

Table S1. Summary demographics of the four studied European cohorts

Cohort	Discovery cohort (Spain) N=1186	Follow-up cohort 1 (The Netherlands) N=962	Follow-up cohort 2 (Norway) N=1095	Follow-up cohort 3 (Germany) N=1948	All combined cohorts (N=5191)
Cases	603	346	532	1226	2707
Gender					
Male	416 (69%)	164 (47%)	295 (55%)	641 (52%)	1513 (56%)
Female	187 (31%)	182 (53%)	237 (45%)	585 (48%)	1194 (44%)
ADHD subtype					
Combined	368 (61%)	229 (67%)	351 (67%)	878 (72%)	1826(67%)
Inattentive	211 (35%)	55 (16%)	54 (10%)	268 (22%)	588 (22%)
Hyperactive/Impulsive	21 (3.5%)	12 (3%)	17 (3%)	80 (6%)	130 (5%)
Sub-threshold	-	-	60 (11%)	-	60 (2%)
Unknown	3 (0.5%)	50 (14%)	50 (9%)	-	103 (4%)
Age (mean and SD)	31.04 (11.7)	36.15 (11.2)	34.2 (10.4)	35.9 (10.5)	33.7 (17.2)
Controls	583	616	563	722	2484
Gender					
Male	402 (69%)	297 (48%)	232 (41%)	371 (51%)	1302 (53%)
Female	181 (31%)	319 (52%)	331 (59%)	351 (49%)	1182 (47%)
Age (mean and SD)	33.6 (21.3)	53.5 (18.9)	28.5 (6.7)	25.2 (6.5)	37.6 (11.9)

Table S2. Selected markers within 10 loci included in the replication stage

SNP	Chr	Base pairs*	Nearest gene	Clinical group of interest
rs1937444#	1	66,463,920	<i>PDE4B</i> **	Inattentive ADHD
rs10594	1	160,247,185	<i>PEX19</i> ** (3'UTR)	Overall ADHD
rs2232429	6	28,359,632	<i>ZSCAN12</i> **	Combined ADHD
rs12333188	6	143,065,590	<i>GPR126</i>	Inattentive ADHD
rs1962749	6	153,551,654		Inattentive ADHD
rs4416909	9	24,095,294	<i>ELAVL2</i>	Combined ADHD
rs1445594	13	58,675,299	<i>PCDH17</i>	Overall ADHD
rs1897792	14	39,697,568		Overall ADHD
rs4902569	14	39,858,941		Overall ADHD and Combined ADHD
rs2415543	14	39,860,216		Combined ADHD
rs2415545	14	39,863,802		Overall ADHD and Combined ADHD
rs3814860	14	39,868,646	<i>FBXO33</i> (3'UTR)**	Combined ADHD
rs17696574	14	39,967,531		Combined ADHD
rs11644983	16	80,314,901	<i>DDYNLRB2</i>	Overall ADHD
rs11646443	16	84,270,476	<i>KCNG4</i> ** (EXON 1)	Overall ADHD and Combined ADHD
rs1988353	17	1,468,941	<i>ACCN1</i> **	Inattentive ADHD

* Base pairs according to hg19 - NCBI Build 36

** SNP within the gene

Not tested in the replication phase due to experimental constraints

Table S3. Pooled analysis of seven SNPs in six independent genomic regions that reached suggestive evidence for association ($PGC < 1e-05$) in the genome-wide association study in 2,707 adulthood ADHD patients and 2,484 controls from four European countries.

Chr	Base pairs**	SNP (Risk Allele)	Spain Discovery Cohort N=1186 (603 cases, 583 controls)		Netherlands Follow-up Cohort 1 N=962 (346 cases, 616 controls)		Norway Follow-up Cohort 2 N=1095 (532 cases, 563 controls)		Germany Follow-up Cohort 3 N=1948 (1,226 cases, 722 controls)		All Follow-up Cohorts N=4005 (2,104 cases, 1901 controls)		All Cohorts N=5191 (2,707 cases, 2,484 controls)	
			OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
1	158,513,809	rs10594 (G)*	1.49	2.3e-06	-	-	0.95	0.54	1.15	0.033	1.06	0.14	1.13	8.4e-04
13	57,573,300	rs1445594 (A)	1.56	3.7e-06	0.92	0.43	1.04	0.70	0.96	0.54	0.97	0.56	1.06	0.15
14	38,767,319	rs1897792 (A)	1.56	5.8e-06	0.94	0.58	1.06	0.63	0.78	0.42	0.99	0.79	1.10	0.05
14	38,928,692	rs4902569 (G)	1.50	6.2e-06	1.07	0.53	1.08	0.44	0.92	0.29	1.02	0.74	1.11	0.014
14	38,933,553	rs2415545 (A)	1.47	3.8e-06	1.03	0.78	1.12	0.20	0.98	0.73	1.02	0.66	1.11	9.7e-03
16	78,872,402	rs11644983 (C)	2.08	5.4e-06	1.07	0.74	1.56	0.014	0.97	0.82	1.12	0.21	1.32	6.6e-04
16	82,827,977	rs11646443 (G)	1.61	3.8e-07	0.94	0.57	1.10	0.30	0.92	0.24	0.98	0.75	1.09	0.049

* Significant departure from HWE in the control sample from The Netherlands
 In bold statistically significant P-values after Bonferroni correction ($P < 3.3e-03$)

Table S4. Pooled analysis of 11 SNPs in seven independent regions that reached suggestive evidence for association ($PGC < 1e-05$) in the genome-wide association study in (a) 1,826 combined ADHD patients or (b) and 588 inattentive ADHD patients and 2,484 controls from four European countries

(a)

Chr	Base pairs**	SNP (Risk Allele)	Spain Discovery Cohort N=951 (368 cases, 583 controls)		Netherlands Follow-up Cohort 1 N=845 (229 cases, 616 controls)		Norway Follow-up Cohort 2 N=914 (351 cases, 563 controls)		Germany Follow-up Cohort 3 N=1,600 (878 cases, 722 controls)			All Follow-up Cohorts N=3,359 (1,458 cases, 1901 controls)		All Cohorts N=4,310 (1,826 cases, 2,484 controls)	
			OR	P	OR	P	O	OR	P	P	OR	P	OR	P	
6	28,467,611	rs2232429 (G)	2.60	7.7e-08	1.12	0.53	1.32	0.26	1.05	0.69	0.75	0.17	1.11	0.19	
9	24,085,294	rs4416909 (C)	1.54	4.5e-06	0.85	0.16	0.91	0.32	1.09	0.22	0.96	0.43	1.06	0.13	
14	38,928,692	rs4902569 (G)	1.60	5.8e-06	1.07	0.58	1.09	0.44	0.96	0.60	1.05	0.41	1.14	5.9e-03	
14	38,929,967	rs2415543 (A)	1.55	7.3e-06	1.01	0.96	1.08	0.44	1.03	0.72	1.04	0.40	1.13	6.4e-03	
14	38,933,553	rs2415545 (A)	1.59	1.8e-06	1.01	0.94	1.14	0.19	1.02	0.77	1.05	0.33	1.14	3.0e-03	
14	38,938,397	rs3814860 (A)	1.61	6.8e-06	1.12	0.35	1.14	0.28	0.97	0.74	1.07	0.24	1.16	2.5e-03	
14	39,037,282	rs17696574 (G)	1.61	2.5e-06	0.95	0.69	1.14	0.15	1.03	0.67	1.05	0.27	1.14	3.1e-03	
16	82,827,977	rs11646443 (G)	1.72	3.6e-07	0.94	0.62	1.10	0.35	0.89	0.14	0.97	0.53	1.07	0.11	

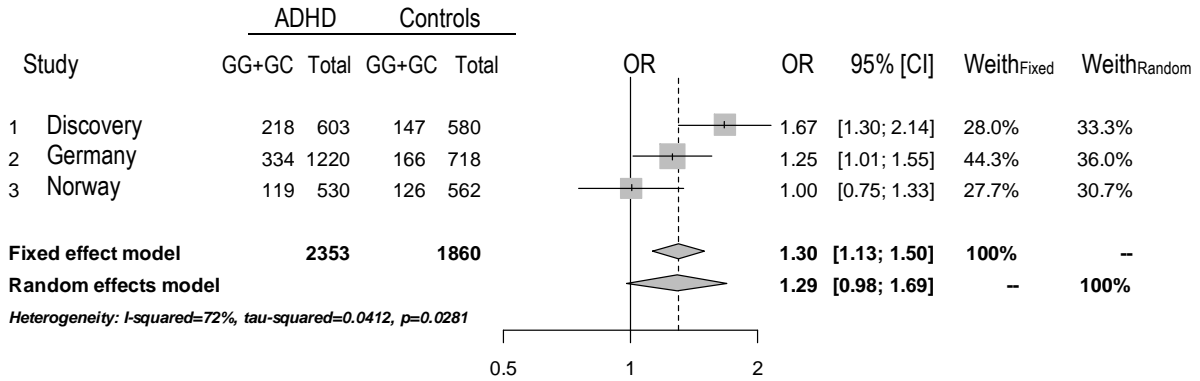
(b)

Chr	Base pairs**	SNP (Risk Allele)	Spain Discovery Cohort N=794 (211 cases, 583 controls)		Netherlands Follow-up Cohort 1 N=671 (55 cases, 616 controls)		Norway Follow-up Cohort 2 N=617 (54 cases, 563 controls)		Germany Follow-up Cohort 3 N=990 (268 cases, 720 controls)		All Follow-up Cohorts N=2,278 (377 cases, 1901 controls)		All Cohorts N=3072 (588 cases, 2,484 controls)	
			OR	P	OR	P	OR	P	OR	P	OR	P	OR	P
6	143,107,283	rs12333188 (T)	4.07	2.3e-05	0.58	0.56	0	0.19	1.62	0.27	1.15	0.69	2.32	3.0e-04
6	153,593,347	rs1962749 (T)	1.29	1.3e-05	0.42	0.039	1.21	0.65	1.28	0.15	1.15	0.32	1.48	2.1e-04
17	28,493,054	rs1988353 (A)	1.88	1.2e-06	1.06	0.80	1.65	0.038	0.94	0.63	1.09	0.35	1.32	2.3e-04

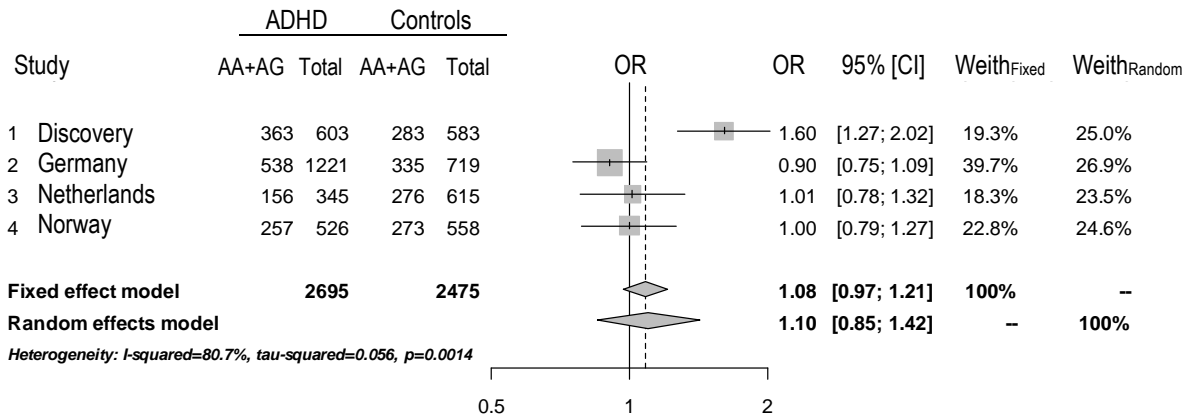
In bold statistically significant P-values after Bonferroni correction ($P < 3.3e-03$)

Table S5. Effect of the seven SNPs from five loci achieving at least suggestive significance ($PGC < 1e-05$) in adulthood ADHD (2,707 cases and 2,484 controls)

