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Method:**Main study sample:**

Body weight was measured in kilograms to the nearest kg. Height was measured to the nearest cm using a height gauge. Body mass index (BMI) was defined as weight/height² (kg/m²). Waist circumference (WC) was measured to the nearest cm. Blood pressure was measured once after 5 minutes of rest in a sitting position. Fasting glucose, triglycerides and HDL-C were analyzed on a routine basis by CHUV's laboratory of clinical chemistry on fresh blood samples using a Modular P apparatus (Roche Diagnostics, Switzerland).

Gene expression analysis

The functional effect of *HSD11B1* rs846910G>A and rs3753519G>A single nucleotide polymorphisms (SNP) on gene expression was investigated in a peripheral model using Peripheral Blood Mononuclear Cells (PBMC). Both SNPs were significantly associated with BMI and the components of the MetS in our sample and they are located in the promoter region, which could influence gene expression. Subjects were selected from a sample of healthy volunteers previously investigated by our group[1]. In a first step, 200 healthy volunteers were genotyped for *HSD11B1* rs846910G>A, while rs3753519G>A genotypes were obtained from the cardiometabochip. None of the subjects were homozygous for the variant allele of rs846910G>A, whereas only 2 subjects were homozygous for the A-allele of rs3753519G>A, thus gene expression was tested in a dominant model for this SNP (GG versus A-allele carriers). For each SNP, the variant A-allele carriers were matched, with 2 controls with the GG genotype. The genotype groups were matched regarding age, sex, BMI, smoking status and oral

contraceptive intake in females. The study was approved by the Ethics Committee of Lausanne University hospital and written informed consents were obtained from the participants. For each subject, two venous blood samples were collected, one into EDTA blood tubes for DNA extraction and *HSD11B1* SNPs genotyping (as described above) and the other into PAXgene Blood RNA tubes (PreAnalytix, Qiagen, Hombrechtikon, Switzerland) for total mRNA extraction. PAXgene tubes were kept at -80°C until RNA isolation. Automated total mRNA isolation was carried out using the PAXgene Blood miRNA kit (PreAnalytix, Qiagen, Hombrechtikon, Switzerland) according to the manufacturer's instructions. Total RNA integrity was assessed using the Agilent BioAnalyser 2100 system (Agilent Technologies, Basel, Switzerland) and RNA concentrations were measured using NanoDrop™ Lite (Thermo Scientific, Wohlen, Switzerland). Three hundred nanograms of RNA was reverse-transcribed to yield complementary DNA with the use of Promega Reverse Transcription System Kit (Promega, Dübendorf, Switzerland) and was used for gene expression analysis. Gene expression assays were performed using the relative quantitative RT-PCR method (ABI PRISM 7000 Sequence Detection System; Applied Biosystems, Rotkreuz, Switzerland). Taqman Gene Expression Assays ID: Hs01547870_m1 was used for *HSD11B1*. In order to correct for differences in RNA sampling and sample variation, two housekeeping genes (GAPDH; ID: Hs00266705_g1 and GUSB; ID: Hs99999908_m1) were used. All gene expression assays were obtained from Applied Biosystems (Rotkreuz, Switzerland).

For Relative Quantitative PCR analyses, data were analyzed using Excel (Microsoft Office Excel 2007) and GraphPad Prism v6. The difference between the threshold cycle (ΔCT) for *HSD11B1* and the mean of the 2 housekeeping genes was calculated ($\Delta CT = CT_{HSD11B1} - \text{mean } CT \text{ of the}$

2 housekeeping genes), which represents the normalization of the relative concentration of target genes in the PCR reaction. Fold change in gene expression for *HSD11B1* gene was calculated using the formula $2^{-\Delta CT}$. Mann-Whitney and Kruskal-Wallis tests were used to compare the $2^{-\Delta CT}$ for the genotype groups of *HSD11B1* polymorphisms.

