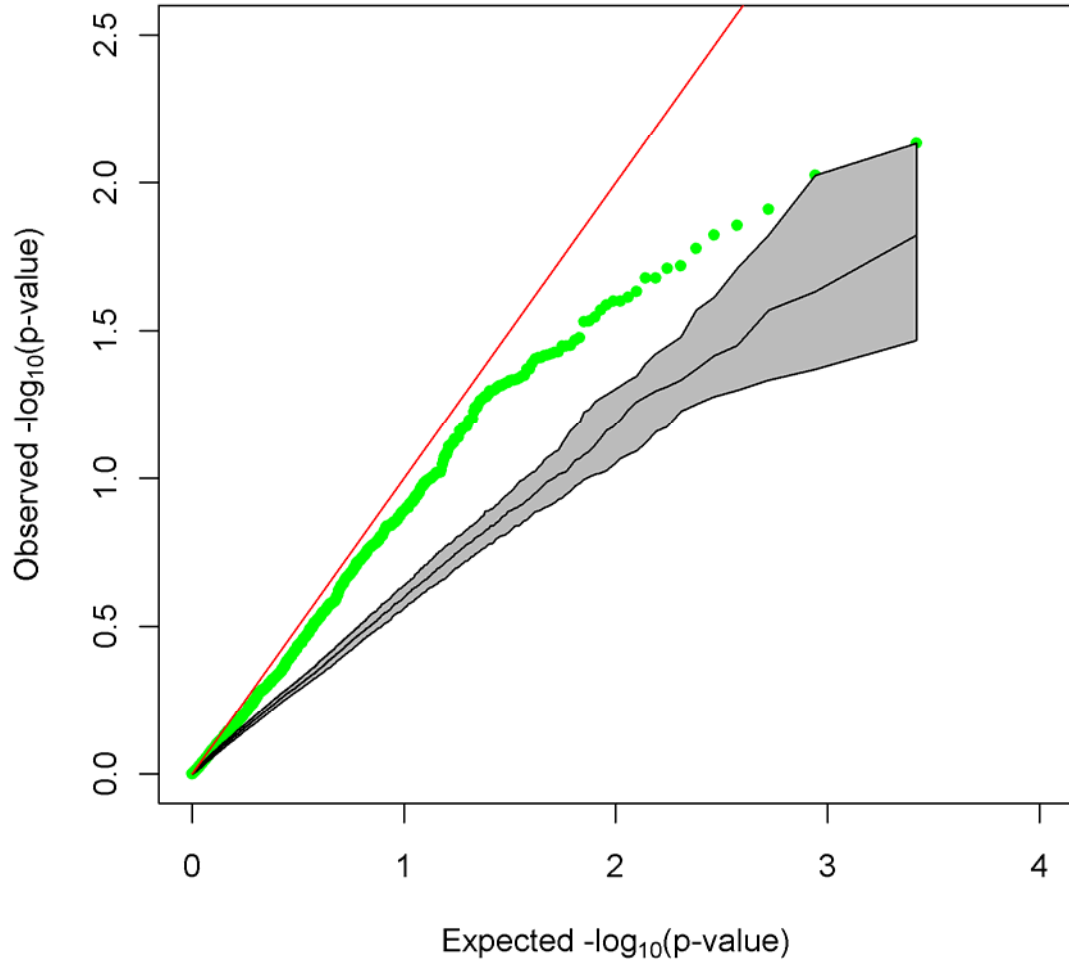# Supplementary Material

Legends to Figures

Figure S1. QQ-plot depicting the excess of significant association signals in the 25 CNVRs detected in the family-based discovery GWAS sample (1,314 CNV markers). The quantiles of the $-\log_{10}$ (p-values) of the observed associations are plotted in green against the quantiles under no association (uniform distribution). The diagonal red line represents the ideal expectancy under the global null hypothesis, whereas the grey shaded funnel is the result of permutation procedure described in "Permutation and Multiple Testing" with the three black lines representing the 97.5, 50, and 2.5 percentile values of 1,000 sets of a random selections.
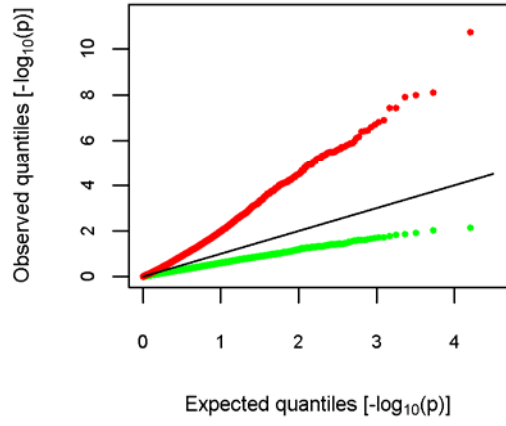
Figure S2. The P-value distributions for all 8,051 CNV markers in all 244 analyzed common CNVRs in the two discovery GWAS samples are depicted. Upper panel: QQ plots for the family-based discovery GWAS sample (green dots) and the case control discovery GWAS sample (red dots). Lower panels: P-value histograms for the family-based (left side) and the case-control (right side) discovery GWAS sample.