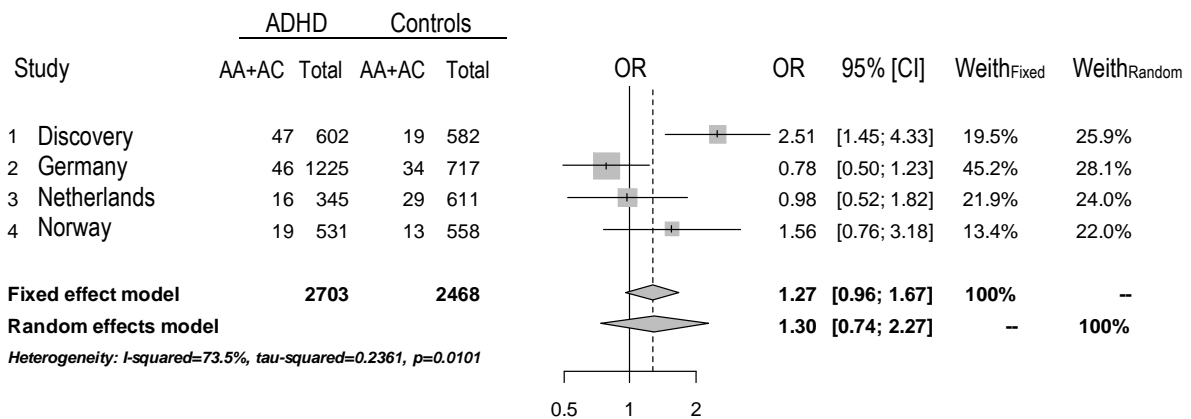
(a) rs10594 (GG+GC versus CC)



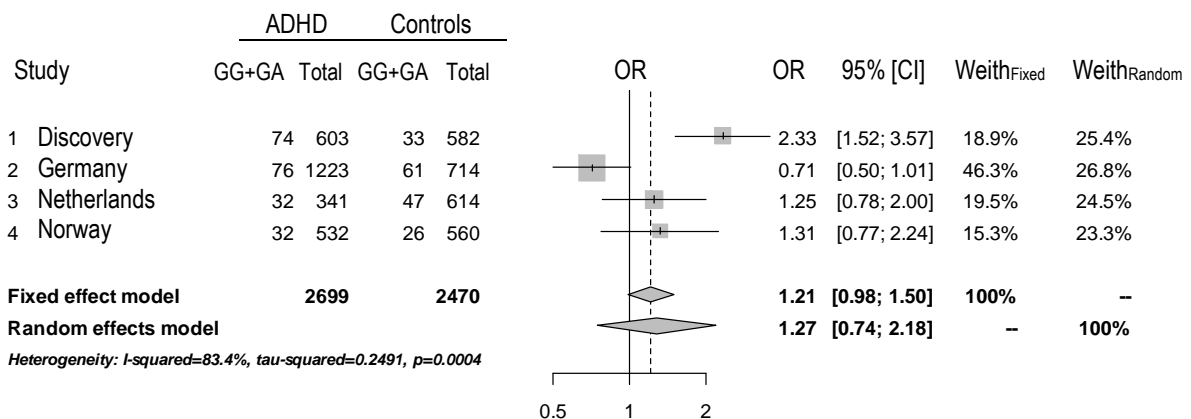
(b) rs1445594 (AA+AG versus GG)



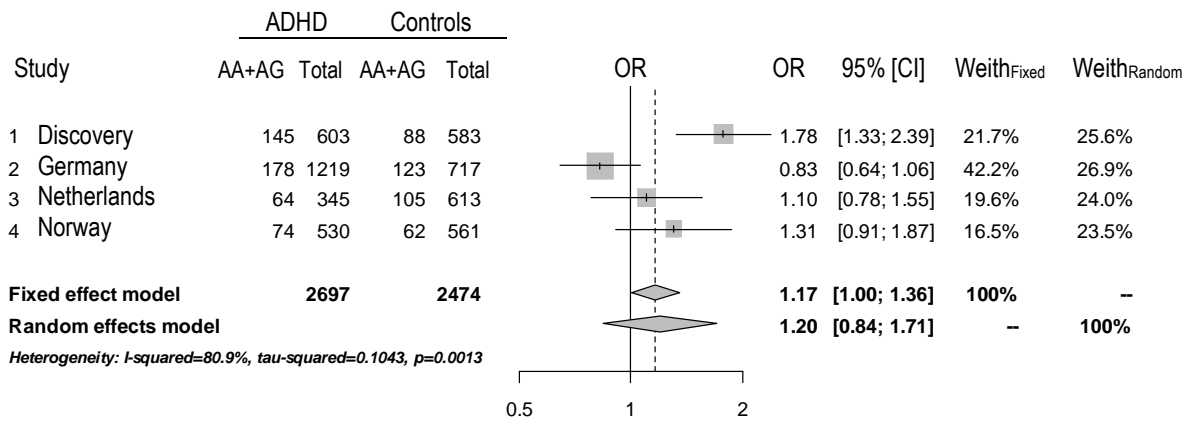
(c) rs1897792 (AA+AC versus CC)



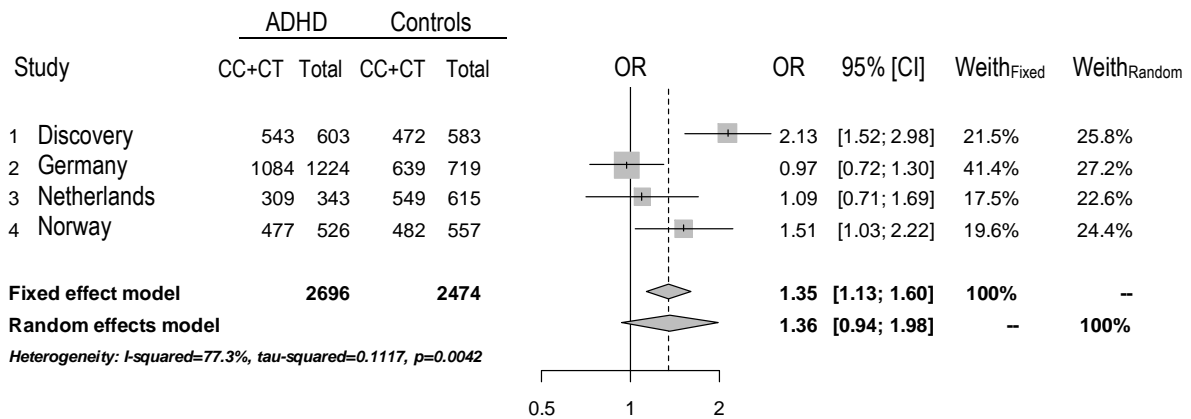
(d) rs4902569 (GG+GA versus AA)



(e) rs2415545 (AA+AG versus GG)



(f) rs11644983 (CC+CT versus TT)



(g) rs11646443 (GG+GA versus AA)

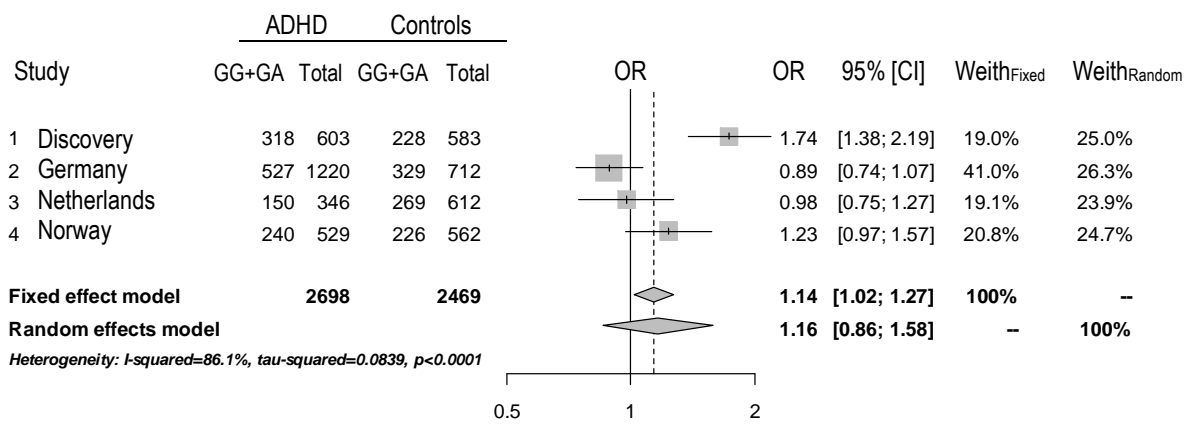
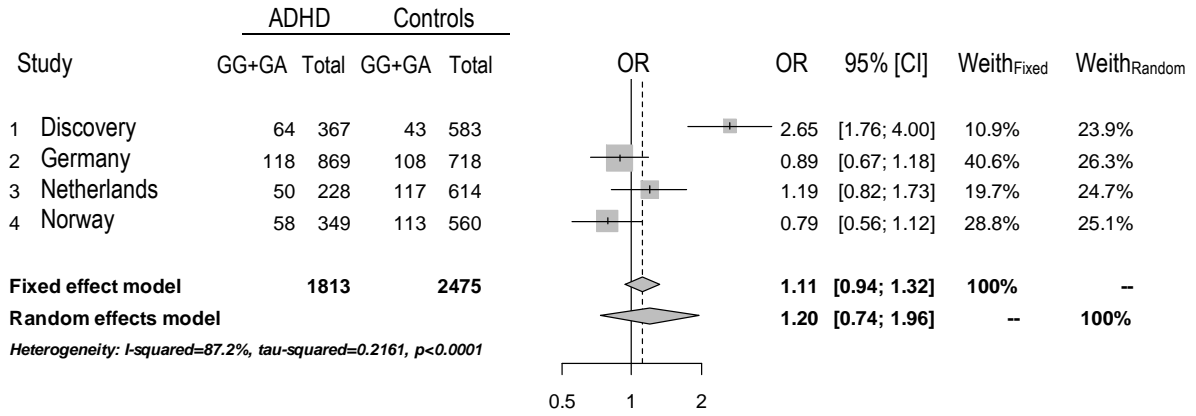
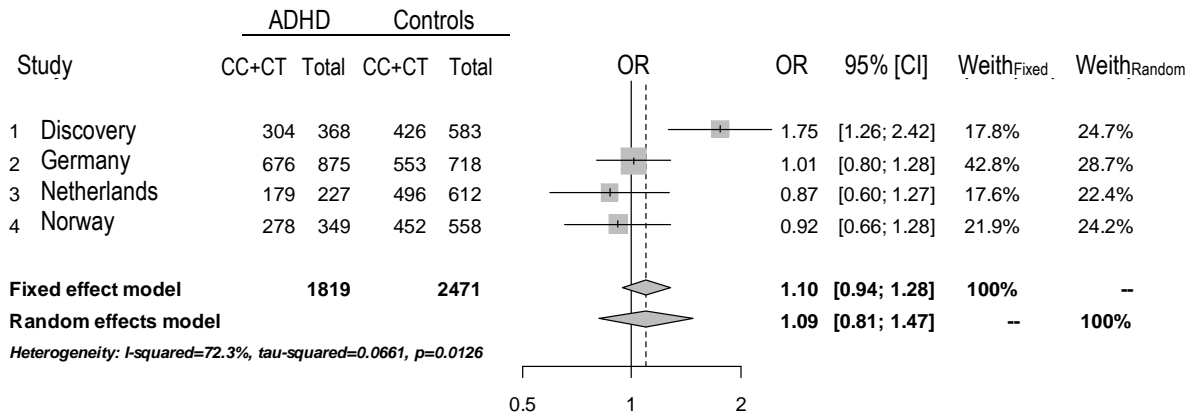


Table S6. Effect of the seven SNPs from four loci achieving at least suggestive significance (PGC < 1e-05) in combined ADHD (1,826 cases and 2,484 controls)

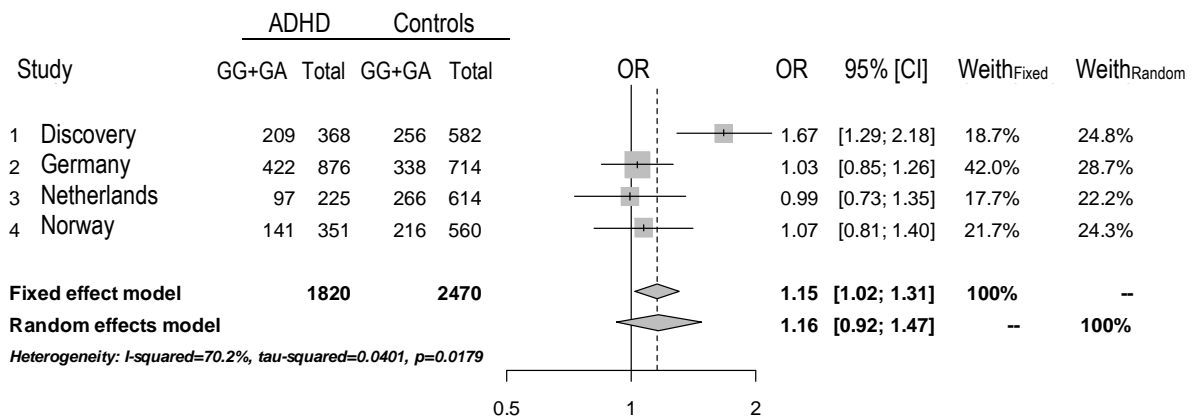
(a) rs2232429 (GG+GA versus AA)



