Cross-disorder genetic analyses implicate dopaminergic signaling as a biological link between Attention-Deficit/Hyperactivity Disorder and obesity measures

SUPPLEMENTARY MATERIAL

<u>Supportive information – Methods</u>

Candidate gene-set association analyses

Gene-set assembly

For our candidate gene-set analyses, we assembled dopaminergic neurotransmission (DOPA) and circadian rhythm (CIRCA) gene-sets based on the *Kyoto Encyclopedia of Genes and Genomes (KEGG)* and the *Gene Ontology (GO)* databases, queried in September 2016.

<u>DOPA gene set:</u> From the KEGG database, we included genes covered by the Dopaminergic synapse (hsa04728) and/or Tyrosine metabolism (hsa00350) pathways and from the GO database we included genes present in (at least) one of the following terms (GO: accession number): dopamine transport (GO:0015872), dopamine receptor signaling pathway (GO:0007212), dopamine receptor binding (GO:0050780), synaptic transmission, dopaminergic (GO:0001963), dopaminergic neuron axon guidance (GO:0036514), dopaminergic neuron differentiation (GO:0071542), response to dopamine (GO:1903350), and dopamine metabolic process (GO:0042417).

This resulted in 155 genes from KEGG database and 144 genes from GO, of which 24 were in common, totalizing 275 genes. From these, we found 273 genes in the MAGMA gene template ("*KIF5C*" and "*PPP2R3B*" were not present), including 9 genes located on chromosome X, which was not covered by our analyses.

CIRCA gene set: From the KEGG database, we included genes comprised by the Circadian rhythm (hsa04710) and/or Circadian entrainment (hsa04713) pathways and, from the GO database we included genes present in the circadian rhythm (GO:0007623) GO term.

This resulted in 123 genes from the KEGG database and 197 genes from GO, of which 27 were in common, totalizing 293 genes. From these, we found 290 genes in the MAGMA software gene reference template ("*H0Y8X5*", "*LOC400927-CSNK1E*", and "*Q59FM5*" were not present), including 6 genes located on chromosome X, which was not covered by our analyses.

Gene-set association analyses

The gene-set association analyses were performed using MAGMA software (version 1.05b; (1)). For such, SNPs were annotated to protein-coding genes, according to the location of their transcribed regions in the Human Genome Build 37, using the NCBI 37.3 gene reference template definitions provided by MAGMA (https://ctg.cncr.nl/software/magma). Genes were considered as present in the GWAS summary statistics being analyzed if they contained at least one SNP located within their transcribed region. Gene-based P-values were then calculated using the SNP-wise mean model (default for summary statistics analysis), which combines the effects of SNPs within a gene and uses the sum of –log(SNP P-value) as test statistic. In order to account for linkage disequilibrium (LD) between the SNPs, we used the European dataset of the 1000 Genomes Phase 3 as reference, provided at MAGMA's website (https://ctg.cncr.nl/software/MAGMA/ref_data/g1000_eur.zip).

We then performed competitive gene-set analyses, which tests whether each gene-set is differently associated with the phenotype compared to the remaining genes on the genome, while taking into account gene size, gene density and LD between genes.

Canonical pathway enrichment analysis

For the pathway enrichment analyses, canonical pathways were defined based on the Ingenuity Knowledge Base, which incorporates experimental data from published literature as well as data from many other sources, including gene expression and gene annotation databases. For each pathway, Ingenuity calculates enrichment P-values using the right-tailed Fisher's exact test and taking into consideration both the total number of molecules from the analyzed data set and the total number of molecules that is in the pathway in question according to the Ingenuity Knowledge Base. To account for multiple testing, the enrichment P-value of each pathway is adjusted using Benjamini-Hochberg correction, and only significantly enriched canonical pathways were reported.

