

ONLINE APPENDIX

Supplementary table 1: Genotype information and quality control statistics for the 17 obesity-susceptibility SNPs

SNP	Nearest gene	Chr.	Position (bp)	GWA reference	Effect-allele	Other allele	Frequency effect-allele (%)	Homozygous effect-allele N (%)	Heterozygous N (%)	Homozygous other allele N (%)	P-value HWE	Call-rate (%)	Δ Effect size
rs2815752	<i>NEGR1</i>	1	72,585,028	3, 4	T	C	61.0	729 (37.7)	901 (46.6)	303 (15.7)	0.38	95.9	0.046
rs10913469	<i>SEC16B</i>	1	176,180,142	4	C	T	18.3	74 (3.8)	567 (29.1)	1310 (67.2)	0.20	96.8	0.069
rs2605100	<i>LYPLAL1</i>	1	217,710,847	5	G	A	69.0	931 (48.1)	806 (41.7)	197 (10.2)	0.25	96.1	-
rs6548238	<i>TMEM18</i>	2	624,905	3, 4	C	T	83.0	1360 (69.1)	547 (27.8)	62 (3.2)	0.44	97.8	0.059
rs7647305	<i>ETV5</i>	3	187,316,984	3, 4	C	T	81.1	1288 (65.7)	605 (30.8)	69 (3.5)	0.84	95.4	0.064
rs10938397	<i>GNPDA2</i>	4	44,877,284	3	G	A	41.2	338 (16.7)	988 (48.9)	694 (34.4)	0.67	98.5	0.045
rs987237	<i>TFAP2B</i>	6	50,911,009	5	G	A	21.0	93 (4.7)	647 (32.7)	1241 (62.7)	0.46	98.3	-
rs545854	<i>MSRA</i>	8	9,897,490	5	C	G	14.4	39 (2.0)	486 (24.8)	1435 (73.2)	0.77	97.2	-
rs1488830	<i>BDNF</i>	11	27,593,461	4	T	C	80.5	1260 (64.2)	638 (32.5)	64 (3.3)	0.12	97.4	-
rs925946	<i>BDNF</i>	11	27,623,778	4	T	G	30.6	188 (9.6)	827 (42.1)	950 (48.4)	0.68	97.5	0.062
rs10838738	<i>MTCH2</i>	11	47,619,625	3	G	A	35.4	237 (12.1)	909 (46.5)	807 (41.3)	0.44	96.9	0.049
rs7138803	<i>BCDIN3D</i>	12	48,533,735	4	A	G	44.1	386 (19.7)	958 (48.9)	617 (31.5)	0.68	97.4	0.054
rs10146997	<i>NRXN3</i>	14	79,014,915	6	G	A	22.3	87 (4.5)	693 (35.6)	1165 (59.9)	0.21	96.6	-
rs8055138	<i>SH2B1</i>	16	28,798,966	3, 4	T	C	42.9	363 (18.6)	953 (48.7)	640 (32.7)	0.80	97.1	0.045
rs1121980	<i>FTO</i>	16	52,366,748	1	T	C	44.9	408 (20.7)	953 (48.3)	611 (31.0)	0.30	96.9	0.045
rs17782313	<i>MC4R</i>	18	56,002,077	2	C	T	21.8	84 (4.3)	676 (34.9)	1177 (60.8)	0.29	96.0	0.052
rs11084753	<i>KCTD15</i>	19	39,013,977	3, 4	G	A	66.1	859 (43.7)	897 (44.8)	226 (11.5)	0.96	97.6	0.049

Chr: Chromosome; GWA study reference: 1) Frayling et al., 2007; 2) Loos et al., 2008; 3) Willer et al., 2009; 4) Thorleifsson et al., 2009; 5) Lindgren et al., 2009; 6) Heard-Costa et al., 2009; HWE: Hardy-Weinberg equilibrium; Call-rate: rate of successful genotyping; ΔEffect size: the minimal difference in effect size between children/adolescents and adults that can be detected at $\alpha=0.05$ with 80% Power.

