LONG-TERM GLUCOCORTICOID CONCENTRATIONS AS A RISK FACTOR FOR CHILDHOOD OBESITY AND ADVERSE BODY FAT DISTRIBUTION

The Generation R study

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INTRODUCTION

In Cushing's syndrome, cortisol is known to induce obesity and cardiometabolic complications, leading to the hypothesis that inter-individual variation of cortisol concentrations could also be implicated in the onset of obesity. Indeed, recent studies showed increased long-term cortisol concentrations in obese adults and adolescents. Additionally, polymorphisms in the glucocorticoid receptor (GR) gene, which increase glucocorticoid (GC) sensitivity, have been associated with metabolically adverse body composition.

AIM

To explore the role of cortisol and cortisone in the onset of obesity, we studied the associations of long-term GC levels and genetically determined GC sensitivity with obesity and body fat distribution in children.

METHODS

We performed a cross-sectional study of cortisol and cortisone concentrations over a 3-month period, measured by LC-MS/MS in scalp hair of 3019 6-year-old children participating in the Generation R study, a population-based cohort study. Four SNPs (GR-9β, ER22/23EK, N363S, *Bcl*I) in the GR gene affecting GC sensitivity were genotyped. Anthropometrics were measured and DEXA-scans were performed to collect information about obesity and body fat distribution. World Obesity Federation criteria for body mass index cutoffs were used.

RESULTS

A total of 4.3% of the children was obese and 13.4% overweight. Hair cortisol was significantly associated with risk of obesity and overweight (Figure 1). Cortisone was associated with risk of obesity (Figure 1). Cortisol and cortisone were both positively associated with body mass index, fat mass index, and android/gynecoid fat mass ratio (Figure 2). GR polymorphisms were not associated with cortisol or cortisone (N=1753, all P's >0.10), nor with obesity or body fat distribution (N=4046, all P's >0.05, Table 1.).

Figure 1. Associations of long-term glucocorticoids with overweight and obesity.

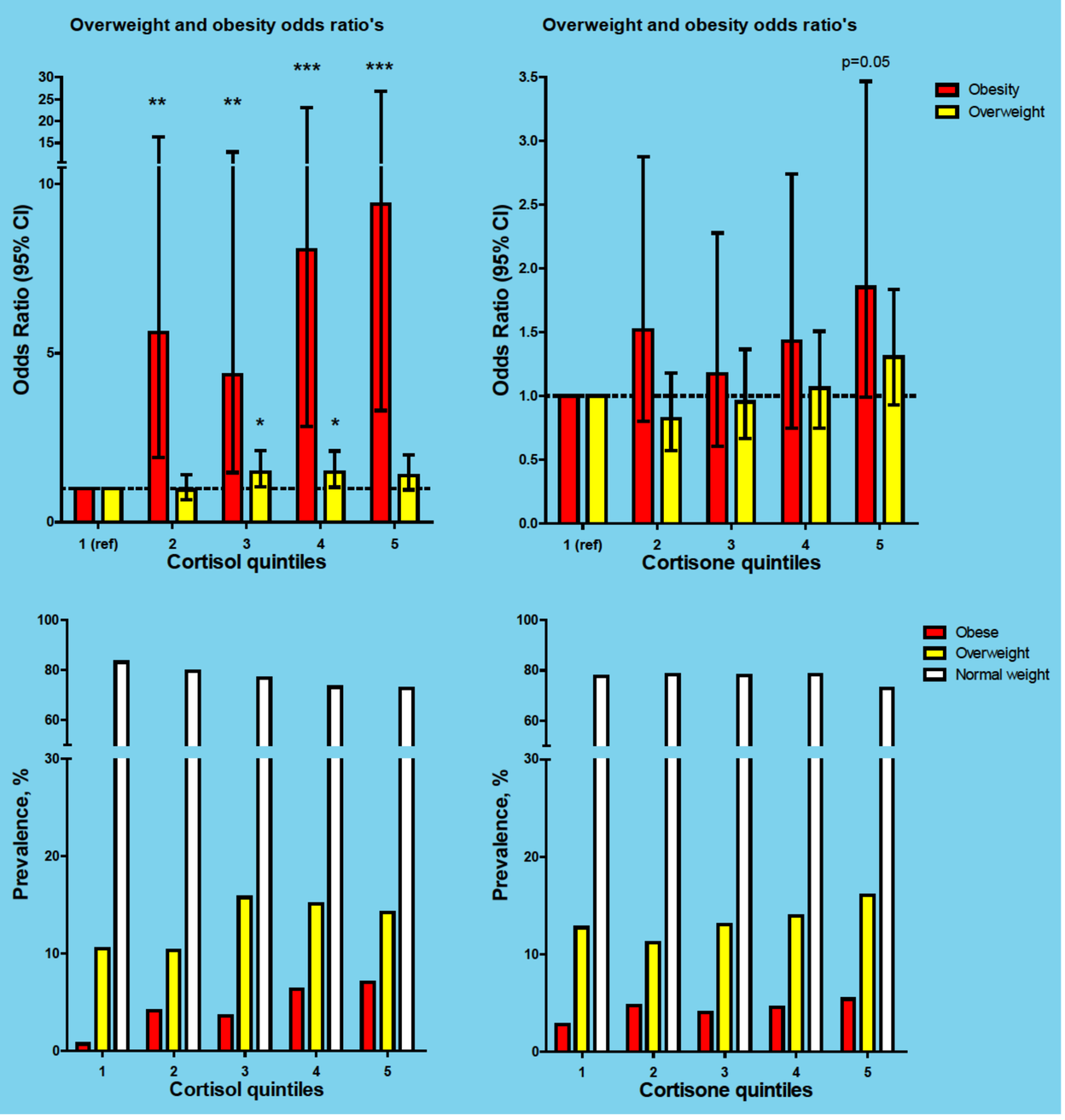

Figure 2. Associations of long-term glucocorticoids with body mass index and body fat distribution