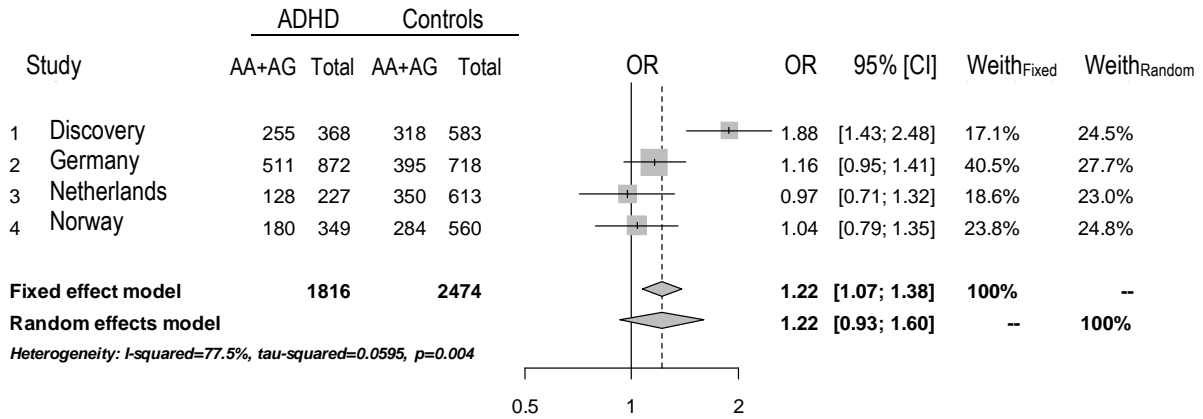
(b) rs4416909 (CC+CT versus TT)



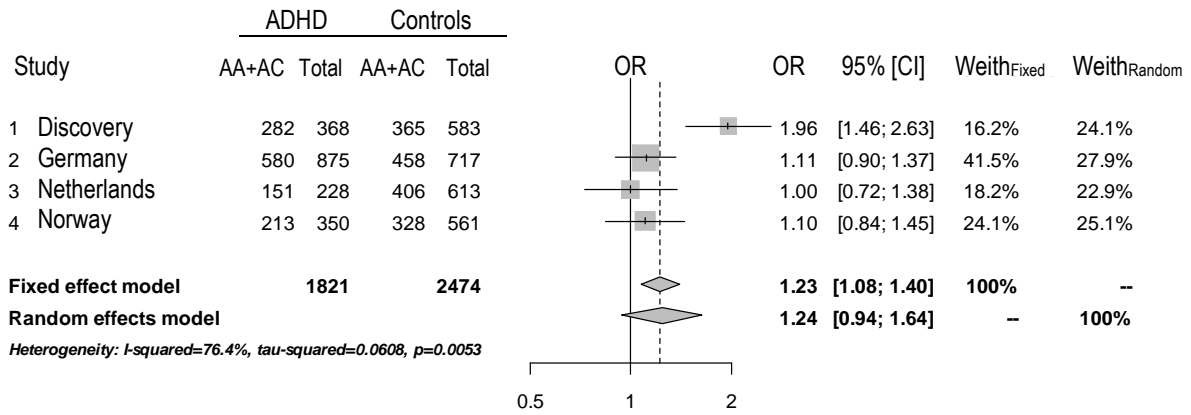
(c) rs4902569 (GG+GA versus AA)



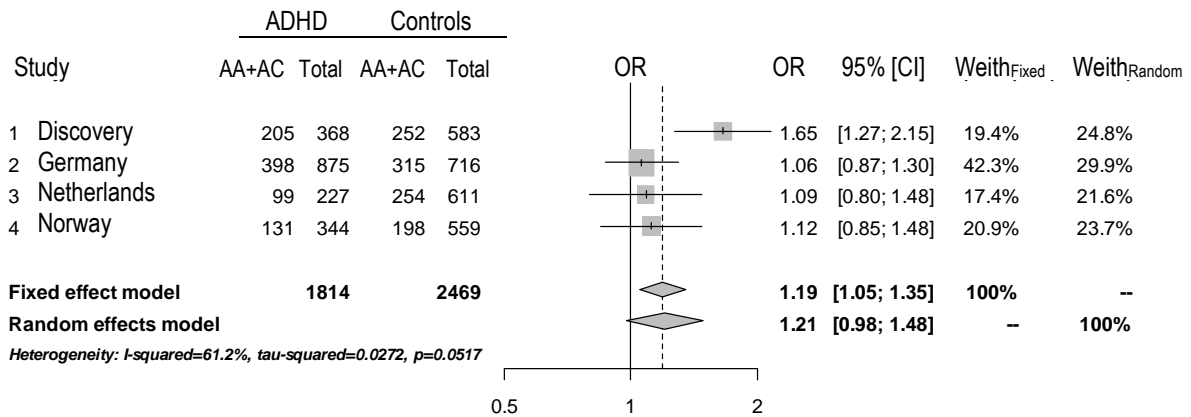
(d) rs2415543 (AA+AG versus GG)



(e) rs2415545 (AA+AC versus CC)



(f) rs3814860 (AA+AC versus CC)



(g) rs11646443 (GG+GA versus AA)

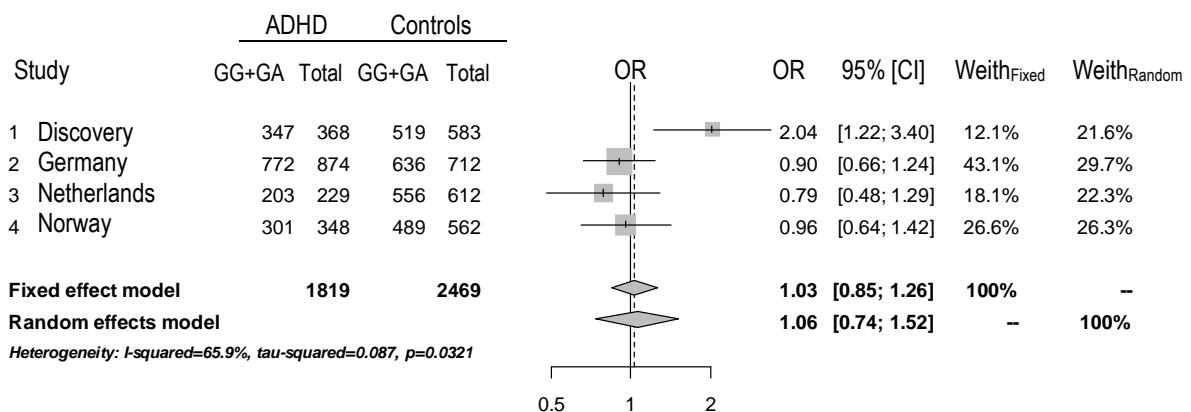
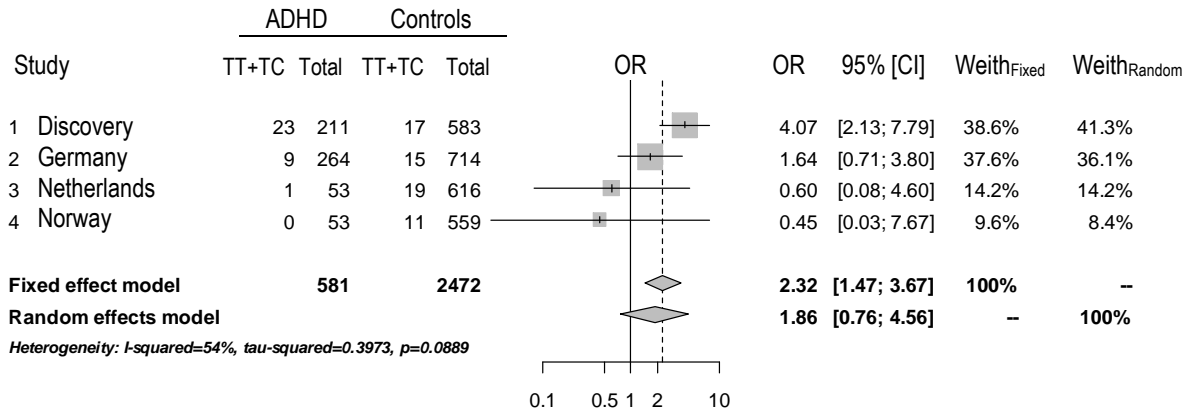
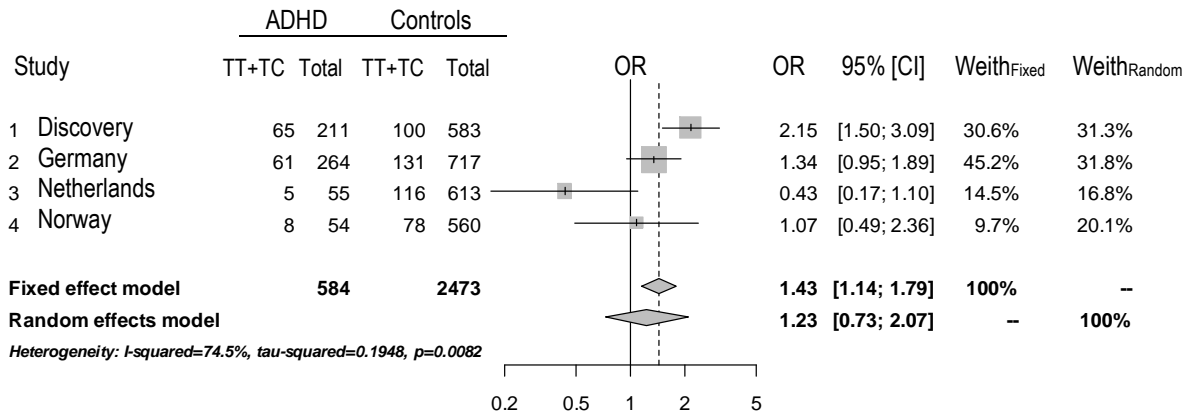


Table S7. Effect of the three SNPs from three loci achieving at least suggestive significance (PGC < 1e-05) on inattentive ADHD (588 cases and 2,484 controls)

(a) rs12333188 (TT+TC versus CC)



(b) rs1962749 (TT+TC versus CC)



(c) rs1988353 (AA+AG versus GG)

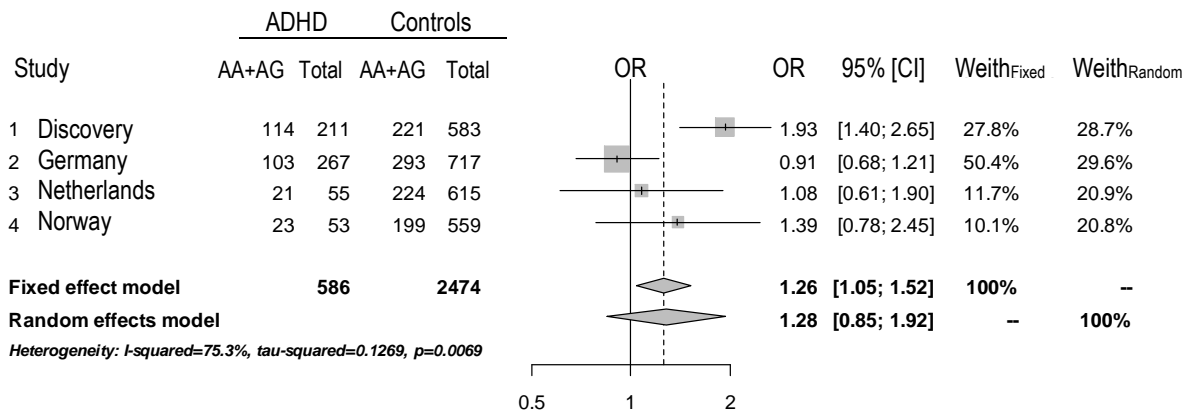


Table S8. Significant genotyped and imputed SNPs within the *FBXO33* locus in the discovery cohort of 368 combined ADHD patients and 583 controls