Supplementary table 2: SNPs genotyped per cohort for the eight loci with proxies to the EYHS SNP available in the CHP study and ALSPAC

Locus	Study	SNP	Effect-allele	Other allele	r²
<i>NEGR1</i>	EYHS	rs2815752	T	C	
	CHP	rs2568958	A	G	1
	ALSPAC	rs2568958	A	G	1
<i>TMEM18</i>	EYHS	rs6548238	C	T	
	CHP	rs4854344	T	G	0.851
	ALSPAC	rs6548238	C	T	
<i>GNPDA2</i>	EYHS	rs10938397	G	A	
	CHP	rs13130484	T	C	1
	ALSPAC	rs10938397	G	A	
<i>BDNF</i> (SNP 1)	EYHS	rs1488830	T	C	
	CHP	rs4074134	G	A	1
<i>SH2B1</i>	EYHS	rs8055138	T	C	
	CHP	rs4788102	A	G	1
	ALSPAC	rs7498665	G	A	0.976
<i>FTO</i>	EYHS	rs1121980	T	C	
	CHP	rs8050136	A	C	0.841
	ALSPAC	rs9939609	A	T	0.841
<i>MC4R</i>	EYHS	rs17782313	C	T	
	CHP	rs12970134	A	G	0.811
	ALSPAC	rs17782313	C	T	
<i>KCTD15</i>	EYHS	rs11084753	G	A	
	CHP	rs29941	C	T	0.64
	ALSPAC	rs368794	T	A	1

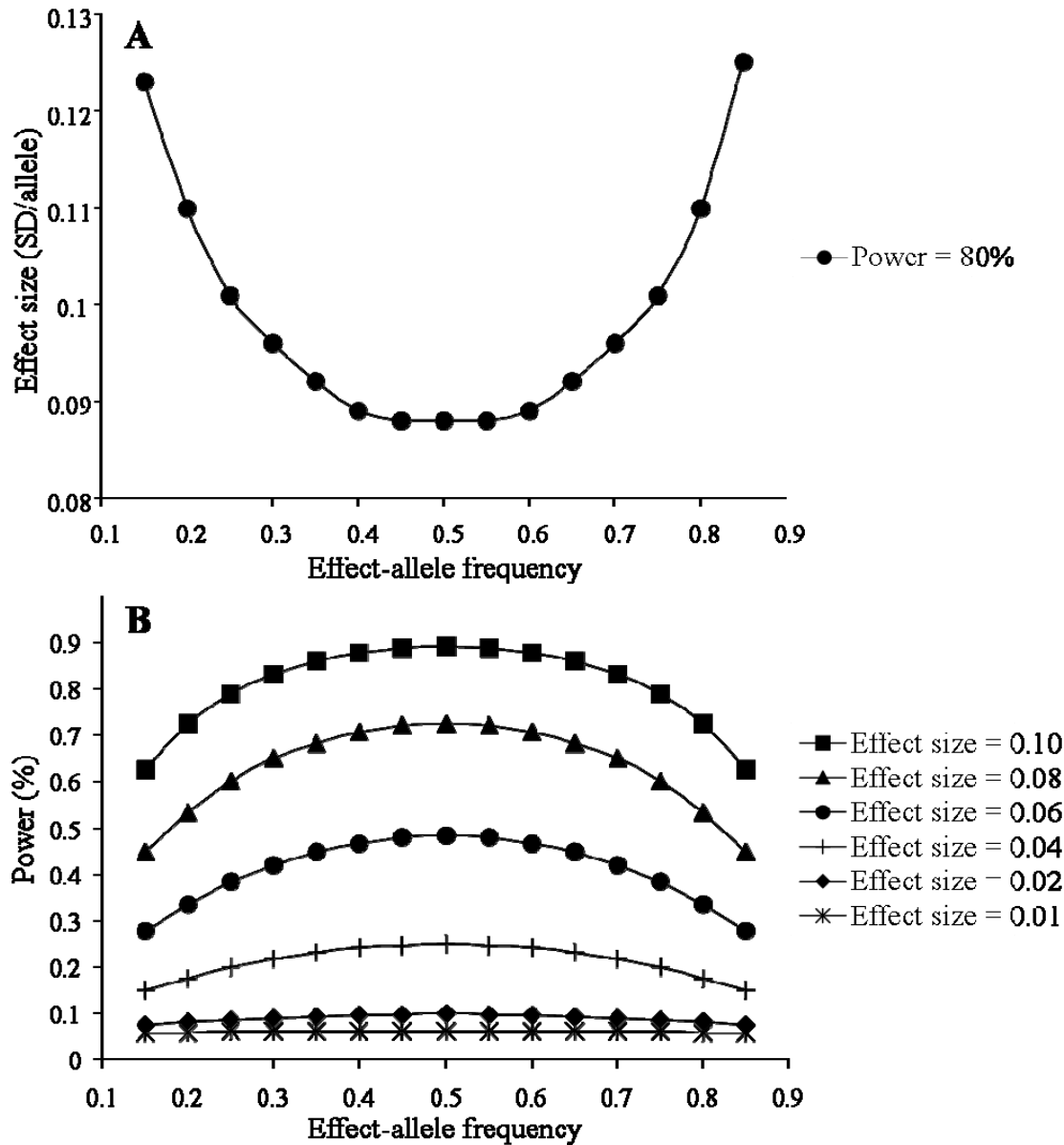
r² represents linkage disequilibrium with the SNP genotyped in the EYHS