Supportive information – Results

Secondary ADHD-BMI gene-based meta-analysis: no sample overlap

Since Welcome Trust participants had been included both in the iPSYCH-PGC (2) and GIANT (3, 4) studies, we performed a secondary analysis to make sure that our results were not driven by this overlap. As described by Demontis *et al.* (2), the ADHD PGC sample from Cardiff is composed of 721 ADHD cases and 5081 Welcome Trust controls. Therefore, we performed a secondary ADHD-BMI gene-based meta-analysis using the leave-one-out summary statistics from the European ancestry iPSYCH-PGC ADHD GWAS without the Cardiff sample (~11% reduction in sample size). Unfortunately, it was not feasible to remove these overlapping samples from the GIANT-UK Biobank BMI GWAS. The canonical pathway enrichment findings from this secondary meta-analysis were reassuring since the *Dopamine-DARPP32 Feedback in cAMP Signaling* pathway remained significantly associated, with seven genes in the pathway and surviving B-H correction ($P = 8.90 \times 10^{-4}$, $P_{B-H} = 4.57 \times 10^{-2}$). Since our secondary results do not show a substantial bias due to sample overlap, we opted for presenting the analysis with the largest sample size as the main analysis.

Detailed description of Figure 1

In **Figure 1,** we show a schematic representation of the *Dopamine-DARPP32 Feedback in cAMP Signaling* pathway. In the description below, we contextualize and highlight in bold the proteins encoded by the eight genes derived from our ADHD-BMI gene-based meta-analysis results that are present in this pathway (highlighted in red in **Figure 1**).

Signaling in the *Dopamine-DARPP32 Feedback in cAMP Signaling* pathway starts at the postsynaptic membrane where dopamine released by midbrain neurons binds and activates two types of dopamine receptors, i.e. the D1 class (DRD1 and DRD5) and D2 class (DRD2, DRD3, and DRD4) of receptors (D1 class and D2 class in **Figure 1**) (5). Subsequently, the D1 and D2 receptors work through different G protein alpha subunits to activate and inhibit the enzyme adenylate cyclase, which results in more and less cyclic AMP (cAMP) being synthesized, respectively (5). cAMP in turn activates protein kinase A (PKA), which is inhibited by the kinase AMPK (6, 7) of which the **AMPKg** subunit is encoded by the *PRKAG1* gene (8). Activated PKA has a large number of downstream effects, including regulating the activity of L-type calcium channels (9) – of which **CACNA1D** is a subunit (8) – that are voltage-sensitive and stimulate the entry of calcium ions into neurons (10). Dopamine binding to D2 receptors also leads to a signaling cascade that results in an increased intraneuronal concentration of calcium (11). In addition, activated PKA is involved in activating transcription factors of the cAMP-dependent CREB complex (12, 13) such as **CREB3L3** (8). The CREB complex transcription factors are inhibited by the phosphatase PP1 (14) – which contains the regulatory subunit **PPP1R3A** - leading to a disruption of dopamine-induced and cAMP/PKA-dependent gene transcription, which may ultimately result in various neuropsychiatric disorders - including ADHD (15) - and somatic disorders such as obesity (16, 17). Dopamine binding and activating D1 receptors also leads to the activation of phospholipase C (PLC) enzymes (9, 18) such as **PLCL1** that binds and functionally interacts with PP1 (interaction not shown in Figure 1) (19). The above described dopamine-induced gene transcription is partially controlled by the protein 'Dopamine and cAMP Regulated Phosphoprotein-32' or DARPP-32, through a feedback loop on the cAMP/PKA cascade. Activated PKA stimulates the phosphatase PP2A - of