Marker*	Position (bp)**	P-value	Location
rs17696574	39,967,531	2,54E-06	5' region
rs10143148	39,964,127	0,009422	5' region
rs1950330	39,955,162	6,50E-04	5' region
rs2057137	39,943,541	4,00E-04	5' region
rs6571939	39,927,605	0,006254	5' region
rs2038281	39,915,197	7,44E-05	5' region
rs2038278	39,912,718	7,71E-06	5' region
rs8006123	39,900,672	1,80E-06	Intron 1
rs2415549	39,899,968	2,82E-06	Intron 1
rs7161403	39,898,349	2,05E-06	Intron 1
rs12588110	39,897,797	1,80E-06	Intron 1
rs36090203	39,897,705	1,36E-06	Intron 1
rs34654496	39,897,415	1,36E-06	Intron 1
rs4902637	39,896,814	1,80E-06	Intron 1
rs10145949	39,896,656	9,98E-07	Intron 1
rs4902636	39,896,638	1,80E-06	Intron 1
rs71407786	39,894,494	1,90E-04	Intron 1
rs34649642	39,894,356	1,80E-06	Intron 1
rs35297616	39,894,204	1,36E-06	Intron 1
rs12588175	39,894,085	1,80E-06	Intron 1
rs12590172	39,893,535	2,82E-06	Intron 1
rs12587625	39,893,525	2,82E-06	Intron 1
rs61999076	39,893,192	0,001675	Intron 1
rs56127968	39,892,757	1,93E-06	Intron 1
rs35459433	39,892,574	2,82E-06	Intron 1
rs34080511	39,892,197	5,42E-04	Intron 1
rs8003397	39,891,459	3,87E-06	Intron 1
rs8003621	39,891,394	3,63E-06	Intron 1
rs8019328	39,890,545	1,62E-06	Intron 1
rs2899889	39,889,812	6,72E-06	Intron 1
rs2899888	39,889,759	1,93E-05	Intron 1
rs4902622	39,888,772	4,42E-06	Intron 1
rs74745468	39,887,676	0,001677	Intron 1
rs12232110	39,887,331	9,02E-07	Intron 1
rs8006893	39,886,707	1,03E-06	Intron 1
rs8006321	39,886,381	2,04E-06	Intron 1
rs10139591	39,885,749	0,001675	Intron 1
rs56046902	39,884,876	2,46E-06	Intron 1
rs7152341	39,884,605	3,18E-06	Intron 1
rs10143351	39,882,971	1,22E-06	Intron 1
rs12882250	39,882,965	2,04E-06	Intron 1
rs34651350	39,881,184	1,36E-06	Intron 1
rs34785385	39,880,920	4,22E-06	Intron 1
rs35693868	39,880,851	9,56E-06	Intron 1
rs12886769	39,880,819	3,18E-06	Intron 1

rs4902599	39,880,284	3,63E-06	Intron 1
rs4902598	39,877,948	3,61E-06	Intron 1
rs2148507	39,877,232	1,66E-06	Intron 1
rs2415546	39,876,289	1,66E-06	Intron 1
rs12880644	39,876,019	3,61E-06	Intron 1
rs12897960	39,875,949	3,61E-06	Intron 1
rs35553183	39,875,672	3,61E-06	Intron 1
rs4899245	39,874,402	4,37E-06	Intron 1
rs147773159	39,873,797	0,01858	Intron 1
rs12885079	39,873,661	1,25E-06	Intron 1
rs79982649	39,873,415	0,008118	Intron 1
rs7142748	39,872,693	1,22E-06	Intron 1
rs72675487	39,872,686	3,63E-06	Intron 1
rs3814860	39,868,646	6,35E-06	3'UTR
rs117538365	39,867,583	0,002579	3'UTR
rs2274395	39,865,764	2,94E-06	3'UTR
rs1056345	39,865,674	2,55E-06	3'UTR
rs2415545	39,863,802	1,91E-06	3' region
rs2415543	39,860,216	7,16E-06	3' region
rs4902569	39,858,941	5,94E-06	3' region

*In bold, genotyped markers; **Base pairs according to hg19 - NCBI Build 36

Table S9. GO categories reaching nominal significance ($P < 0.05$) for overrepresentation in the GWAS dataset.

GO NUMBER	TYPE*	TOTAL GENES IN CATEGORY	GENES ON LIST	EXPECTED GENES ON LIST	P-VALUE	EXPECTED HITS/STUDY	FUNCTION
GO:0008366	P	30	21	12,82	0,0007	1,68	axon ensheathment
GO:0007272	P	30	21	12,82	0,0007	1,68	ensheathment of neurons
GO:0009887	P	473	232	200,56	0,0009	2,12	organ morphogenesis
GO:0003700	F	866	380	341,16	0,001	2,35	transcription factor activity
GO:0042552	P	27	19	11,36	0,0012	2,8	myelination
GO:0048706	P	53	28	18,65	0,0014	3,25	embryonic skeletal system development
GO:0001764	P	41	28	19,42	0,0015	3,48	neuron migration
GO:0051336	P	266	140	117,69	0,0015	3,48	regulation of hydrolase activity
GO:0006144	P	12	10	5,02	0,0021	4,88	purine base metabolic process
GO:0030225	P	11	10	5,44	0,0024	5,59	macrophage differentiation
GO:0030154	P	1156	541	499,76001	0,0028	6,57	cell differentiation
GO:0048598	P	207	101	82,08	0,0028	6,57	embryonic morphogenesis
GO:0048704	P	40	21	13,39	0,0031	7,31	embryonic skeletal system morphogenesis
GO:0009653	P	950	448	412,29001	0,0033	7,81	anatomical structure morphogenesis
GO:0007275	P	2202	992	940,84998	0,0034	8,06	multicellular organismal development
GO:0004540	F	60	31	21,11	0,0035	8,32	ribonuclease activity
GO:0001975	P	7	7	3,68	0,0036	8,56	response to amphetamine
GO:0008589	P	10	8	3,61	0,0038	9,07	regulation of smoothened signaling pathway
GO:0030528	F	1311	555	513,66998	0,0039	9,34	transcription regulator activity
GO:0021522	P	11	9	4,85	0,0041	9,88	spinal cord motor neuron differentiation
GO:0048869	P	1247	583	543,13	0,0045	10,93	cellular developmental process
GO:0022037	P	22	16	10,52	0,0045	10,93	metencephalon development
GO:0007389	P	193	89	73,2	0,005	12,27	pattern specification process
GO:0032502	P	2821	1239	1184,85999	0,0052	12,81	developmental process
GO:0048522	P	1229	555	515,01001	0,0052	12,81	positive regulation of cellular process
GO:0016331	P	36	24	16,4	0,0055	13,63	morphogenesis of embryonic epithelium
GO:0021510	P	29	19	12,49	0,0055	13,63	spinal cord development
GO:0048468	P	548	270	244,06	0,0056	13,91	cell development
GO:0005097	F	45	29	21	0,0058	14,47	Rab GTPase activator activity
GO:0042391	P	84	51	40,27	0,0061	15,31	regulation of membrane potential
GO:0003676	F	2934	1078	1025,46997	0,0062	15,59	nucleic acid binding
GO:0042440	P	38	23	15,6	0,0064	16,18	pigment metabolic process
GO:0015250	F	10	8	4,02	0,0064	16,18	water channel activity
GO:0051216	P	46	30	21,89	0,0068	17,34	cartilage development
GO:0070461	C	4	4	1,27	0,0075	19,36	SAGA-type complex
GO:0042176	P	25	17	11,02	0,0077	19,94	regulation of protein catabolic process
GO:0035239	P	70	42	32,36	0,0078	20,23	tube morphogenesis
GO:0009790	P	377	175	154,08	0,0082	21,39	embryonic development
GO:0007194	P	31	21	14,71	0,0082	21,39	negative regulation of adenylate cyclase activity
GO:0031280	P	31	21	14,71	0,0082	21,39	negative regulation of cyclase activity
GO:0051350	P	31	21	14,71	0,0082	21,39	negative regulation of lyase activity
GO:0007399	P	776	384	355,59	0,0085	22,26	nervous system development
GO:0046112	P	10	8	4,14	0,0086	22,55	nucleobase biosynthetic process
GO:0009113	P	6	5	1,83	0,0087	22,83	purine base biosynthetic process
GO:0055072	P	25	15	8,99	0,0088	23,11	iron ion homeostasis
GO:0033135	P	8	7	3,35	0,0089	23,4	regulation of peptidyl-serine phosphorylation
GO:0032405	F	6	5	1,83	0,0092	24,26	MutLalpha complex binding
GO:0032313	P	44	28	20,67	0,0092	24,26	regulation of Rab GTPase activity
GO:0032483	P	44	28	20,67	0,0092	24,26	regulation of Rab protein signal transduction
GO:0048856	P	1888	859	817,71997	0,0095	25,14	anatomical structure development
GO:0051239	P	597	289	263,95999	0,0097	25,72	regulation of multicellular organismal

							process
							regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
GO:0019219	P	2445	946	899,77002	0,0098	26,01	
GO:0008016	P	58	37	28,47	0,0098	26,01	regulation of heart contraction
GO:0045604	P	3	3	0,76	0,0098	26,01	regulation of epidermal cell differentiation
GO:0021515	P	19	13	8,22	0,0099	26,29	cell differentiation in spinal cord
GO:0014020	P	19	14	8,93	0,0101	26,88	primary neural tube formation
GO:0006572	P	4	4	1,4	0,0102	27,18	tyrosine catabolic process
GO:0001843	P	17	13	8,23	0,0105	28,06	neural tube closure
GO:0043025	C	62	38	29,48	0,0107	28,62	cell soma
GO:0001894	P	28	18	12,25	0,0108	28,9	tissue homeostasis
GO:0048871	P	28	18	12,25	0,0108	28,9	multicellular organismal homeostasis
GO:0048705	P	64	32	23,8	0,0108	28,9	skeletal system morphogenesis
GO:0021517	P	13	10	6,02	0,0108	28,9	ventral spinal cord development
GO:0048518	P	1345	601	563,64001	0,0109	29,19	positive regulation of biological process
GO:0048731	P	1685	768	729,97998	0,011	29,48	system development
GO:0044057	P	179	99	85,26	0,011	29,48	regulation of system process
GO:0048878	P	353	174	154,38	0,0111	29,76	chemical homeostasis
GO:0006919	P	42	25	17,8	0,0111	29,76	activation of caspase activity
GO:0048513	P	1184	537	503,70001	0,0112	30,05	organ development
GO:0007423	P	151	74	60,89	0,0112	30,05	sensory organ development
GO:0050482	P	8	7	3,48	0,0112	30,05	arachidonic acid secretion
GO:0065009	P	735	335	308,22	0,0116	31,2	regulation of molecular function
GO:0019228	P	37	24	17,43	0,0121	32,62	regulation of action potential in neuron
GO:0045449	P	2299	885	841,41998	0,0122	32,9	regulation of transcription
GO:0022008	P	369	186	166,52	0,0123	33,19	neurogenesis
GO:0030424	C	52	35	27,27	0,0125	33,76	axon
GO:0043565	F	497	212	190,34	0,0126	34,04	sequence-specific DNA binding
GO:0048858	P	132	77	65,47	0,0127	34,32	cell projection morphogenesis
GO:0032990	P	132	77	65,47	0,0127	34,32	cell part morphogenesis
GO:0048699	P	346	176	157,19	0,0128	34,6	generation of neurons
GO:0004521	F	41	22	14,9	0,0128	34,6	endoribonuclease activity
GO:0031326	P	2572	992	945,92999	0,0129	34,89	regulation of cellular biosynthetic process
							regulation of transcription, DNA-dependent
GO:0006355	P	2167	833	790,40002	0,013	35,18	positive regulation of tyrosine phosphorylation of Stat3 protein
GO:0042517	P	11	8	4,03	0,013	35,18	transcription corepressor activity
GO:0003714	F	117	57	45,72	0,0131	35,47	1-alkyl-2-acetyl-glycerophosphocholine esterase activity
GO:0003847	F	5	4	1,27	0,0133	36,05	regulation of gene expression
GO:0010468	P	2501	960	914,59998	0,0134	36,33	neuromuscular process
GO:0050905	P	47	31	23,73	0,0135	36,62	adult locomotory behavior
GO:0008344	P	32	22	15,92	0,0135	36,62	ion homeostasis
GO:0050801	P	283	140	122,88	0,0136	36,91	porphyrin metabolic process
GO:0006778	P	24	16	10,36	0,0136	36,91	tetrapyrrole metabolic process
GO:0033013	P	24	16	10,36	0,0136	36,91	regulation of RNA metabolic process
GO:0051252	P	2190	840	797,98999	0,0139	37,78	
GO:0007409	P	119	70	59,3	0,0143	38,98	axonogenesis
GO:0042592	P	566	268	244,53	0,0145	39,58	homeostatic process
							inhibition of adenylate cyclase activity by G-protein signaling pathway
GO:0007193	P	18	12	7,26	0,0146	39,88	positive regulation of hydrolase activity
GO:0051345	P	137	73	60,85	0,0148	40,46	nucleobase metabolic process
GO:0009112	P	20	14	8,97	0,015	41,07	midbody
GO:0030496	C	12	9	4,85	0,015	41,07	regulation of biosynthetic process
GO:0009889	P	2580	994	949,20001	0,0159	43,82	JAK-STAT cascade
GO:0007259	P	30	19	13,12	0,0161	44,44	regulation of GTPase activity
GO:0043087	P	101	58	47,71	0,0165	45,67	response to progesterone stimulus
GO:0032570	P	4	4	1,55	0,0165	45,67	structural constituent of nuclear pore
GO:0017056	F	4	4	1,58	0,0166	45,99	
GO:0030182	P	270	139	123,15	0,0167	46,3	neuron differentiation
GO:0030027	C	42	28	21,36	0,0171	47,57	lamellipodium
							positive regulation of cellular metabolic process
GO:0031325	P	569	262	239,78999	0,0173	48,2	

