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Author's Reply

To the Editor: Dr Murphy and his colleagues raise interesting potential methodological points about our observation of a positive relation between paternal insulin resistance and fetal birth weight in a rural Indian population. They have suggested that the relation between paternal BMI, insulin resistance and fetal birth weight is confounded by socio-economic status (SES) rather than having a genetic basis.

We present the figure with confidence intervals for birth weight (Fig. 1). The confidence intervals do not encompass a zero nor an inverse correlation. Paternal insulin resistance (r=0.10, p<0.05) and paternal BMI (r=0.13, p<0.01) are both positively associated with fetal birth weight. The association of insulin resistance with birth weight becomes non-significant if corrected for the father's BMI, suggesting that it depends on paternal BMI. Maternal and paternal BMI are significantly related which is not unexpected ('assortative mating'). Correcting for maternal BMI did not change the relation between paternal BMI and fetal birth weight which remained significant (p=0.009). The statistical correction allows us to test the independence of relation, though we appreciate it might not correct for biological effects.

Murphy *et al.* suggest that BMI could be an acquired rather than a genetic attribute. The evidence suggests that the origin of BMI (obesity) is multifactorial. While there can be no doubt that BMI is to an extent acquired, there is strong evidence that it is inherited [1, 2] and recent molecular genetic findings have supported the critical role of the father, suggesting that the obesity in the offspring is paternally imprinted [3]. As more genetic markers are discovered, it is probable that we will have a better picture of the gene-environment interactions in the genesis of obesity and the associated insulin resistance; one such interaction between PPAR-γ and dietary fatty acid ratio has been reported [4].

We derived a composite socio-economic score (SES) [5], based on occupation and education of the head of the family, caste, type of housing and family ownership of animals, land and material possessions. There are five groups of decreasing affluence; the majority of our study cohort (78%) belonged to the middle and lower-middle class, nineteen percent belonged to the upper-middle and less than one percent belonged to upper class. Foetal birth weight was not related to SES (r=0.05, p=0.45) nor were paternal BMI, paternal insulin resistance and maternal BMI. After adjustment for SES, the relationship between paternal BMI, paternal insulin resistance and fetal birth weight still remained positive and significant (p<0.05, both). Thus, in the present study SES is not a significant determinant of fetal size and parental size and paternal insulin resistance. A possible reason for this rather unexpected finding is the predominantly low SES of the majority of the population and lack of numerical spread. The SES could act indirectly on the fetal size through maternal food intake and her physical activity during pregnancy which we have reported [6].

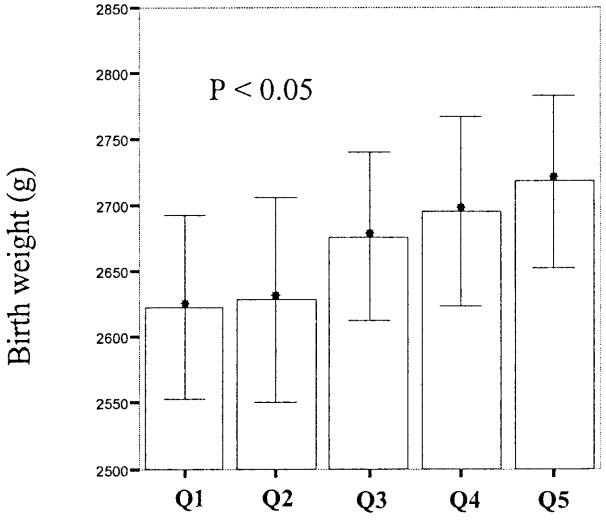

Fig. 1. Fetal birthweight (mean and 95%-CI) by quintiles of paternal insulin resistance. The significance is corrected for gestational age and sex, p<0.05

The purpose of our letter was to show that an inverse relationship between paternal insulin resistance and fetal birth weight as predicted in the fetal insulin hypothesis was absent in our study. In fact, the relationship was direct. We suggested that this relationship could operate through paternal size which has been reported before [7] and probably has a genetic basis. This view is strengthened by the above analysis of SES. Further investigation of this relationship will depend on study of appropriate molecular genetic markers.

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