which **PPP2R3A** is a regulatory subunit (8) - that phosphorylates DARPP-32 at Threonine(Thr)34, which makes DARPP-32 a potent inhibitor of PP1 (14). Conversely, an increase of intracellular calcium - through being pumped into the neuron by L-type calcium channels such as **CACNA1D**, downstream of dopamine binding to D2 receptors (see above) and/or trough being released from the endoplasmic reticulum (ER), a process that is mediated by the ER membrane-receptor **ITPR3 (20)** - leads to a dephosphorylation of DARPP-32 at Thr34 (21), rendering the protein inactive again. Interestingly, DARPP-32 can also be phosphorylated at Thr75 by CDK5 (14)- a kinase that itself is activated by CK1 (22), of which **CSNK1G2** is an isoform (8) - which converts DARPP-32 into an inhibitor of PKA (14). In this way, DARPP-32 is a dual-function protein that, depending on where it is phosphorylated, can act either as an inhibitor of PP1 or of PKA, which makes DARPP-32 a critical regulator of dopamine/cAMP/PKA signaling.

Supplementary Table S1. Summary of gene-based association results of the ADHD, BMI, and obesity individual GWASs, as well as of the ADHD-BMI and ADHD-obesity gene-based meta-analyses, displaying the number of genome-wide significant (GWsig) genes and if they are included in the candidate DOPA and/or CIRCA gene sets:

	GWsig genes	Presence of GWsig genes in gene sets:		
		DOPA	CIRCA	DOPA and CIRCA
ADHD[a]	20	.	.	.
BMI[b]	1747	41	49	22
		(*ADCY5, ADCY6, AKT3, ARNTL, CACNA1C, CACNA1D, CALML6, COMT, CREB1, CREB3L1, CREB3L3, CTNNB1, DDC, DNM1, DNM2, DRD2, GNAI3, GNAQ, GNAS, GNB1, GNG7, GRIA1, GRIN2A, GSK3B, ITPR3, KLF16, LMX1B, OPRK1, OPRM1, PARK2, PLCB1, PLCB4, PPP1CB, PPP2R3A, PPP2R5C, PPP3CA, PTGS2, RAC1, SCN1A, SLC22A3, SLC6A4*)	(*ADCY3, ADCY5, ADCY6, ADCY9, ADK, AHR, ARNTL, BTBD9, BTRC, CACNA1C, CACNA1D, CALML6, CREB1, CRTC1, DDC, DRD2, EP300, GNAI3, GNAQ, GNAS, GNB1, GNG7, GRIA1, GRIN2A, GSK3B, GUCY1A2, HCRTR1, HCRTR2, ITPR3, LGR4, NCOR1, NFIL3, NLGN1, NOS1AP, NR1H3, NTRK2, OPRL1, PLCB1, PLCB4, PPARG, PPARGC1A, PPP1CB, PRKG1, RORA, RPS6KA5, SLC6A4, SYNCRIP, TP53, ZFHX3*)	(*ADCY5, ADCY6, ARNTL, CACNA1C, CACNA1D, CALML6, CREB1, DDC, DRD2, GNAI3, GNAQ, GNAS, GNB1, GNG7, GRIA1, GRIN2A, GSK3B, ITPR3, PLCB1, PLCB4, PPP1CB, SLC6A4*)
Obesity[c]	26	.	1 (*ADCY3*)	.
ADHD-BMI[d] meta-analysis	211	8 (*CACNA1D, CREB3L1, CREB3L3, CTNNB1, DNM1, GRIA1, ITPR3, PPP2R3A*)	7 (*CACNA1D, GRIA1, ITPR3, PRKAG1, RPS6KA5, SYNCRIP, ZFHX3*)	3 (*CACNA1D, GRIA1, ITPR3*)
ADHD-Obesity[e] meta-analysis	9	2 (*CACNA1D, DNM1*)	1 (*CACNA1D*)	1 (*CACNA1D*)

[a.] European ancestry iPSYCH-PGC ADHD GWAS (2).
[b.] GIANT-UK Biobank BMI GWAS (4).
[c] GIANT Obesity (class I) GWAS (3).
[d,e] Meta-analysis of [d.]ADHD-BMI and [e.]ADHD-obesity gene-based results. Only genome-wide significant genes are shown with association P-values lower by at least one order of magnitude in the meta-analysis compared to both the ADHD and the [d.]BMI or [e.]obesity results individually.