GO:0006890	P	18	12	7,28	0,0173	48,2	retrograde vesicle-mediated transport, Golgi to ER
GO:0016504	F	19	13	8,23	0,0175	48,82	peptidase activator activity
GO:0005634	C	4694	1708	1656,72998	0,0177	49,44	nucleus
GO:0002573	P	27	19	13,5	0,0178	49,77	myeloid leukocyte differentiation
GO:0042995	C	427	230	210,59	0,0178	49,77	cell projection
GO:0007625	P	4	4	1,53	0,0178	49,77	grooming behavior
GO:0003712	F	297	136	119,35	0,018	50,4	transcription cofactor activity
GO:0042168	P	19	13	8,1	0,0181	50,72	heme metabolic process
GO:0040014	P	44	24	17,18	0,0182	51,05	regulation of multicellular organism growth
GO:0043280	P	47	27	20,14	0,0184	51,69	positive regulation of caspase activity
GO:0002246	P	4	4	1,49	0,0188	52,95	healing during inflammatory response
GO:0031252	C	80	48	39,08	0,0189	53,27	cell leading edge
GO:0007164	P	7	6	2,93	0,0189	53,27	establishment of tissue polarity
GO:0045217	P	3	3	0,9	0,0189	53,27	cell-cell junction maintenance
GO:0034331	P	3	3	0,9	0,0189	53,27	cell junction maintenance
GO:0043954	P	3	3	0,9	0,0189	53,27	cellular component maintenance
GO:0000124	C	3	3	0,84	0,0189	53,27	SAGA complex
GO:0043005	C	121	75	64,59	0,0192	54,23	neuron projection
GO:0021548	P	4	4	1,76	0,0192	54,23	pons development
GO:0032446	P	87	43	33,72	0,0195	55,2	protein modification by small protein conjugation
GO:0009615	P	93	39	29,8	0,0197	55,83	response to virus
GO:0001736	P	5	5	2,42	0,0202	57,45	establishment of planar polarity
GO:0048148	P	6	6	3,24	0,0208	59,41	behavioral response to cocaine
GO:0033138	P	7	6	2,97	0,021	60,07	positive regulation of peptidyl-serine phosphorylation
GO:0030326	P	55	32	24,98	0,0211	60,4	embryonic limb morphogenesis
GO:0035113	P	55	32	24,98	0,0211	60,4	embryonic appendage morphogenesis
GO:0007009	P	12	9	5,25	0,0211	60,4	plasma membrane organization
GO:0043014	F	4	4	1,58	0,0212	60,74	alpha-tubulin binding
GO:0009893	P	590	271	249,25999	0,0217	62,41	positive regulation of metabolic process
GO:0002029	P	5	4	1,5	0,0218	62,75	desensitization of G-protein coupled receptor protein signaling pathway
GO:0022401	P	5	4	1,5	0,0218	62,75	adaptation of signaling pathway
GO:0035295	P	126	69	58,1	0,0219	63,08	tube development
GO:0019902	F	30	21	15,45	0,022	63,44	phosphatase binding
GO:0001601	F	3	3	0,96	0,0221	63,77	peptide YY receptor activity
GO:0007267	P	537	258	236,97	0,0225	65,14	cell-cell signaling
GO:0046717	P	10	8	4,55	0,0226	65,49	acid secretion
GO:0005246	F	13	10	6,38	0,0226	65,49	calcium channel regulator activity
GO:0043009	P	198	92	79,22	0,0227	65,81	chordate embryonic development
GO:0007219	P	44	27	20,68	0,0229	66,5	Notch signaling pathway
GO:0002028	P	9	8	4,73	0,023	66,85	regulation of sodium ion transport
GO:0016567	P	80	40	31,29	0,023	66,85	protein ubiquitination
GO:0005372	F	11	8	4,47	0,0233	67,87	water transporter activity
GO:0043393	P	21	15	10,4	0,0234	68,2	regulation of protein binding
GO:0048812	P	126	73	63	0,0236	68,88	neuron projection morphogenesis
GO:0009792	P	201	93	80,26	0,0238	69,57	embryonic development ending in birth or egg hatching
GO:0046483	P	81	45	36,31	0,024	70,24	heterocycle metabolic process
GO:0051926	P	7	6	3,12	0,0242	70,91	negative regulation of calcium ion transport
GO:0006350	P	1506	576	543,90002	0,0243	71,26	transcription
GO:0045744	P	8	6	2,9	0,0243	71,26	negative regulation of G-protein coupled receptor protein signaling pathway
GO:0007626	P	209	99	86,15	0,0243	71,26	locomotory behavior
GO:0052548	P	61	33	25,75	0,0243	71,26	regulation of endopeptidase activity
GO:0048667	P	128	74	64,08	0,0244	71,59	cell morphogenesis involved in neuron differentiation
GO:0008283	P	307	144	128,39999	0,0248	72,93	cell proliferation
GO:0043558	P	3	3	0,87	0,0252	74,24	regulation of translational initiation in response to stress
GO:0043555	P	3	3	0,87	0,0252	74,24	regulation of translation in response to stress

GO:0007492	P	12	9	5,36	0,0253	74,58	endoderm development
GO:0015721	P	6	6	3,4	0,0254	74,92	bile acid and bile salt transport
GO:0010556	P	2485	948	908,07001	0,0255	75,25	regulation of macromolecule biosynthetic process
GO:0000305	P	6	5	2,34	0,0263	77,91	response to oxygen radical
GO:0004904	F	4	4	1,64	0,0264	78,23	interferon receptor activity
GO:0019961	F	4	4	1,64	0,0264	78,23	interferon binding
GO:0055117	P	5	5	2,58	0,0267	79,25	regulation of cardiac muscle contraction
GO:0035108	P	62	36	28,87	0,027	80,22	limb morphogenesis
GO:0035107	P	62	36	28,87	0,027	80,22	appendage morphogenesis
GO:0009124	P	22	14	9,31	0,0271	80,55	nucleoside monophosphate biosynthetic process
GO:0009123	P	22	14	9,31	0,0271	80,55	nucleoside monophosphate metabolic process
GO:0030126	C	10	7	3,52	0,0272	80,88	COPI vesicle coat
GO:0030663	C	10	7	3,52	0,0272	80,88	COPI coated vesicle membrane
GO:0000122	P	181	88	76,08	0,0273	81,21	negative regulation of transcription from RNA polymerase II promoter
GO:0045822	P	4	3	0,91	0,0275	81,85	negative regulation of heart contraction
GO:0009168	P	16	10	5,91	0,0276	82,18	purine ribonucleoside monophosphate biosynthetic process
GO:0009127	P	16	10	5,91	0,0276	82,18	purine nucleoside monophosphate biosynthetic process
GO:0009167	P	16	10	5,91	0,0276	82,18	purine ribonucleoside monophosphate metabolic process
GO:0009126	P	16	10	5,91	0,0276	82,18	purine nucleoside monophosphate metabolic process
GO:0006833	P	13	9	5,28	0,0279	83,14	water transport
GO:0042044	P	13	9	5,28	0,0279	83,14	fluid transport
GO:0033018	C	5	5	2,58	0,0279	83,14	sarcoplasmic reticulum lumen
GO:0005911	C	146	80	69,33	0,0283	84,45	cell-cell junction
GO:0003002	P	148	63	52,55	0,0284	84,76	regionalization
GO:0045932	P	8	6	3,27	0,0284	84,76	negative regulation of muscle contraction
GO:0000904	P	145	81	70,83	0,0285	85,09	cell morphogenesis involved in differentiation
GO:0001838	P	25	16	11,11	0,0289	86,4	embryonic epithelial tube formation
GO:0015802	P	4	4	1,8	0,0292	87,4	basic amino acid transport
GO:0055082	P	266	129	114,7	0,0293	87,74	cellular chemical homeostasis
GO:0030426	C	27	19	14,08	0,0295	88,41	growth cone
GO:0042789	P	3	3	1,07	0,0295	88,41	mRNA transcription from RNA polymerase II promoter
GO:0046148	P	32	18	12,69	0,0297	89,07	pigment biosynthetic process
GO:0008134	F	419	189	171,64	0,0301	90,41	transcription factor binding
GO:0043073	C	13	9	5,29	0,0303	91,07	germ cell nucleus
GO:0002262	P	3	3	0,99	0,0309	93,11	myeloid cell homeostasis
GO:0032318	P	89	51	42,53	0,031	93,44	regulation of Ras GTPase activity
GO:0016323	C	143	85	74,65	0,0314	94,8	basolateral plasma membrane
GO:0051927	P	3	3	0,97	0,0316	95,49	negative regulation of calcium ion transport via voltage-gated calcium channel activity
GO:0045935	P	421	195	177,73	0,0317	95,84	positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
GO:0014075	P	10	8	5,09	0,0319	96,54	response to amine stimulus
GO:0010243	P	10	8	5,09	0,0319	96,54	response to organic nitrogen
GO:0003677	F	2127	793	758,60999	0,0328	99,65	DNA binding
GO:0006873	P	261	126	112,26	0,0328	99,65	cellular ion homeostasis
GO:0045941	P	392	182	165,39	0,0329	99,99	positive regulation of transcription
GO:0010740	P	138	65	54,69	0,0331	100,68	positive regulation of protein kinase cascade
GO:0048485	P	3	3	1,09	0,0334	101,71	sympathetic nervous system development
GO:0000303	P	5	4	1,61	0,0335	102,06	response to superoxide
GO:0016192	P	469	227	208,85001	0,0342	104,43	vesicle-mediated transport
GO:0051704	P	504	209	190,78	0,0342	104,43	multi-organism process

GO:0017134	F	5	4	1,61	0,0345	105,46	fibroblast growth factor binding
GO:0006885	P	26	16	11,2	0,0353	108,2	regulation of pH
GO:0019226	P	277	149	135,77	0,0354	108,54	transmission of nerve impulse
GO:0044445	C	129	49	39,7	0,0356	109,23	cytosolic part
GO:0060173	P	64	37	30,15	0,0358	109,9	limb development
GO:0048736	P	64	37	30,15	0,0358	109,9	appendage development
GO:0010604	P	558	255	236,22	0,036	110,59	positive regulation of macromolecule metabolic process
GO:0021871	P	6	5	2,53	0,0364	111,95	forebrain regionalization
GO:0032965	P	5	4	1,64	0,0365	112,29	regulation of collagen biosynthetic process
GO:0010628	P	402	186	169,74001	0,0369	113,68	positive regulation of gene expression
GO:0016505	F	16	11	7,17	0,0371	114,37	apoptotic protease activator activity
GO:0021695	P	14	10	6,73	0,0372	114,72	cerebellar cortex development
GO:0009156	P	21	13	8,71	0,0372	114,72	ribonucleoside monophosphate biosynthetic process
GO:0009161	P	21	13	8,71	0,0372	114,72	ribonucleoside monophosphate metabolic process
GO:0007260	P	6	5	2,43	0,0382	118,2	tyrosine phosphorylation of STAT protein
GO:0060043	P	7	6	3,41	0,0382	118,2	regulation of cardiac muscle cell proliferation
GO:0051864	F	3	3	1,08	0,0385	119,26	histone demethylase activity (H3-K36 specific)
GO:0004518	F	141	61	50,93	0,0388	120,35	nuclease activity
GO:0052547	P	65	34	27,23	0,0391	121,42	regulation of peptidase activity
GO:0070198	P	5	4	1,81	0,0392	121,78	protein localization to chromosome, telomeric region
GO:0050790	P	653	292	272,04001	0,0398	123,94	regulation of catalytic activity
GO:0022612	P	7	6	3,48	0,0406	126,91	gland morphogenesis
GO:0006928	P	351	174	159,33	0,0411	128,8	cellular component movement
GO:0051674	P	351	174	159,33	0,0411	128,8	localization of cell
GO:0001654	P	87	44	36,38	0,0413	129,55	eye development
GO:0048568	P	34	21	15,99	0,0414	129,92	embryonic organ development
GO:0030277	P	3	3	1,07	0,0414	129,92	maintenance of gastrointestinal epithelium
GO:0043492	F	93	58	50,41	0,0415	130,29	ATPase activity, coupled to movement of substances
GO:0030802	P	76	42	34,89	0,0419	131,8	regulation of cyclic nucleotide biosynthetic process
GO:0030808	P	76	42	34,89	0,0419	131,8	regulation of nucleotide biosynthetic process
GO:0032501	P	3327	1390	1350,44995	0,042	132,18	multicellular organismal process
GO:0001841	P	24	15	10,63	0,042	132,18	neural tube formation
GO:0019222	P	2947	1129	1090,68994	0,0422	132,95	regulation of metabolic process
GO:0005160	F	17	12	8,34	0,0424	133,72	transforming growth factor beta receptor binding
GO:0006942	P	15	10	6,34	0,0425	134,09	regulation of striated muscle contraction
GO:0045597	P	145	78	68,17	0,0426	134,47	positive regulation of cell differentiation
GO:0008066	F	29	25	21,4	0,0436	138,25	glutamate receptor activity
GO:0060255	P	2810	1073	1036,18005	0,0439	139,4	regulation of macromolecule metabolic process
GO:0051240	P	128	68	58,71	0,044	139,79	positive regulation of multicellular organismal process
GO:0006937	P	49	27	21,27	0,044	139,79	regulation of muscle contraction
GO:0045666	P	15	9	5,49	0,044	139,79	positive regulation of neuron differentiation
GO:0022601	P	3	3	1,21	0,0442	140,54	menstrual cycle phase
GO:0004983	F	8	6	3,17	0,0442	140,54	neuropeptide Y receptor activity
GO:0000149	F	23	15	10,89	0,0446	142,05	SNARE binding
GO:0032002	C	3	3	1,23	0,0451	143,98	interleukin-28 receptor complex
GO:0045892	P	250	114	101,85	0,0453	144,75	negative regulation of transcription, DNA-dependent
GO:0032451	F	7	5	2,36	0,0453	144,75	demethylase activity
GO:0008109	F	3	3	1,18	0,0453	144,75	N-acetyllactosaminide beta-1,6-N-acetylglucosaminyltransferase activity
GO:0051383	P	4	4	1,89	0,0454	145,13	kinetochore organization