Supplementary Table 3: Associations of the individual obesity-susceptibility SNPs and the genetic predisposition score with the risk of obesity or overweight in children and adolescents of the EYHS study (N=2,042)

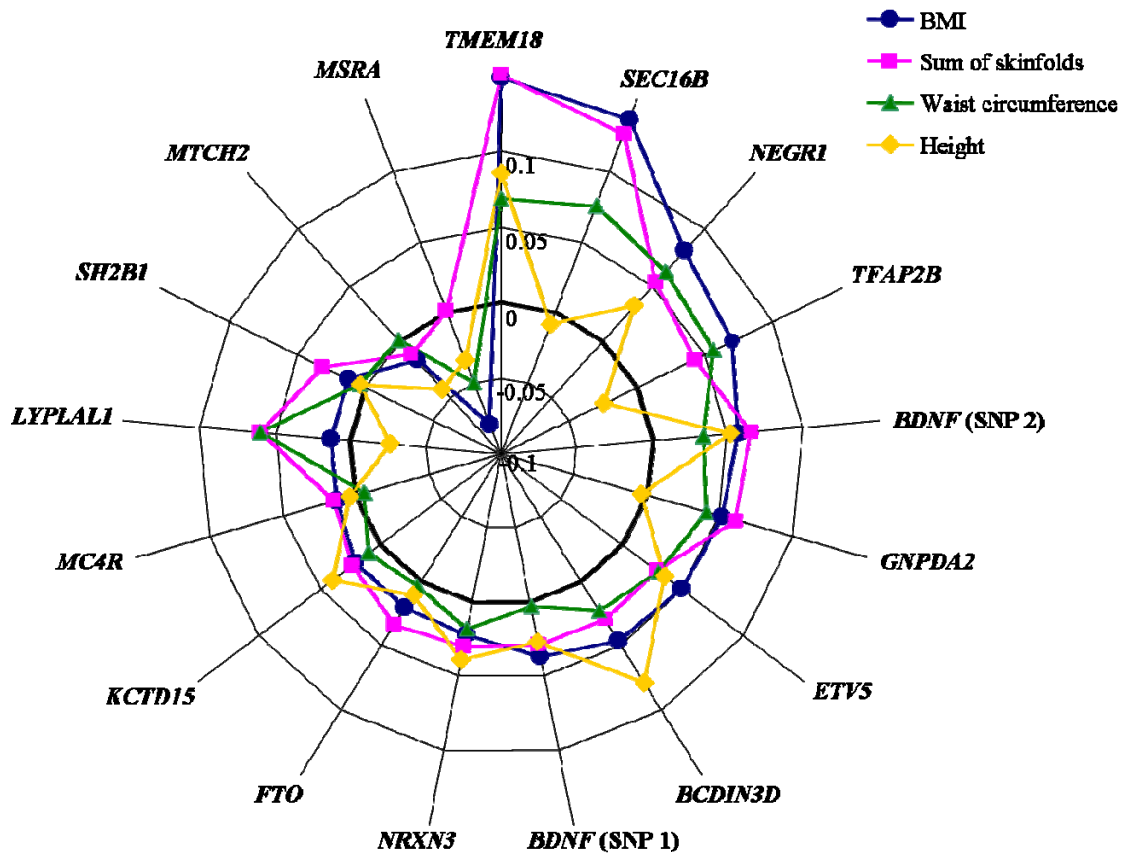
SNPs	Nearest gene	Obesity				Overweight			
		OR	L 95% CI	U 95% CI	P-value	OR	L 95% CI	U 95% CI	P-value
rs2815752	<i>NEGR1</i>	1.065	0.79	1.43	0.67	1.214	1.01	1.46	4.3·10 ⁻²
rs10913469	<i>SEC16B</i>	1.281	0.90	1.81	0.16	1.221	0.98	1.52	0.08
rs2605100*	<i>LYPLALI</i>	0.993	0.73	1.36	0.97	0.971	0.80	1.18	0.77
rs6548238	<i>TMEM18</i>	1.597	1.02	2.49	3.9·10 ⁻²	1.302	1.01	1.68	4.3·10 ⁻²
rs7647305	<i>ETV5</i>	1.639	1.08	2.50	2.2·10 ⁻²	1.264	0.99	1.61	0.06
rs10938397	<i>GNPDA2</i>	1.314	0.98	1.76	0.07	1.321	1.10	1.58	2.5·10 ⁻³
rs987237*	<i>TFAP2B</i>	1.023	0.70	1.49	0.91	1.229	0.98	1.53	0.07
rs545854*	<i>MSRA</i>	0.995	0.66	1.50	0.98	0.890	0.68	1.16	0.39
rs1488830	<i>BDNF</i>	1.132	0.77	1.66	0.52	1.059	0.84	1.34	0.63
rs925946	<i>BDNF</i>	1.388	1.03	1.88	3.4·10 ⁻²	1.069	0.88	1.30	0.50
rs10838738	<i>MTCH2</i>	0.840	0.61	1.15	0.28	0.834	0.69	1.01	0.07
rs7138803	<i>BCDIN3D</i>	1.042	0.77	1.41	0.79	1.173	0.98	1.41	0.09
rs10146997*	<i>NRXN3</i>	0.903	0.63	1.30	0.58	1.038	0.83	1.29	0.74
rs8055138	<i>SH2B1</i>	1.205	0.90	1.62	0.22	1.103	0.92	1.33	0.30
rs1121980	<i>FTO</i>	1.416	1.06	1.90	1.9·10 ⁻²	1.097	0.92	1.31	0.31
rs17782313	<i>MC4R</i>	1.039	0.73	1.48	0.83	1.094	0.88	1.36	0.42
rs11084753	<i>KCTD15</i>	0.999	0.73	1.36	0.99	1.063	0.88	1.29	0.53
GPS-12		1.184	1.08	1.30	4.7·10 ⁻⁴	1.126	1.06	1.20	8.7·10 ⁻⁵