Results:

HSD11B1 polymorphisms in the psychiatric replication studies

In order to highlight the effect of *HSD11B1* SNPs on BMI in the subgroup of patients with psychotropic drugs that has potentially similar mechanisms and propensity to induce weight gain, additional subgroup analyses were performed in the combined psychiatric sample. Psychotropic drugs were classified as follow: patients treated with aripiprazole or amisulpride, olanzapine or clozapine, risperidone or quetiapine and with mood stabilizers MS (lithium or valproate). *HSD11B1* SNPs were mostly associated with BMI in the subgroup of patients treated with olanzapine/clozapine or with risperidone/quetiapine. No influence of *HSD11B1* SNPs in the subgroup of patients treated with MS (**Supplementary table ...**). In the subgroup of patients treated with aripiprazole or amisulpride, although the BMIs were different between genotype groups, the significance were not consistent between the three SNPs, which could be explained by the small sample size of this subgroup. Only small number of patients were treated with mirtazapine, and therefore, this subgroup could not be analyzed.

***HSD11B1* haplotype blocks and combinations:**

Two haplotype blocks were observed from the seven studied *HSD11B1* SNPs: *rs846910-rs3753519* and *rs12565406-rs10863782* (supplementary Figure 1). Regarding the former haplotype block, by combining the 2 SNPs *rs846910G>A* and *rs3753519G>A*: 3 groups were formed, patients with wild-type genotype for both SNPs (*rs846910GG/rs3753519GG*), wild-type for *rs846910* and carriers of the variant allele of *rs3753519* (*rs846910GG/rs3753519GA-AA*) and carriers of the variant allele of both SNPs (*rs846910GA-AA/rs3753519GA-AA*). None of the patients were carriers of the variant allele of *rs846910* and wild-type for *rs3753519* (*rs846910GA-AA /rs3753519GG*). A small increase of the effect was observed in patients carrying the variant alleles of the 2 SNPs compared to the other genotypes and also as compared to the carriers of the variant allele of each SNP separately (Supplementary Table 9). This effect was mainly observed in the female subgroup, in which carriers of the variant allele of both SNPs (*rs846910* and *rs3753519*) showing 4.2 kg/m², 9.0 cm and 5.1 mmHg lower BMI, WC and diastolic blood pressure (DBP), respectively, as compared to patients with wild-type genotype explaining 5.05, 5.09 and 2.02% of BMI, WC and DBP variance, respectively.

Haplotypes formed from the second block, *rs12565406-rs10863782*, did not show any significant association with the investigated components of the MetS and BMI (data not shown).

***HSD11B1* SNPs in newly diagnosed patients**

The effect of *HSD11B1* SNPs on BMI and the components of the MetS (mainly WC and DBP) was more pronounced in a subgroup of patients from the main psychiatric study sample that were

newly diagnosed with a psychiatric disorder (within the same year of study inclusion) and started psychotropic treatment within the 1st year following the first psychiatric diagnosis (n=178). For these patients, most *HSD11B1* SNPs (except for *rs12086634T>G*) were associated with BMI (supplementary Table 10). This association was mainly observed in the female subgroup (n=101) explaining, for example, up to 10%, 5% and 7% of BMI, WC and DBP variance for the *rs846910G>A* SNP (supplementary Table 10). Due to small sample number, we weren't able to apply the GAMM model for most of men' analyses.

No association between *HSD11B1* SNPs and systolic blood pressure (SBP), triglycerides and HDL-C was observed in this subgroup (supplementary Table 10). We were not able to analyze the impact of *HSD11B1* SNPs on fasting glucose due to the small sample size.

Additionally, by combining the 2 SNPs (*rs846910* and *rs3753519*), the effect of both SNPs on BMI and different components of the MetS was also pronounced specially in the female subgroup, in which women who carries the variant allele of both SNPs had 5.5 kg/m², 10.2 cm and 9.8 mmHg lower and WC and DBP, respectively, as compared to patients with the wild-type genotypes (p<0.01 for the three variables, explaining nearly 11%, 5% and 7% of BMI and WC and DBP variance, respectively)(supplementary Table 11).