GO:0030162	P	32	18	13,08	0,0455	145,52	regulation of proteolysis
GO:0005913	C	18	14	10,35	0,0455	145,52	cell-cell adherens junction
GO:0016820	F	95	59	51,54	0,0456	145,9	hydrolase activity, acting on acid anhydrides, catalyzing transmembrane movement of substances
GO:0005581	C	33	26	21,57	0,0456	145,9	collagen
GO:0008156	P	25	13	8,67	0,0462	148,24	negative regulation of DNA replication
GO:0048703	P	4	4	2,09	0,0463	148,62	embryonic viscerocranium morphogenesis
GO:0032092	P	5	5	2,8	0,0465	149,38	positive regulation of protein binding
GO:0016892	F	18	9	5,45	0,0465	149,38	endoribonuclease activity, producing 3'-phosphomonoesters
GO:0032635	P	4	4	1,88	0,0465	149,38	interleukin-6 production
GO:0042626	F	92	57	49,67	0,0468	150,53	ATPase activity, coupled to transmembrane movement of substances
GO:0043266	P	6	6	3,62	0,0468	150,53	regulation of potassium ion transport
GO:0051384	P	22	14	10,04	0,0469	150,91	response to glucocorticoid stimulus
GO:0034404	P	12	8	4,83	0,0472	152,06	nucleobase, nucleoside and nucleotide biosynthetic process
GO:0034654	P	12	8	4,83	0,0472	152,06	nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process
GO:0005655	C	6	5	2,54	0,0473	152,44	nucleolar ribonuclease P complex
GO:0030681	C	6	5	2,54	0,0473	152,44	multimeric ribonuclease P complex
GO:0030677	C	6	5	2,54	0,0473	152,44	ribonuclease P complex
GO:0002248	P	3	3	1,11	0,0474	152,83	connective tissue replacement during inflammatory response
GO:0050793	P	1006	453	429,35999	0,0475	153,21	regulation of developmental process
GO:0030799	P	78	43	36,08	0,0476	153,59	regulation of cyclic nucleotide metabolic process
GO:0030427	C	28	19	14,49	0,0476	153,59	site of polarized growth
GO:0019003	F	8	6	3,26	0,0477	153,99	GDP binding
GO:0010742	P	5	5	3,07	0,0479	154,76	macrophage derived foam cell differentiation
GO:0008656	F	14	10	6,58	0,0482	155,9	caspase activator activity
GO:0016477	P	186	92	81,45	0,0483	156,28	cell migration
GO:0006357	P	537	235	217,61	0,0484	156,66	regulation of transcription from RNA polymerase II promoter
GO:0031328	P	479	219	202,53999	0,0485	157,04	positive regulation of cellular biosynthetic process
GO:0031323	P	2813	1076	1040,51001	0,0488	158,16	regulation of cellular metabolic process
GO:0006465	P	8	6	3,47	0,0494	160,44	signal peptide processing
GO:0043502	P	7	6	3,42	0,0495	160,82	regulation of muscle adaptation
GO:0004519	F	83	38	30,56	0,0495	160,82	endonuclease activity
GO:0042472	P	39	18	12,88	0,0497	161,58	inner ear morphogenesis
GO:0048532	P	5	4	1,86	0,0499	162,36	anatomical structure arrangement

*In bold, gene set/pathway related with neuronal development, differentiation and activity; **F: Function, P: Process, C: Cellular.

Table S10. P-value and OR of SNPs achieving the significance threshold of 1e-05 in four previous GWAS

SNP	Chr	Base pairs**	Nearest gene	Risk allele	Childhood ADHD				Adulthood ADHD		
					Neale et al		Yang et al		Hinney et al		Lesch et al*
					P-value	OR	P-value	OR	P-value	OR	P-value
rs1937444	1	66,463,920	PDE4B***	A	0.94	0.07	0.35	0.94	0.72	0.97	0.052
rs1557524	1	160,246,485		T	0.88	0.15	0.46	1.05	0.60	0.96	-
rs7522166	1	160,276,709	COPA***	C	0.95	16.6	-	-	0.60	1.04	-
rs12333188	6	143,065,590	GPR126	T	0.88	0.15	-	-	-	-	-
rs1962749	6	153,551,654		A	0.85	0.19	-	-	-	-	-
rs1445594	13	58,675,299	PCDH17	A	0.067	1.82	0.47	1.05	0.26	1.09	0.90
s4902569	14	39,858,941		G	0.17	0.73	-	-	0.97	1.00	0.16
rs2415543	14	39,860,216		A	-	-	0.31	0.93	0.57	1.05	0.38
rs2415545	14	39,863,802		A	0.58	0.55	-	-	0.26	1.09	-
rs3814860	14	39,868,646	FBXO33***	A	0.096	1.66	-	-	0.66	0.96	-
rs17696574	14	39,967,531		G	0.49	1.44			0.19	1.10	-
rs11646443	16	84,270,476	KCNG4***	G	0.35	1.08			-	-	-

* Pooled analysis with no OR available

** Base pairs according to hg19 - NCBI Build 36

*** SNP within the gene

Neale BM, Medland SE, Ripke S, Asherson P, Franke B, Lesch KP, et al (2010). Meta-analysis of genome-wide association studies of attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 49(9): 884-897.

Yang L, Neale BM, Liu L, Lee SH, Wray NR, Ji N, et al (2013). Polygenic transmission and complex neuro developmental network for attention deficit hyperactivity disorder: genome-wide association study of both common and rare variants. *Am J Med Genet B Neuropsychiatr Genet* 162B(5): 419-430.

Hinney A, Scherag A, Jarick I, Albayrak O, Putter C, Pechlivanis S, et al (2011). Genome-wide association study in German patients with attention deficit/hyperactivity disorder. *Am J Med Genet B Neuropsychiatr Genet* 156B(8): 888-897.

Lesch KP, Timmesfeld N, Renner TJ, Halperin R, Roser C, Nguyen TT, et al (2008). Molecular genetics of adult ADHD: converging evidence from genome-wide association and extended pedigree linkage studies. *J Neural Transm* 115(11): 1573-1585.

Figure S1. Quantile-quantile (QQ) plot from the genome-wide data

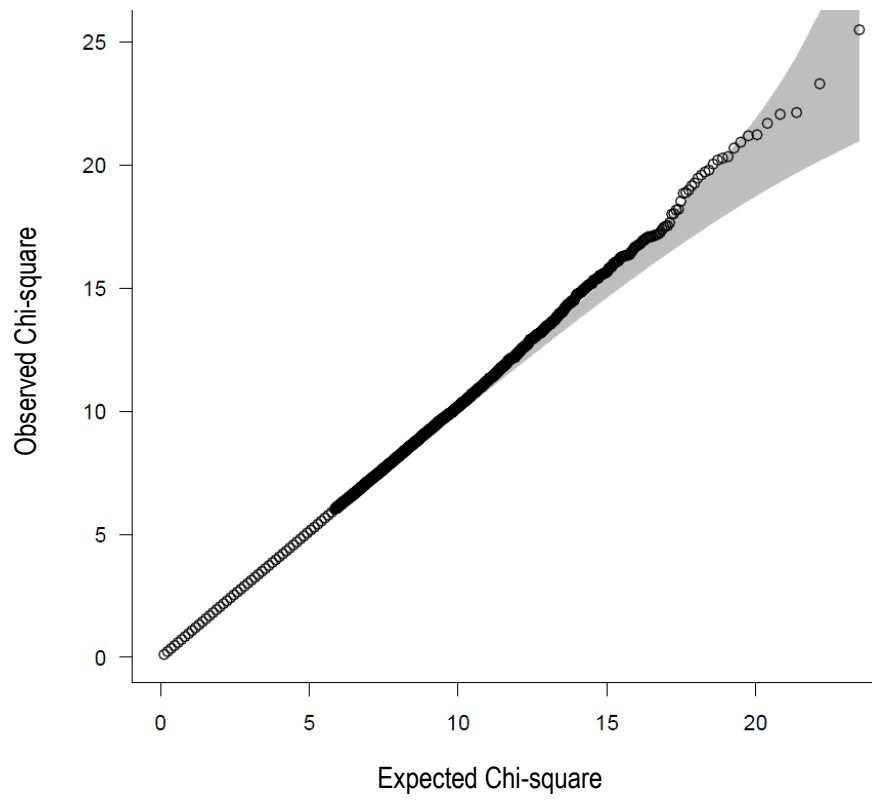


Figure S2.