Supplementary Table S2. Results of the ADHD-BMI gene-based meta-analysis showing the 211 genome-wide significant genes that increased significance in the meta-analysis by at least one order of magnitude compared to both individual GWASs.

GENE	CHR	START	STOP	ADHD-BMI gene-based meta-analysis
SEMA3F	3	50192562	50226508	**1.70X10-26**
FBXL17	5	107194734	107718080	**2.52X10-26**
XKR6	8	10753654	11058875	**1.84X10-22**
GNAT1	3	50229043	50235129	**2.14X10-22**
MAML3	4	140637545	141075233	**4.04X10-22**
CCDC171	9	15552872	15971897	**1.16X10-21**
SOX5	12	23682438	24715383	**9.86X10-21**
PCDH7	4	30721951	31148423	**8.31X10-20**
GATA4	8	11534433	11617510	**2.34X10-19**
SEMA6D	15	47476403	48066420	**2.42X10-19**
TENM2	5	166406083	167691162	**9.78X10-19**
CALN1	7	71244476	71912136	**6.42X10-18**
CACNA1D	3	53529076	53847179	**3.96X10-17**
TRAF3	14	103243816	103377837	**4.01X10-17**
NLRC3	16	3589033	3627392	**6.38X10-17**
STAG1	3	136055077	136471245	**8.34X10-17**
CSMD2	1	33979609	34631443	**2.04X10-16**
ADARB1	21	46494493	46646478	**3.67X10-16**
RSRC1	3	157823690	158262624	**3.94X10-16**
PCCB	3	135969167	136056737	**9.39X10-16**
MSL2	3	135867760	135915522	**9.87X10-16**
MSI2	17	55333931	55762050	**1.48X10-15**
TRAIP	3	49866028	49893992	**1.61X10-15**
IP6K1	3	49761728	49823973	**1.71X10-15**
CAMKMT	2	44589043	44999731	**1.86X10-15**
IGF1R	15	99192272	99507759	**1.94X10-15**
PPL	16	4932508	4987136	**2.00X10-15**
PDE1C	7	31791666	32339016	**2.44X10-15**
TEX29	13	111973015	111996594	**2.73X10-15**
DNASE1	16	3661772	3712689	**3.08X10-15**
ABHD17C	15	80987635	81047962	**3.14X10-15**
PTBP2	1	97187161	97280605	**3.62X10-15**
MST1	3	49721380	49726196	**5.45X10-15**
BSN	3	49591922	49708982	**5.61X10-15**
RNF123	3	49726950	49758962	**7.21X10-15**
ARHGEF7	13	111767624	111958081	**7.22X10-15**
PCDH9	13	66876966	67804468	**7.48X10-15**
MEF2C	5	88014058	88199922	**7.80X10-15**
TSHZ2	20	51588946	52111869	**1.37X10-14**