Figure S3. QQ-Plots comparing the quantiles of the 8,051 true (asymptotic) observed p-values in the 244 common CNVRs with those quantiles of approximate exact p-values based on 1,000 permutations in the family-based GWAS discovery sample (left panal) and case-control GWAS discovery sample (right panel), respectively. In each plot the red line represents the ideal situation, where observed and permutation-based quantiles equal each other.
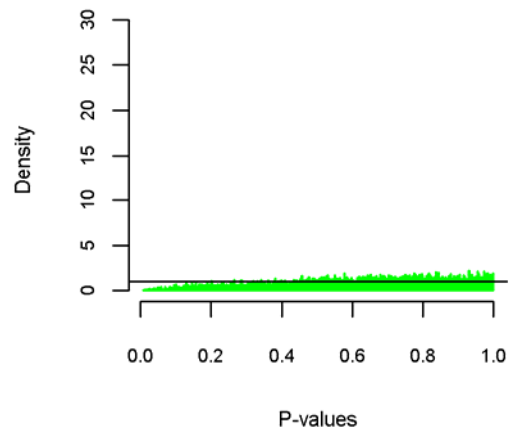
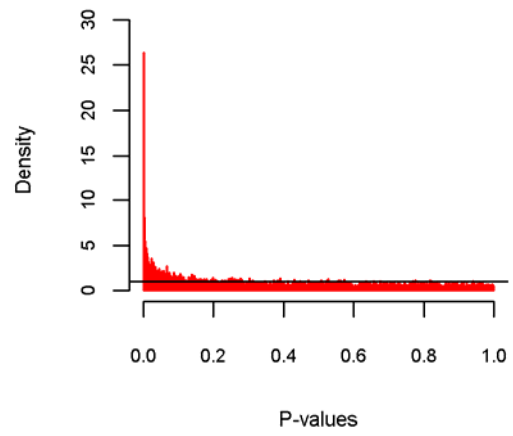**QQ-Plot**

QQ-Plots
[green: family-based,
red: case-control]

Observed quantiles [-log₁₀(p)]

Expected quantiles [-log₁₀(p)]

Histogram
[family-based]

Density

P-values

Histogram
[case-control]

Density

P-values

QQ-Plot
[family-based GWAS discovery sample]

QQ-Plot
[case-control GWAS discovery sample]
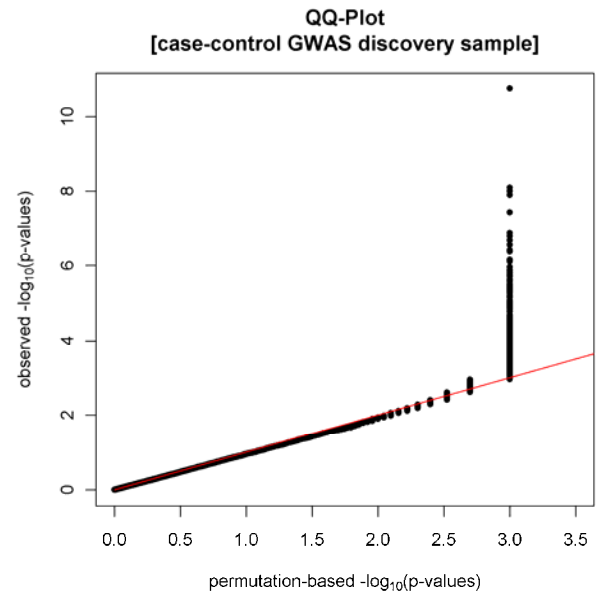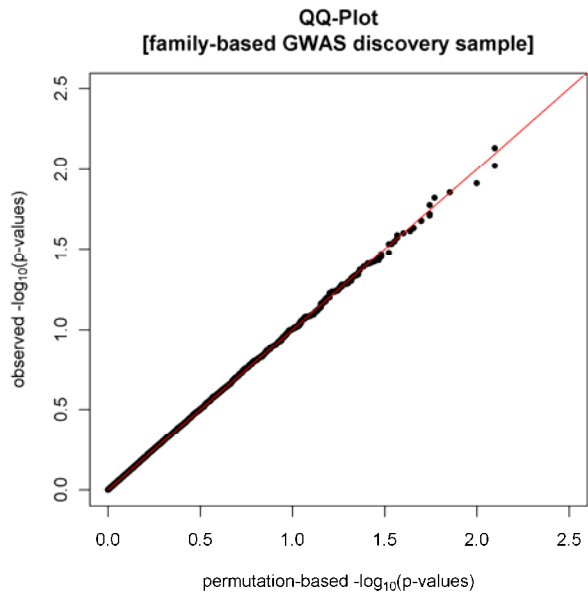
Tables