Gene expression analyses and *HSD11B1* polymorphism

The functional consequence of *HSD11B1 rs846910G>A* and *rs3753519G>A polymorphisms* on gene expression was tested in a peripheral model using PBMC. The mean age of the subjects was 39.1 years (range 20-62) of which 53.7 % were women. Regarding *rs846910G>A*, no significant difference was observed on *HSD11B1* gene expression between GA group (n=14) and

their matched control GG group (n=28, p-value>0.05), neither in men nor in women (Supplementary Figure 2). Due to insufficient RNA quality control for some samples, two subjects with *rs3753519 G-Allele* carriers were only matched with one GG genotype, so 18 subjects with G-Allele carriers were matched with 34 subjects with the GG genotype. Non-significant association was observed when analyzing gene expression of this SNP and also when analyzing men and women separately (Supplementary Figure 3). Same non-significant results were obtained by combining the 2 SNPs and comparing subjects with the variant alleles of both SNPs (*rs846910GA-AA/rs3753519GA-AA*) (n=10) to subjects with the wild-type genotypes (*rs846910GG/rs3753519GG*) (n=20, p-value>0.05) as shown in Supplementary Figure 4.

HSD11B1 gene expression analysis in PBMC was not different between carriers of the variant alleles (*rs846910-A* and/or *rs3753519-A*) and patients with the GG genotype. These results were comparable with the published data regarding the functionality of *rs846910* polymorphism. In-vitro, lower 11 β -HSD1 transcriptional activity was associated with the variant G allele of the *rs12086634* polymorphism[2], whereas no difference of activity was observed between *rs846910* variants[3]. An in-vivo study showed that *rs846910* was not associated with differences of *HSD11B1* mRNA levels from human subcutaneous adipose tissue biopsies[4]. In a second in-vivo study, it was shown that carriers of both *rs846910GA* and *rs12086634TT* genotypes had higher *HSD11B1* mRNA levels in female adipose tissue samples, however, the association of each SNP separately with *HSD11B1* mRNA levels was not shown or discussed[5]. Altogether, these data suggest that the *rs846910* polymorphism has no direct influence on *HSD11B1* expression in humans. No previous studies investigated the functional activity of *rs3753519G>A* polymorphism. We also used the Genotype-Tissue Expression (GTEx) portal[6]

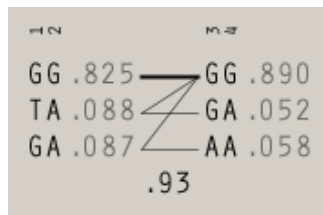
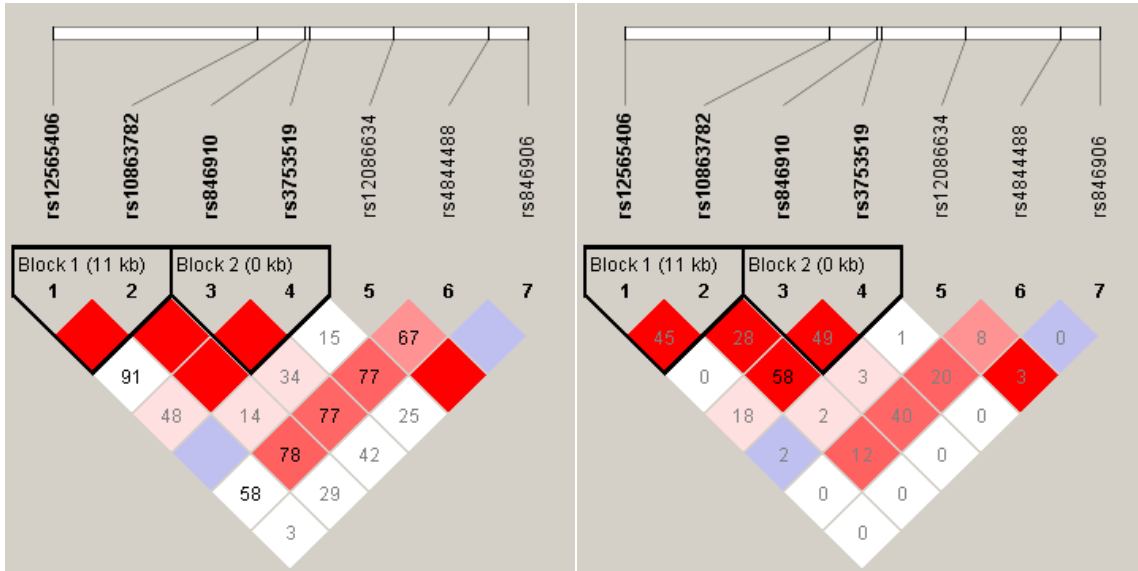
which analyzes global RNA expression within different tissues and helps in identifying expression quantitative trait loci, or eQTLs. Both SNPs were not identified as eQTLs and no other SNPs were identified as eQTLs for the *HSD11B1* gene in the tested tissues as well.