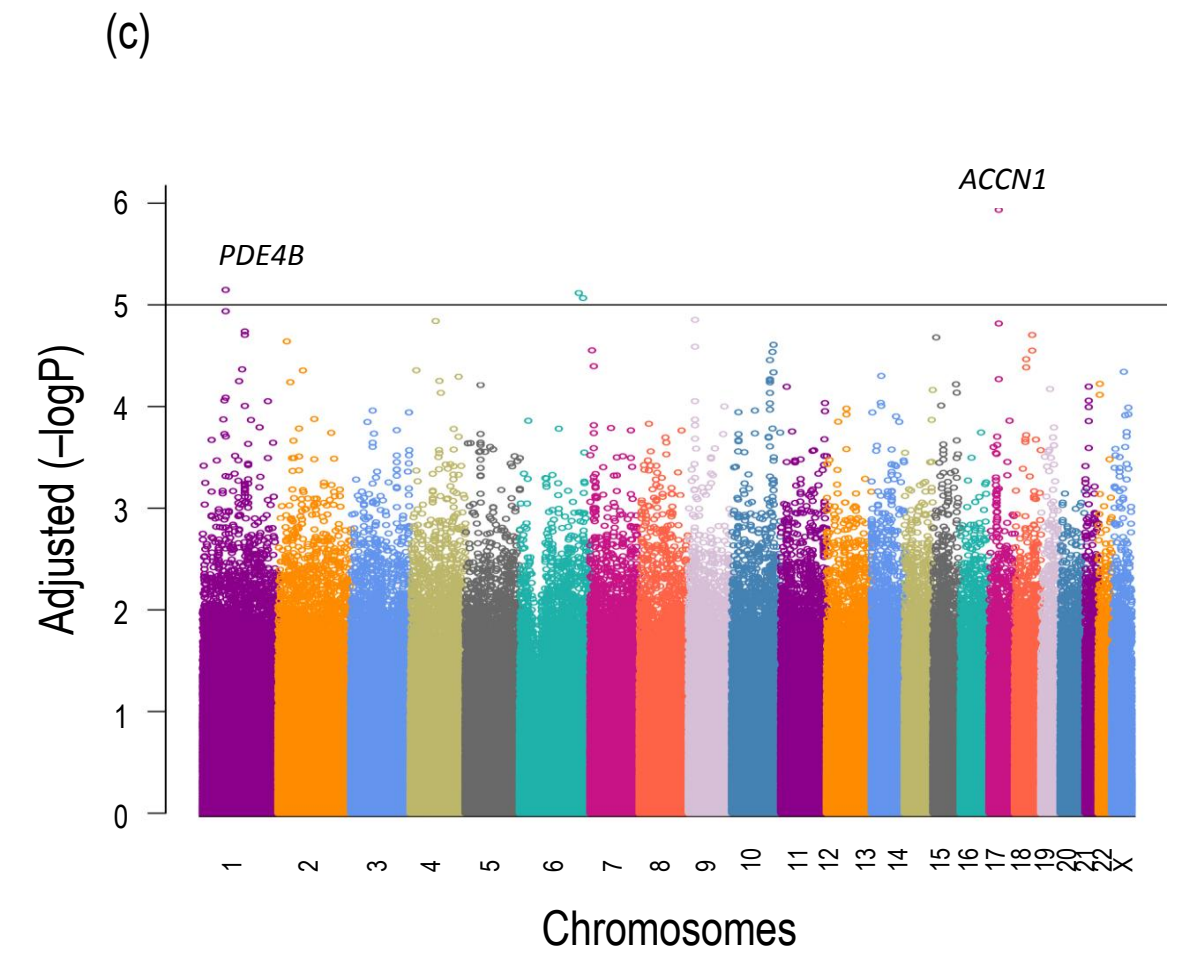
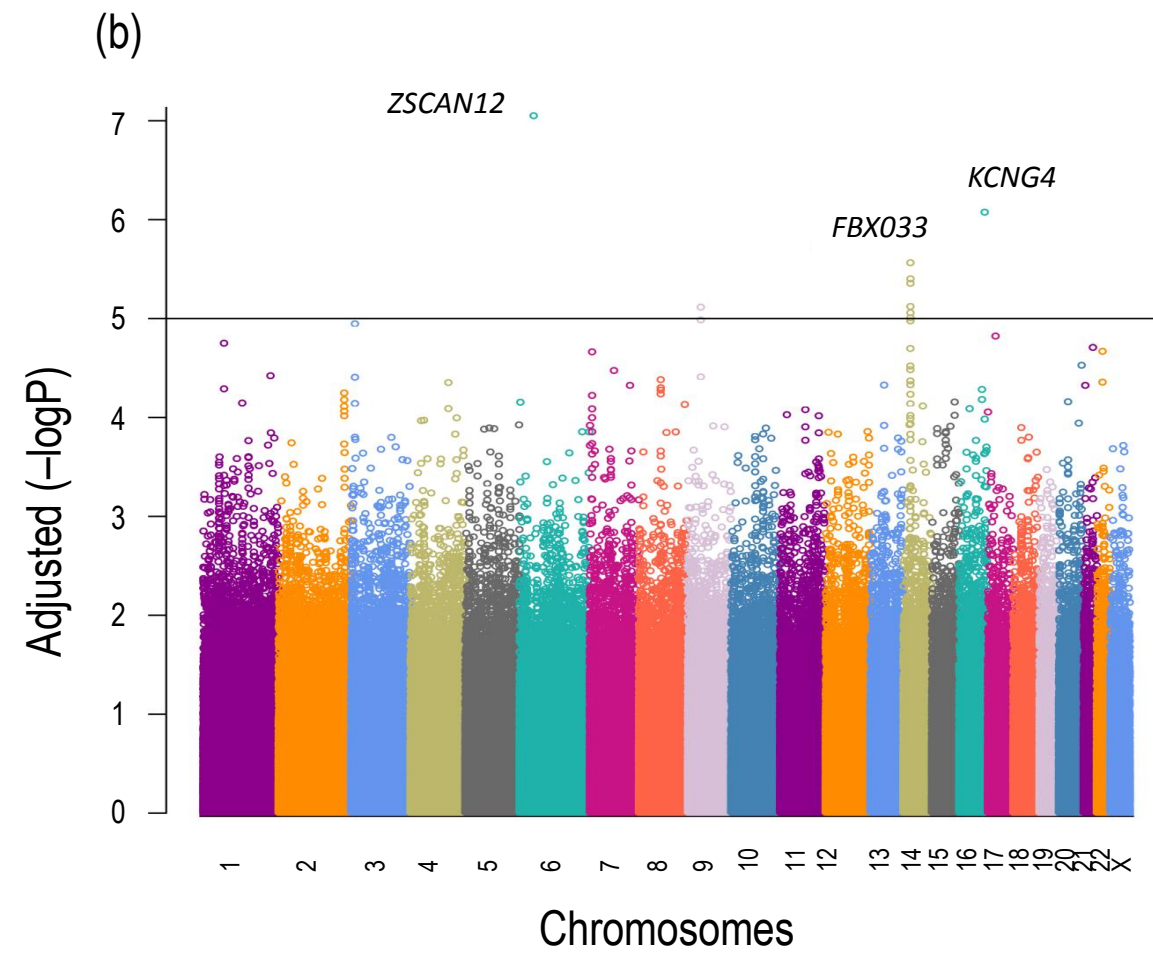
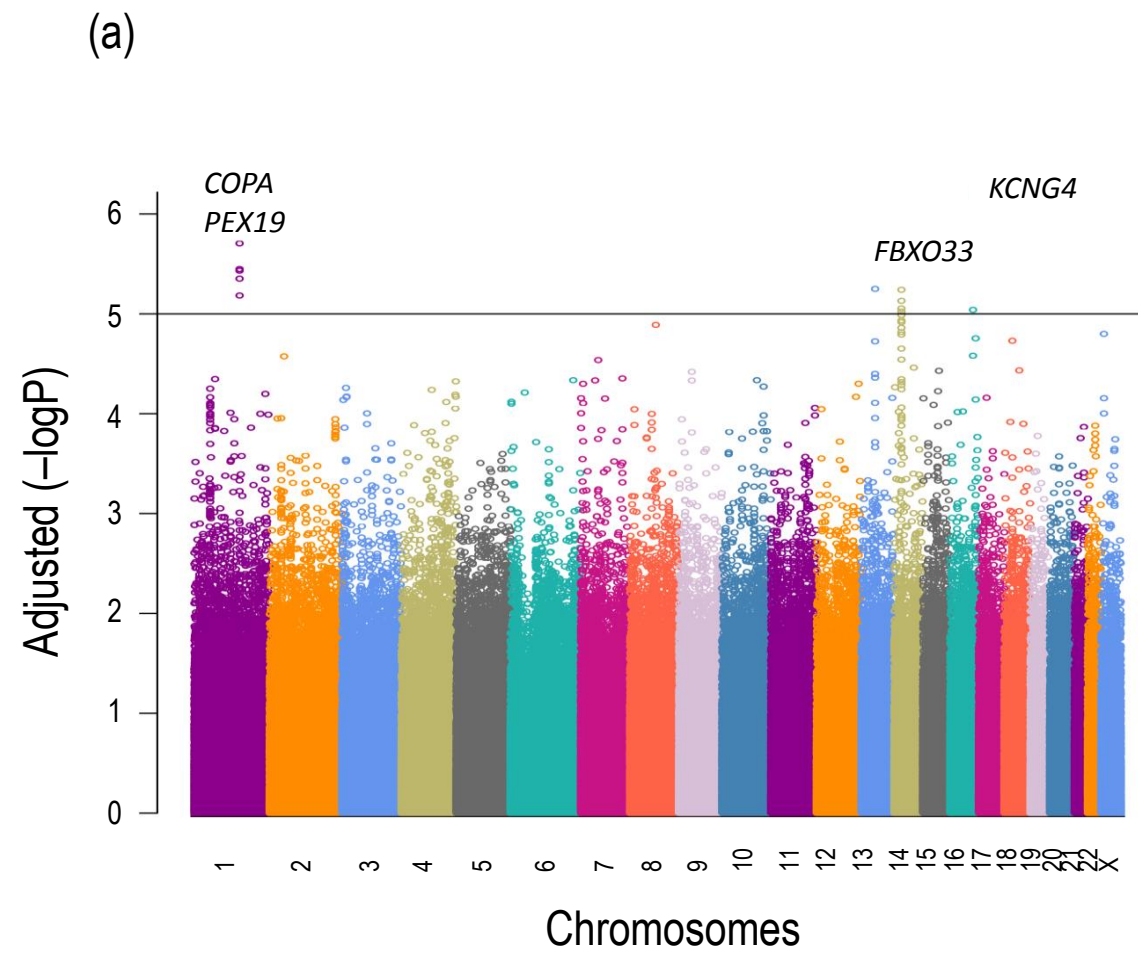


Figure S3.

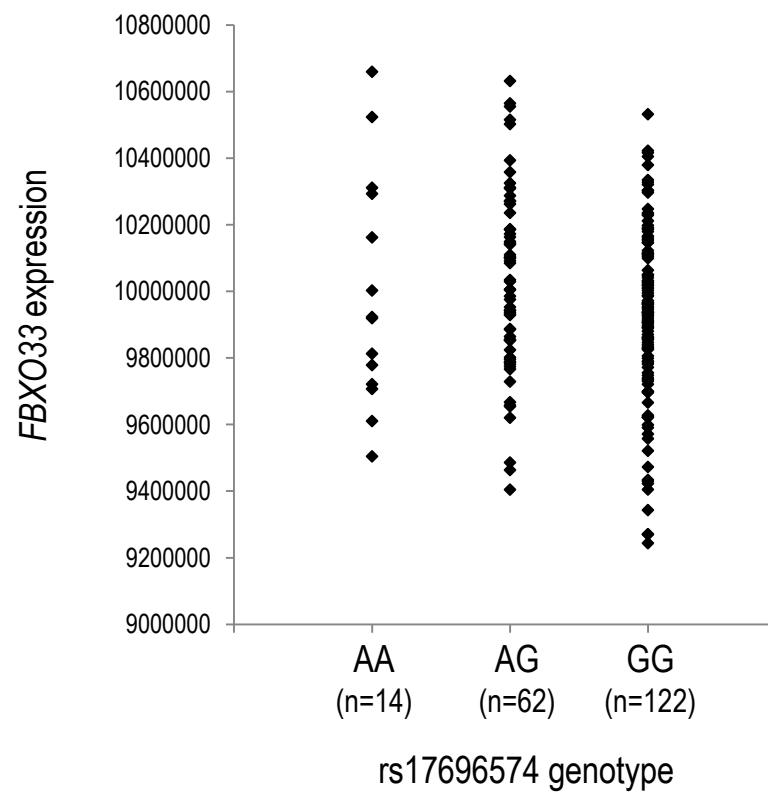
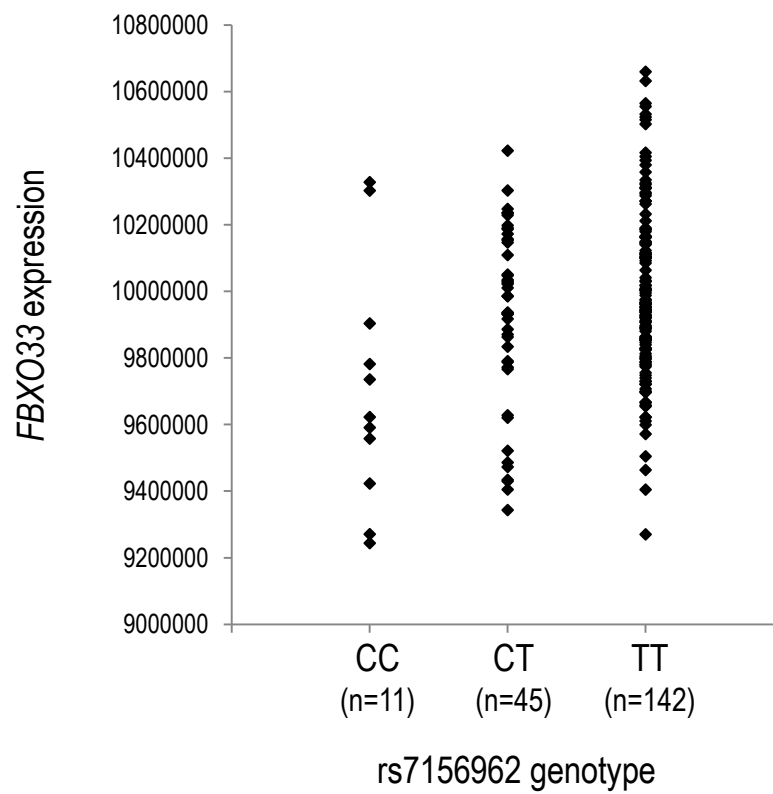
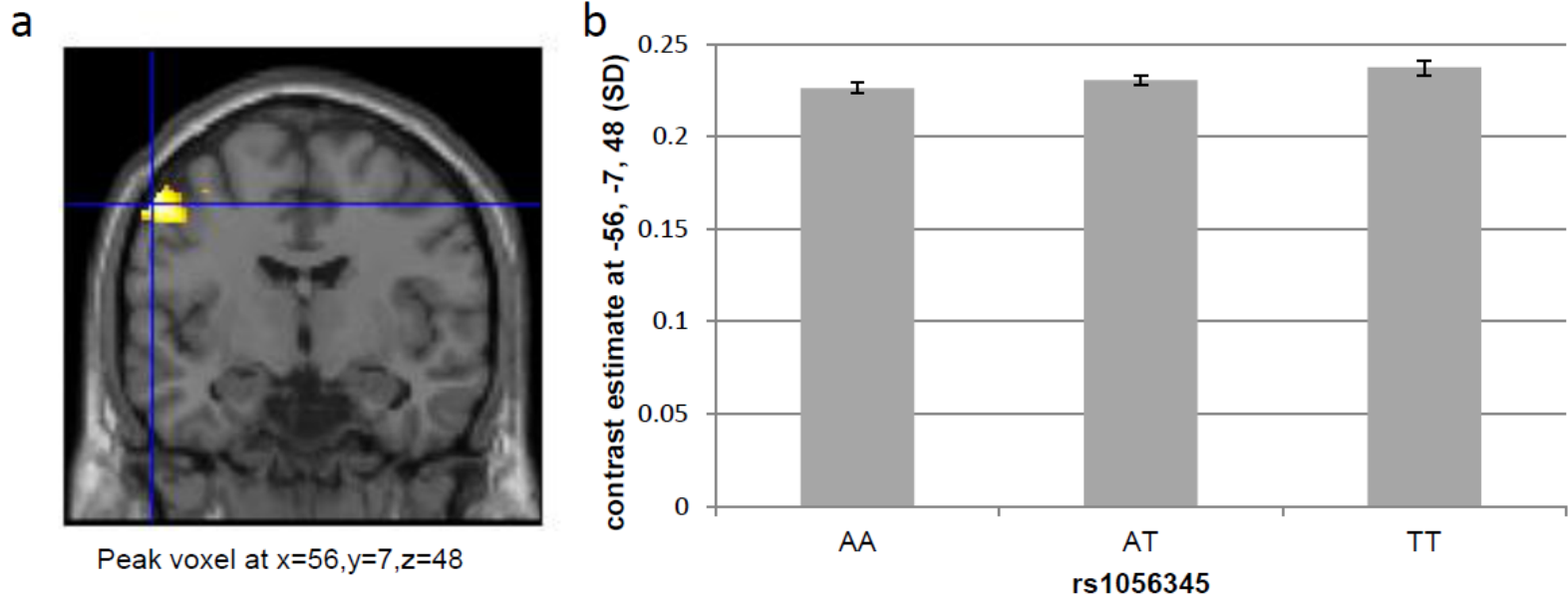