DNM1	9	130965634	131017528	**1.76X10-14**
TNKS	8	9412756	9639856	**1.91X10-14**
UBN1	16	4896666	4932363	**1.99X10-14**
CLUAP1	16	3550945	3589048	**2.10X10-14**
UBA7	3	49842638	49851391	**2.32X10-14**
PURG	8	30853320	30891231	**2.68X10-14**
RPS6KA5	14	91335086	91526993	**2.74X10-14**
MON1A	3	49946302	49967445	**2.92X10-14**
ZFPM2	8	106330917	106816767	**3.04X10-14**
HIVEP2	6	143072604	143267495	**4.49X10-14**
SLC38A3	3	50242692	50258406	**6.19X10-14**
TMEM161B	5	87485450	87564665	**6.86X10-14**
RPLP2	11	808841	827592	**7.01X10-14**
TCTA	3	49449639	49453909	**9.80X10-14**
NKAIN2	6	124124991	125146786	**1.03X10-13**
LONRF2	2	100889753	100939195	**1.56X10-13**
C14orf159	14	91526677	91691976	**1.66X10-13**
DUSP6	12	89741837	89746296	**2.46X10-13**
BACE2	21	42539728	42654461	**2.63X10-13**
PPP1R3A	7	113516882	113559082	**3.82X10-13**
APEH	3	49711427	49720936	**3.92X10-13**
C3orf38	3	88198875	88207115	**4.02X10-13**
MLIP	6	53883714	54131078	**5.42X10-13**
BTBD2	19	1985437	2015702	**7.05X10-13**
ZNF131	5	43120985	43176351	**7.18X10-13**
NIM1K	5	43192170	43280952	**7.31X10-13**
GRIA1	5	152870084	153193429	**8.11X10-13**
SWI5	9	131037663	131051268	**8.94X10-13**
DIABLO	12	122692209	122712081	**9.36X10-13**
PPP2R3A	3	135684515	135866752	**1.07X10-12**
CGGBP1	3	88101100	88199016	**1.40X10-12**
TEAD3	6	35441374	35464884	**1.46X10-12**
PPARD	6	35310335	35395968	**1.52X10-12**
ATP5G1	17	46970148	46973233	**1.58X10-12**
ARHGAP1	11	46698625	46722215	**1.71X10-12**
CADPS2	7	121958478	122526813	**1.81X10-12**
TRIM38	6	25962917	25987557	**1.87X10-12**
JADE2	5	133860003	133918918	**1.94X10-12**
LOC101929490	8	11537185	11555493	**2.26X10-12**
IQSEC1	3	12938542	13114652	**2.47X10-12**
HYAL1	3	50337320	50349812	**3.27X10-12**
ZNF654	3	88108394	88193814	**3.46X10-12**
GTF2I	7	74071991	74175022	**3.59X10-12**
PIDD1	11	799179	809872	**4.17X10-12**
ULK4	3	41288090	42056080	**4.88X10-12**
HIST1H2BD	6	26157419	26171577	**5.98X10-12**

MAP4	3	47892180	48130769	**6.04X10-12**
BBX	3	107241783	107530176	**7.34X10-12**
BAK1	6	33540323	33548072	**7.71X10-12**
PNPLA2	11	818901	825573	**9.37X10-12**
ZFHX3	16	72816784	73092534	**1.16X10-11**
SLX4	16	3631182	3661585	**1.22X10-11**
DAG1	3	49506136	49573051	**2.09X10-11**
RHOA	3	49396569	49449526	**2.87X10-11**
PLCL1	2	198669426	199014608	**2.99X10-11**
TM6SF2	19	19374841	19384074	**3.26X10-11**
DHX30	3	47844399	47891686	**3.35X10-11**
SUGP1	19	19387320	19431321	**3.54X10-11**
ANTXR2	4	80822771	80994626	**3.82X10-11**
SMARCC1	3	47627378	47823405	**4.11X10-11**
KMT2D	12	49412758	49453935	**4.33X10-11**
CTNNB1	3	41236401	41281939	**5.75X10-11**
ICA1L	2	203637873	203736708	**6.40X10-11**
SCN2A	2	165986659	166248820	**7.44X10-11**
CSNK1G2	19	1941148	1981337	**8.74X10-11**
CSE1L	20	47662783	47713497	**8.92X10-11**
CSRNP3	2	166326157	166545917	**9.06X10-11**
WDPCP	2	63348518	63815867	**1.21X10-10**
ANKRD28	3	15708743	15901053	**1.29X10-10**
SLC9B2	4	103946647	103998480	**1.37X10-10**
SLC25A22	11	790475	798269	**1.39X10-10**
STK32C	10	133996038	134145377	**1.42X10-10**
ITPR3	6	33587951	33664351	**1.45X10-10**
CSPG5	3	47603728	47621730	**1.68X10-10**
IP6K3	6	33689415	33714762	**2.05X10-10**
ATP13A2	1	17312453	17338467	**2.12X10-10**
CDHR4	3	49828165	49837254	**2.52X10-10**
UQCC2	6	33664538	33679528	**2.67X10-10**
TOX3	16	52471682	52581714	**2.73X10-10**
AMBRA1	11	46417962	46615619	**2.80X10-10**
MANBA	4	103552643	103682151	**3.70X10-10**
RASGRF1	15	79252289	79383215	**3.79X10-10**
MFAP2	1	17300997	17308081	**3.87X10-10**
FOXP2	7	113726365	114333827	**4.03X10-10**
GLYR1	16	4853204	4897383	**4.15X10-10**
HIST1H4A	6	26021907	26022278	**5.22X10-10**
WDR12	2	203745323	203776949	**5.73X10-10**
BTD	3	15642864	15689147	**6.11X10-10**
GRIK5	19	42502468	42574278	**6.48X10-10**
DAGLA	11	61447905	61514474	**7.09X10-10**
LEMD2	6	33738990	33756906	**7.21X10-10**
NBEAL1	2	203879597	204091101	**7.56X10-10**