It should be noted that we performed gene expression analyses in a peripheral model using PBMC on healthy subjects, while using adipose tissue on a psychiatric sample treated with weight-gain inducing psychotropic drugs (especially in drug naïve patients) would be more appropriate as model.

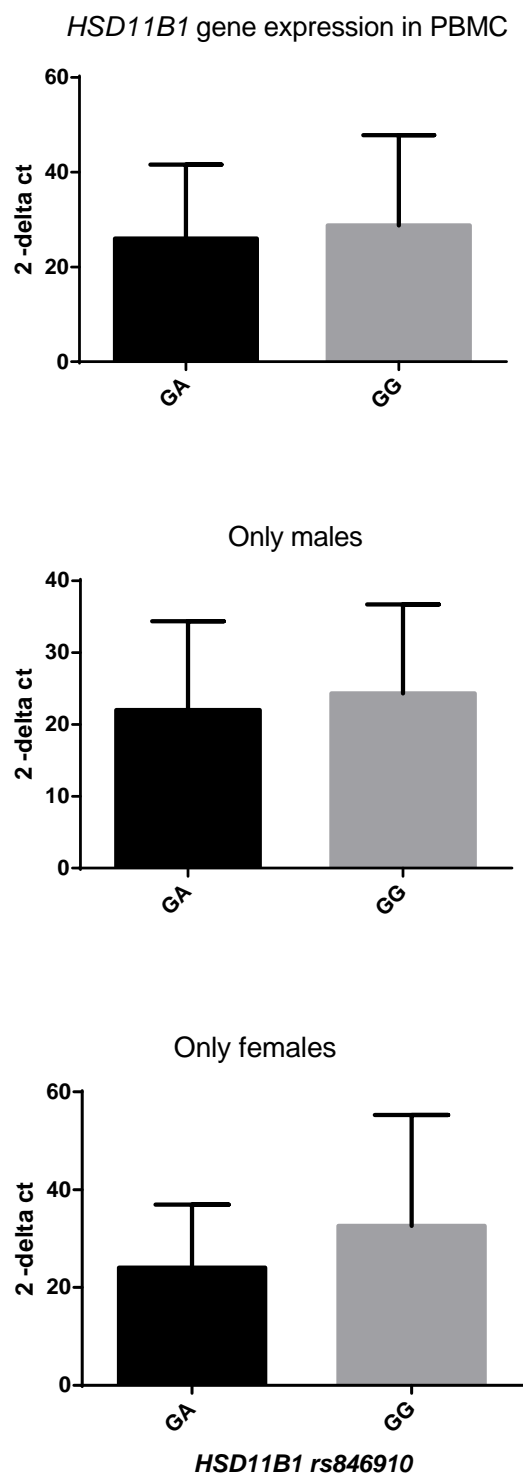
Supplementary Figure 1: HSD11B1 SNPs haplotype blocks

1a.D'