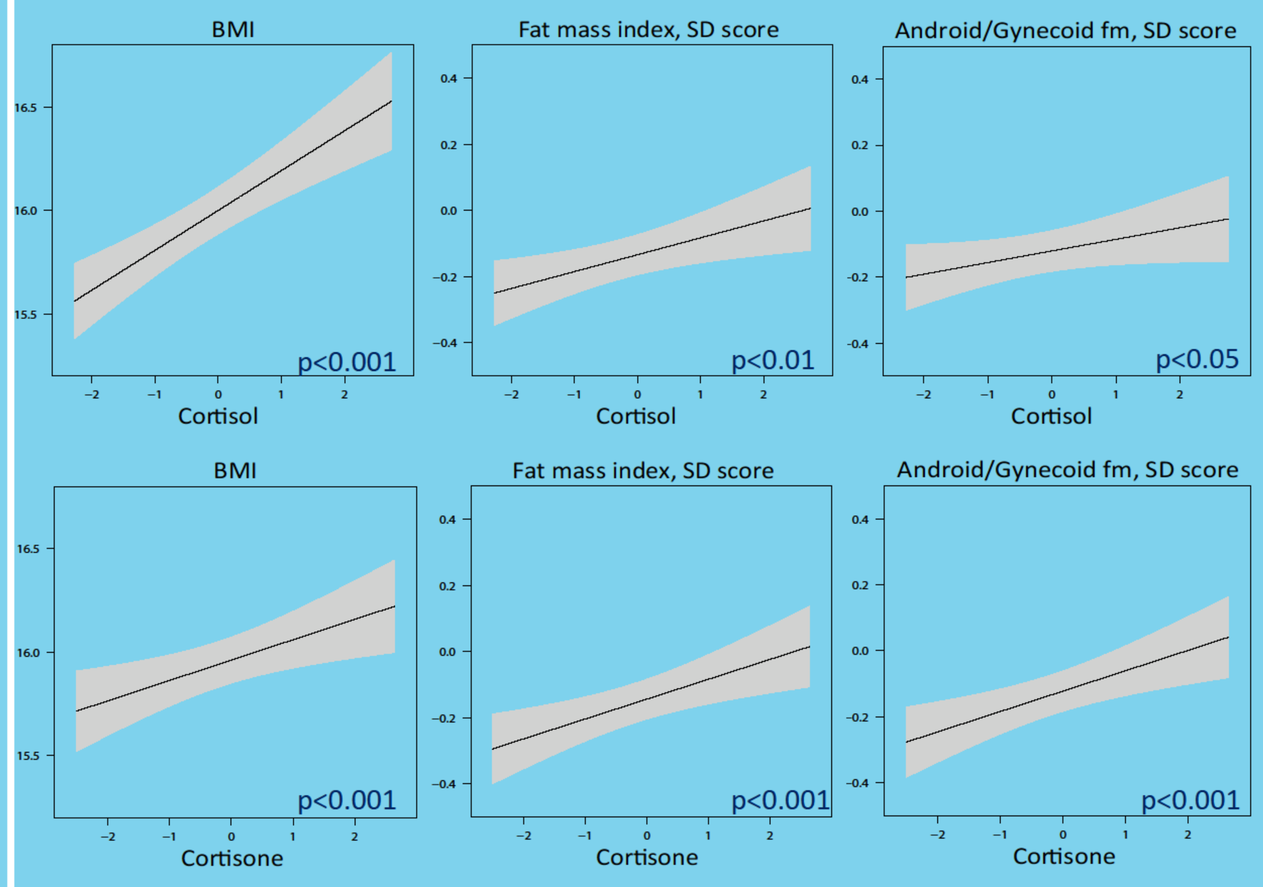

Table 1. Associations of glucocorticoid receptor gene polymorphisms with body composition and body fat distribution. N=4046.

	ER22/23EK	GR-9β	N363S	*Bcl*I
Overw./obese	1.08 (0.5 - 1.4)	0.98 (0.8 - 1.2)	1.35 (0.9 - 2.0)	1.05 (0.9 - 1.2)
BMI	-0.05, p=0.73	0.06, p=0.30	-0.04, p=0.74	0.04, p=0.13
FMI	-0.04, p=0.62	0.02, p=0.53	-0.02, p=0.72	0.04, p=0.09
A/G FM	-0.14, p=0.06	0.01, p=0.76	0.00, p=0.99	0.04, p=0.08

Results shown are logistic regression OR (95%CI) or linear regression β, p-value, all models adjusted for age, sex and ethnicity, A/G FM additionally adjusted for height. FMI, Fat mass index; A/G FM, Android/gynecoid fat mass ratio.

CONCLUSION

Long-term cortisol concentrations are strongly associated with an increased risk of childhood obesity, and show linear associations with adverse body fat distribution. Whether this is a causal relationship and whether cortisol may be a future target for therapeutic strategies to combat obesity remains to be explored. The contribution of GR gene polymorphisms to body composition at the age of 6 years seems limited.

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