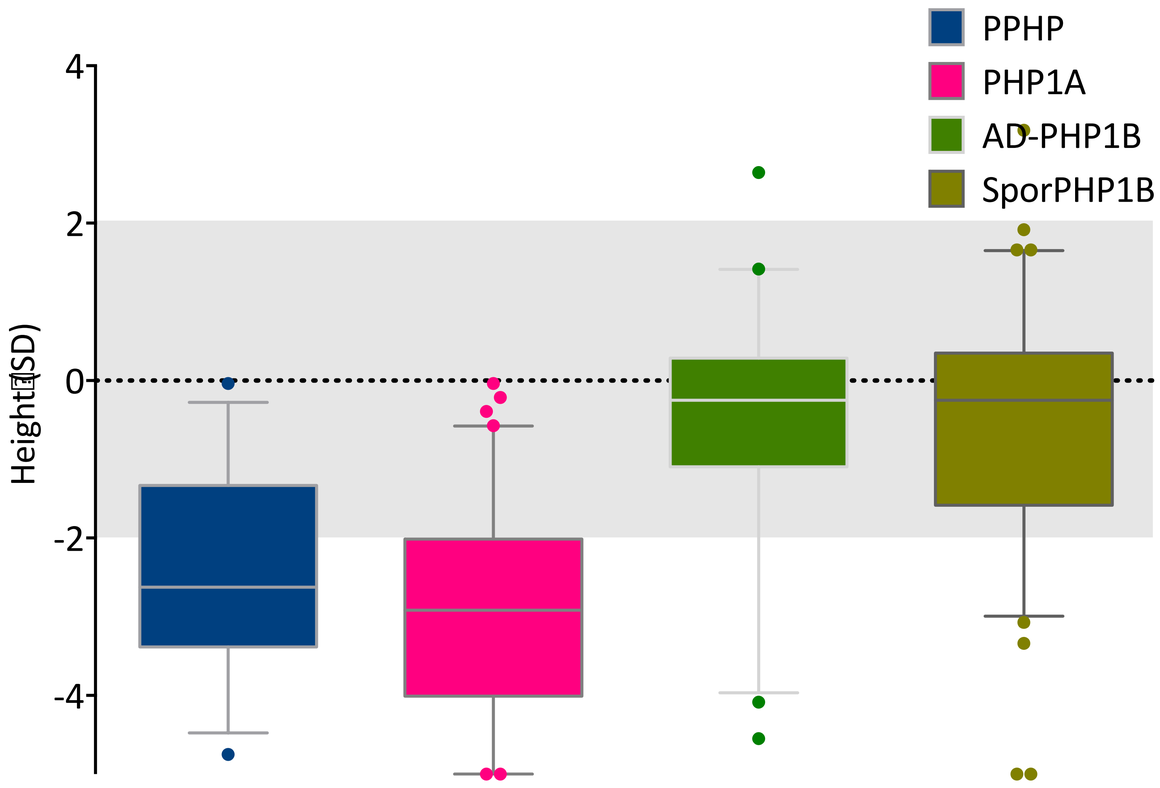
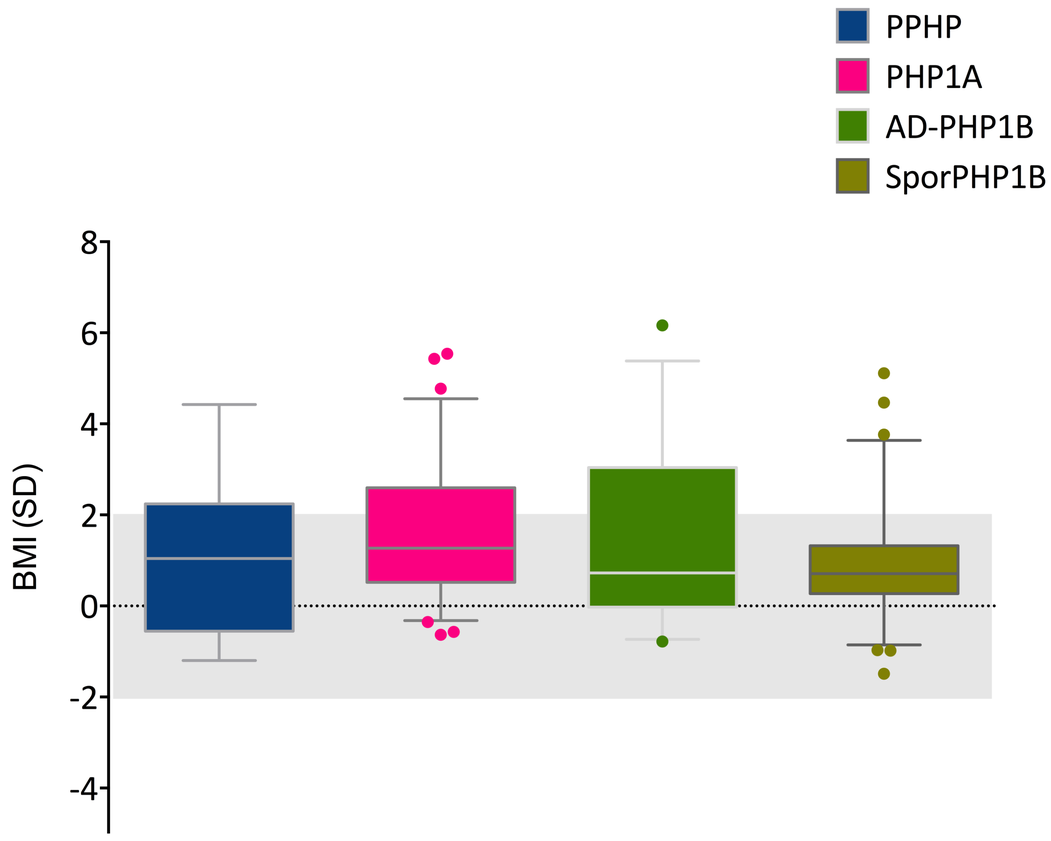


Figure 2: final heights in 28 PPHP, 84 PHP1A, 41 AD-PHP1B and 85 sporPHP1B patients



BMIs of females affected by PHP1B were higher than those of males. sporPHP1B patients (F: n=31; M: n=32): 1.2 vs 0.3, p=0.0001; AD-PHP1B patients (F: n=17; M: n=10): 1.8 vs 0.7, p=0.16. 52% and 16% of the female PHP1B patients are overweighed (z-BMI>1.0) or obese (z-BMI>2.0), respectively.

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

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