Figure S4.



Clinical assessment

Discovery Cohort

The discovery cohort consisted of 607 adulthood ADHD cases (61% combined, 35% inattentive, 3.5% hyperactive-impulsive and 0.5% with undefined subtype) and 584 healthy controls from Spain. All patients were adults of Caucasian origin, recruited and evaluated at the Hospital Universitari Vall d'Hebron located in Barcelona (Spain), and met Diagnostic and Statistical Manual for Mental Disorders-IV (DSM-IV) criteria for ADHD. The diagnosis of ADHD was evaluated with the Structured Clinical Interview for DSM-IV Axis I and II Disorders (SCID-I and SCID-II) and the Conner's Adult ADHD Diagnostic Interview for DSM-IV (CAADID Parts I and II). Severity of ADHD symptoms was evaluated with the long version of the Conners' ADHD Rating Scale (self-report form CAARS-S:L and observer form CAARS-O:L), the ADHD Rating Scale (ADHD-RS), the ADHD Screening Checklist and the Wender Utah Rating Scale (WURS) for retrospective symptomatology. The level of impairment was measured with the Clinical Global Impression (CGI), included in the CAADID Part II, and the Sheehan Disability Inventory (SDI). For the evaluation of psychiatric symptoms, patients were filled in the Beck Depression Inventory (BDI), the State Trait Anxiety Inventory (STAI) and the Millon Clinical Multiaxial Inventory (MCMI-II). Full-Scale IQ was estimated with the Vocabulary and Block Design subtests of the WAIS-III. Patients also completed the digit span, arithmetic, Letter-Number Sequencing and Symbol Search subtests of the WAISIII, the Conners' Continuous Performance Test (CPT), the California Verbal Learning Test (CVLT), the Logical Memory I-II and Visual Memory I-II of the WMS-R and the trail-making test (Parts A and B). The control sample consisted of two subsets: (i) 584 unrelated blood donors frequency-matched for gender with the ADHD group in which DSM-IV life-time ADHD symptoms were excluded under the following criteria: (1) Not having previously been diagnosed with ADHD and (2) answering negatively to the life-time presence of the following DSM-IV ADHD symptoms: (a) often has trouble keeping attention on tasks, (b) often loses things

needed for tasks, (c) often fidgets with hands or feet or squirms in seat and (d) often gets up from seat when remaining in seat is expected and (ii) 149 control subjects from the Infancia y Medio Ambiente (INMA; (<http://www.proyectoima.org>)) (Guxens et al. 2012). All of them were assessed for ADHD symptoms using the DSM-IV test at the age of 4 years and controls were defined as fulfilling less or equal to four DSM-IV symptoms. All of them were born from white European parents and did not show any population substructure in the principal components analysis (PCA) using genome-wide genotypic data. The average age at assessment was 31.0 years (SD=11.7) for patients and 33.6 (SD=21.3) for control subjects.

Replication Cohorts

In total, 2,104 adult ADHD patients and 1,901 controls of Caucasian origin from three European countries (Germany, The Netherlands and Norway) were recruited at three sites of The International Multicentre Persistent ADHD CollaboraTion (IMpACT; Table S1). Consensus eligibility criteria for the current study across all sites were a diagnosis of ADHD according to the diagnostic criteria of DSM-IV, onset before the age of 7 years via retrospective diagnosis (which was confirmed by a family member, wherever possible), lifelong persistence and current diagnosis. Patients were extensively examined by psychiatrists experienced in adult ADHD using open and semi-structured interviews. Other psychiatric disorders were evaluated with the Structured Clinical Interview of DSM-IV for axis-I and axis-II disorders (SCID-I, SCID-II) or semi-structured interviews. Most controls (except for the Norwegian samples and part of the German samples) were screened for the presence of ADHD and those scoring high on symptoms of the disorder were excluded. Each of these datasets has been described elsewhere (Franke et al. 2010 ; Landaas et al. 2010) For a more detailed description of the different diagnostic instruments, see Sanchez-Mora et al. et al.et al.(Sánchez-Mora et al. 2010).

The study was approved by the ethics committee of each institution and informed consent was obtained from all participants in accordance with the Helsinki Declaration.

Brain imaging studies

Structural brain changes were tested by Voxel Based Morphometry (VBM) using structural T1 brain scans acquired at 1.5 Tesla and 3 Tesla scanners (Siemens, Erlangen, Germany). The scanning protocols included small variations to a standard T1-weighted 3D MPRAGE sequence (TR 2300 ms, TI 1100 ms, TE 3.03 ms, 192 sagittal slices, field of view 256 mm); however, these variations have been shown to not affect the reliability of the imaging results (Jovicich et al. 2010). Raw DICOM images were converted to NIFTI format using the conversion tool implemented in SPM5 (www.fil.ion.ucl.ac.uk/spm/software/spm5/). As a next step, the VBM 5.1 toolbox version 1.19 in SPM using priors (default settings) was used to normalize, perform a bias-correction, and segment the images into grey and white matter. This method includes an optimized VBM protocol as well as a model to increase the signal to noise ratio (Hidden Markov Random Fields) (Cuadra et al. 2005). Total Brain Volume (TBV) was defined as the sum of resulting tissue probabilities of grey and white matter volumes. The VBM analysis was performed in SPM5 and included the Diffeomorphic Anatomical registration using Exponentiated Lie Algebra (DARTEL) toolbox. Subsequently, Jacobian-scaled images were calculated and an affine transformation was used to transform to Montreal Neurological Institute (MNI) space, after which all data were smoothed with an 8 mm FWHM Gaussian smoothing kernel. Images with poor quality, artifacts or more than 1.5 times the interquartile range from the median were excluded.

References

- Cuadra MB, Cammoun L, Butz T, Cuisenaire O, Thiran JP (2005): Comparison and validation of tissue modelization and statistical classification methods in T1-weighted MR brain images. *IEEE Trans Med Imaging* 24: 1548-1565.
- Guxens M, Ballester F, Espada M, Fernandez MF, Grimalt JO, Ibarluzea J, et al (2012). Cohort Profile: the INMA-INfancia y Medio Ambiente-(Environment and Childhood) Project. *Int J Epidemiol* 41: 930-940.
- Franke B, Vasquez AA, Johansson S, Hoogman M, Romanos J, Boreatti-Hümmer A, et al (2010). Multicenter analysis of the SLC6A3/DAT1 VNTR haplotype in persistent ADHD suggests differential involvement of the gene in childhood and persistent ADHD. *Neuropsychopharmacology*. Feb;35(3):656-64
- Jovicich J, Czanner S, Han X, Salat D, van der Kouwe A, Quinn B, et al (2009). MRI-derived measurements of human subcortical, ventricular and intracranial brain volumes: Reliability effects of scan sessions, acquisition sequences, data analyses, scanner upgrade, scanner vendors and field strengths. *Neuroimage* 46: 177-192.
- Landaas ET, Johansson S, Jacobsen KK, Ribasés M, Bosch R, Sánchez-Mora C et al (2010). An international multicenter association study of the serotonin transporter gene in persistent ADHD. *Genes Brain Behav*. Jul;9(5):449-58.
- Sánchez-Mora C, Ribasés M, Ramos-Quiroga JA, Casas M, Bosch R, Boreatti-Hümmer A et al (2010). Meta-analysis of brain-derived neurotrophic factor p.Val66Met in adult ADHD in four European populations. *Am J Med Genet B Neuropsychiatr Genet*. Mar 5;153B(2):512-23.

German ADHD GWAS GROUP:

Anke Hinney, Özgür Albayrak, Anna-Lena Volckmar, Johannes Hebebrand; Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Universitätsklinikum Essen, University of Duisburg-Essen, Essen, Germany

André Scherag; Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University of Duisburg-Essen, Essen, Germany and Clinical Epidemiology, Integrated Research and Treatment Center, Center for Sepsis Control and Care (CSCC), Jena University Hospital, Jena, Germany

Ivonne Jarick, Astrid Dempfle; Institute for Medical Biometry and Epidemiology, Philipps-University Marburg, Marburg, Germany

Sven Cichon, Per Hoffmann; Institute of Neuroscience and Medicine (INM-1), Structural and Functional Organization of the Brain, Genomic Imaging, Research Center Juelich, Juelich, Germany and Institute of Human Genetics, University of Bonn, Bonn, Germany and Human Genomics Research Group, Division of Medical Genetics, Universityhospital Basel, Department of Biomedicine

Markus M. Nöthen; Institute of Human Genetics, University of Bonn, Bonn, Germany and Department of Genomics, Life & Brain Center, University of Bonn, Bonn, Germany

Stefan Schreiber; Institute of Clinical Molecular Biology, University Hospital Schleswig-Holstein, Kiel, Germany

Karl-Heinz Jöckel; Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University of Duisburg-Essen, Essen, Germany

H.-Erich Wichmann; Institute of Epidemiology, Helmholtz Center Munich, German Research Center for Environmental Health, Munich, Germany

Beate Herpertz-Dahlmann; Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, RWTH Aachen, University Clinics, Aachen, Germany

Judith Sinzig; Department of Child and Adolescent Psychiatry, University of Cologne, Cologne, Germany and Department of Child and Adolescent Psychiatry and Psychotherapy, LVR – Clinic Bonn, Bonn, Germany

Gerd Lehmkuhl; Department of Child and Adolescent Psychiatry, University of Cologne, Cologne, Germany

Tobias J. Renner; Department of Child and Adolescent Psychiatry, Universitätsklinikum Tübingen, Tübingen, Germany

Marcel Romanos; Department of Child and Adolescent Psychiatry, University of Würzburg, Würzburg, Germany

Benno G. Schimmelmann; University Hospital of Child- and Adolescent Psychiatry, University of Bern, Bern, Switzerland