Table S1. Basic phenotypical characteristics of the family-based GWAS sample, the case-control GWAS sample and the family-based replication sample.

sample	description	status	n total {% female}	age in years [a] {female} (male)	BMI in kg/m^2 [a] {female} (male)	BMI SDS [a,b] {female} (male)
(1) discovery: family-based GWAS	(extremely) obese children and adolescents	cases	424 {53}	13.2 ± 2.8 {13.4 ± 2.9} (13.0 ± 2.7)	32.0 ± 5.4 {32.3 ± 5.8} (31.5 ± 4.9)	4.22 ± 1.84 {4.53 ± 1.98} (3.87 ± 1.61)
	parents of the (extremely) obese children and adolescents	parents	848 {50}	42.3 ± 6.1 {40.6 ± 5.4} (44.0 ± 6.2)	30.4 ± 6.4 {30.6 ± 7.4} (30.2 ± 5.4)	1.66 ± 1.85 {1.84 ± 1.94} (1.48 ± 1.73)
	subgroup reference sample I [c] for CNV calling	parents	212 {50}	41.8 ± 5.9 {40.0 ± 5.1} (43.6 ± 6.1)	30.1 ± 5.9 {29.8 ± 6.1} (30.4 ± 5.6)	1.62 ± 1.77 {1.67 ± 1.65} (1.57 ± 1.89)
	subgroup reference sample II [c] for CNV calling	parents	212 50 50	41.5 ± 5.7 {40.0 ± 5.1} (43.1 ± 5.8)	25.2 ± 2.7 {24.4 ± 2.8} (26.1 ± 2.3)	0.18 ± 0.72 {0.18 ± 0.69} (0.17 ± 0.75)
(2) discovery: case-control GWAS	(extremely) obese children and adolescents	cases	453 {58}	14.4 ± 3.8 {14.5 ± 3.7} (14.2 ± 3.9)	33.1 ± 6.7 {33.2 ± 6.8} (33.1 ± 6.5)	4.55 ± 2.16 {4.66 ± 2.18} (4.40 ± 2.12)
	lean or normal weight subjects	controls	435 {61}	26.1 ± 5.8 {26.5 ± 6.4} (25.4 ± 4.6)	18.3 ± 1.1 {17.9 ± 1.0} (19.0 ± 0.9)	-1.45 ± 0.34 {-1.35 ± 0.30} (-1.60 ± 0.36)
(3) replication: family-based	(extremely) obese children and adolescents	cases	365 {58}	13.75 ± 3.40 {13.77 ± 3.48} (13.74 ± 3.29)	32.41 ± 6.47 {32.65 ± 6.50} (32.09 ± 6.42)	4.34 ± 2.15 {4.51 ± 2.17} (4.10 ± 2.10)
	parents of the (extremely) obese children and adults	parents	730 {50}	41.67 ± 9.38 {7.85 ± 7.85} (10.59 ± 10.59)	30.42 ± 6.13 {30.18 ± 6.68} (30.66 ± 5.52)	1.71 ± 1.80 {1.74 ± 1.77} (1.69 ± 1.83)
(3a) array-based replication: family-based [subsample of Sample 3]	(extremely) obese children and adolescents	cases	281 {58}	13.80 ± 3.29 {13.76 ± 3.26} (13.84 ± 3.32)	32.15 ± 6.41 {32.45 ± 6.36} (31.74 ± 6.46)	4.26 ± 2.121 {4.46 ± 2.10} (3.98 ± 2.10)

| parents of the (extremely) obese children and adults | parents | 562 {50} | 42.89 ± 5.93 {41.31 ± 5.48} (44.52 ± 5.94) | 30.10 ± 6.16 {29.69 ± 6.71} (30.52 ± 5.53) | 1.63 ± 1.82 {1.61 ± 1.79} (1.65 ± 1.85) |

[a] Data is shown as mean ± standard deviation.

[b] Age and BMI SDS (standard deviation score) values were available for only 422 mothers and 421 fathers of the family-based discovery GWAS sample. For the family-based replication [array-based replication] sample age was available for 358 [274] mothers and 350 [266] fathers, BMI was available for 358 [274] mothers and 356 [272] fathers and BMI SDS was available for 355 [271] mothers and 349 [265] fathers. Calculation of the BMI SDS values has been based on population reference values following the National Nutrition Survey I (Hebebrand et al. 1994).

[c] Reference sample I is a random sample of all parents whereas reference sample II is based on parents representing lowest BMI SDS values out of all parents in our sample.