CHST10	2	101008322	101034130	**8.25X10-10**
RMDN1	8	87479627	87526567	**8.43X10-10**
CALB2	16	71392616	71424341	**9.69X10-10**
CRIM1	2	36583370	36778278	**1.01X10-9**
SLC3A1	2	44502597	44547963	**1.07X10-9**
FOXP1	3	71003865	71633140	**1.19X10-9**
HMGB4	1	34326076	34330392	**1.33X10-9**
DGKZ	11	46354455	46402104	**1.37X10-9**
ATG13	11	46638826	46697569	**1.39X10-9**
ZKSCAN4	6	28212404	28227030	**1.66X10-9**
MAD1L1	7	1855428	2272583	**1.93X10-9**
MAU2	19	19431496	19469563	**2.09X10-9**
MMP24	20	33814539	33864804	**2.38X10-9**
PREPL	2	44544746	44589001	**2.59X10-9**
DDN	12	49388933	49393088	**3.47X10-9**
UBE2D3	4	103715540	103790050	**3.52X10-9**
SLC9B1	4	103806205	103947552	**3.70X10-9**
PDDC1	11	767222	777501	**3.80X10-9**
OR4C13	11	49973943	49974971	**3.98X10-9**
BCL2L13	22	18111621	18213621	**4.14X10-9**
LOC101927844	1	87678352	87717014	**4.94X10-9**
SIDT2	11	117049626	117068161	**6.49X10-9**
GATAD2A	19	19496642	19619741	**6.56X10-9**
RPS10	6	34385231	34393902	**7.21X10-9**
NICN1	3	49459766	49466777	**7.21X10-9**
CISD2	4	103749224	103813964	**9.11X10-9**
SNX14	6	86215214	86303850	**9.14X10-9**
PHF2	9	96338909	96441869	**9.72X10-9**
GRK4	4	2965232	3042474	**1.19X10-8**
STYX	14	53196883	53241707	**1.23X10-8**
RASSF1	3	50367217	50378367	**1.40X10-8**
GRM4	6	33989623	34123399	**1.44X10-8**
HYAL3	3	50330259	50336899	**1.69X10-8**
HPS5	11	18300217	18343751	**1.74X10-8**
PMFBP1	16	72152996	72206349	**1.86X10-8**
PKP4	2	159313476	159537941	**1.95X10-8**
TMEM184B	22	38612415	38669040	**1.96X10-8**
DIS3L	15	66585633	66626236	**2.12X10-8**
FAM13A	4	89647105	90032549	**2.25X10-8**
SYNCRIP	6	86317502	86353568	**2.62X10-8**
MDH1	2	63815743	63834331	**2.93X10-8**
BANK1	4	102711764	102995969	**2.99X10-8**
SDK1	7	3341080	4308632	**3.60X10-8**
NOP14	4	2939663	2965233	**3.74X10-8**
OLFM4	13	53602876	53626196	**4.30X10-8**
KAT2B	3	20081524	20195896	**4.75X10-8**