GPS-17		1.122	1.04	1.22	4.7·10 ⁻³	1.094	1.04	1.15	4.2·10 ⁻⁴

Results were obtained using logistic regression analysis assuming an additive effect, while adjusting for sex, age, age-group, country and maturity. Odds ratios (OR) represent the change in outcome for each additional effect-allele, that is, the obesity-susceptibility increasing allele in the initial GWA study (see Supplementary table 1). SNPs marked by * are located in or near loci identified in GWA studies for waist circumference, all others were identified in GWA studies for BMI.

Supplementary figure 1: Power calculations for associations of genetic variants with anthropometric traits. A shows the effect size in SD/allele of a single SNP association that can be detected with a power of 80% as a function of effect-allele frequency; B shows the power to detect an association as a function of the effect-allele frequency for different effect sizes. Both assume a sample size of 2,042 individuals (EYHS).



Supplementary figure 2: Effect sizes in SD/allele across traits for the obesity-susceptibility SNPs in EYHS (N=2,042). Results were obtained using multiple linear regression analysis assuming an additive effect, while adjusting for sex, age, age-group, country and maturity. Sum of skinfolds and waist circumference were additionally adjusted for height.



Supplementary figure 3: Odds ratios for obesity and overweight for the obesity-susceptibility SNPs in EYHS. Results were obtained using logistic regression analysis assuming an additive effect, while adjusting for sex, age, age-group, country and maturity.