Gene	CHR	START	STOP	p-value
GRID2	4	93225453	94695707	**5.31X10-8**
PEAK1	15	77400498	77712446	**8.30X10-8**
PKD1L3	16	71963441	72033877	**8.97X10-8**
CREB3L1	11	46299189	46342972	**1.09X10-7**
CREB3L3	19	4153598	4173051	**1.12X10-7**
MALRD1	10	19337700	20023407	**1.23X10-7**
THUMPD3	3	9404660	9428475	**1.26X10-7**
ADGRB2	1	32192718	32230494	**1.27X10-7**
PBXIP1	1	154916553	154928624	**1.40X10-7**
CD247	1	167399877	167487847	**1.43X10-7**
OR4C12	11	50003009	50004071	**1.44X10-7**
ZAK	2	173940440	174132737	**1.51X10-7**
PRKAG1	12	49396055	49413012	**1.56X10-7**
CELF4	18	34823003	35146000	**1.97X10-7**
TALDO1	11	747417	765024	**2.07X10-7**
MRPL21	11	68658744	68671303	**2.73X10-7**
DCC	18	49866542	51062273	**3.02X10-7**
ZNF521	18	22641888	22932214	**3.88X10-7**
CEND1	11	787110	790126	**3.92X10-7**
MARCH5	10	94050920	94113721	**3.93X10-7**
FOXO1	13	41129801	41240734	**4.38X10-7**
GALNT13	2	154728426	155310489	**4.50X10-7**
CARF	2	203776978	203851060	**5.51X10-7**
RNF115	1	145610990	145689005	**7.08X10-7**
PCSK7	11	117075788	117102811	**8.45X10-7**
ZNF564	19	12636184	12691789	**9.83X10-7**
ANO10	3	43407818	43663560	**1.42X10-6**
LIN28B	6	105384874	105531207	**1.50X10-6**
CYP20A1	2	204103164	204170563	**1.72X10-6**
ETF1	5	137841782	137878989	**2.01X10-6**
CPEB3	10	93806452	94050875	**2.09X10-6**
DPYSL5	2	27070969	27173219	**2.16X10-6**
KLHDC8B	3	49208987	49213919	**2.87X10-6**
UBE2J1	6	90036344	90062619	**2.94X10-6**

Gene locations are given as chromosome (CHR) and transcribed region (START and STOP sites) in the Human Genome Build 37, according to the NCBI 37.3 gene definitions.

Supplementary Table S3. Results of the ADHD-obesity gene-based cross-disorder meta-analysis showing the 9 genome-wide significant genes that increased significance in the meta-analysis by at least one order of magnitude compared to both individual GWASs.

GENE	CHR	START	STOP	ADHD-obesity gene-based meta-analysis
BDNF	11	27676440	27743605	**1.23x10-12**
TFAP2B	6	50786439	50815326	**1.48x10-11**
DNM1	9	130965634	131017528	**4.60x10-8**
CACNA1D	3	53529076	53847179	**9.89x10-8**
BTBD2	19	1985437	2015702	**1.22x10-7**
FBXL17	5	107194734	107718080	**1.43x10-7**
SWI5	9	131037663	131051268	**2.18x10-7**
CSNK1G2	19	1941148	1981337	**8.60x10-7**
CAMKMT	2	44589043	44999731	**1.17x10-6**

Gene locations are given as chromosome (CHR) and transcribed region (START and STOP sites) in the Human Genome Build 37, according to the NCBI 37.3 gene definitions.

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