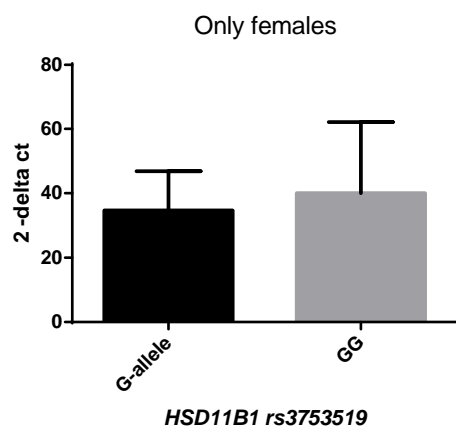
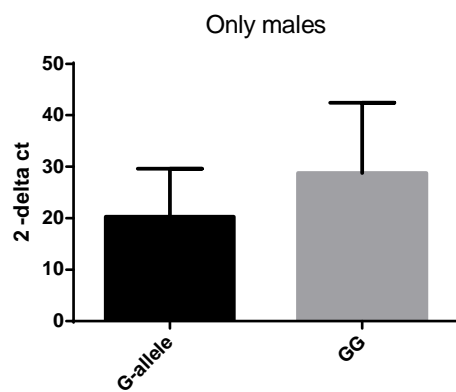
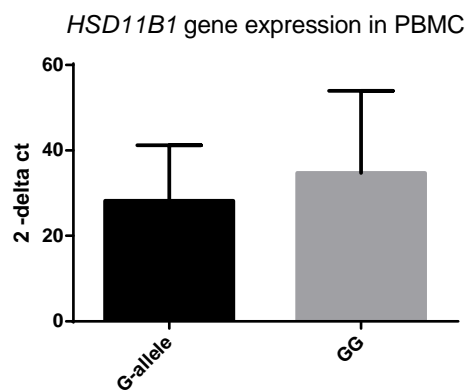
1b. r²



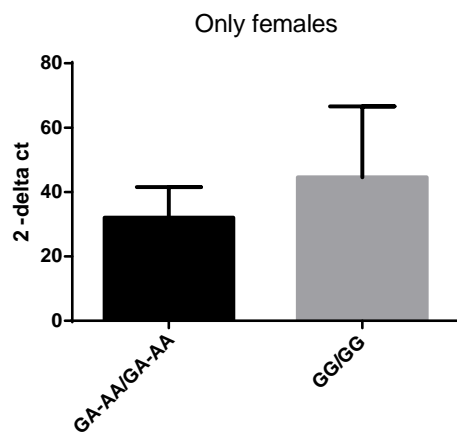
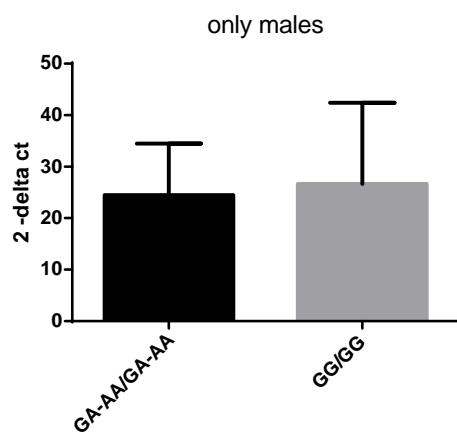
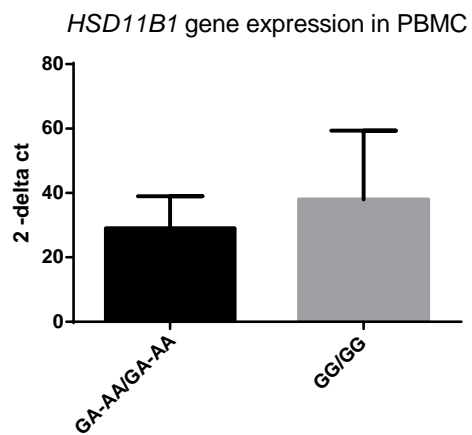
Supplementary Figure 2: *HSD11B1* gene expression according to *rs846910* genotypes in Peripheral Blood Mononuclear Cells (PBMC) in healthy volunteers.



Supplementary Figure 3: *HSD11B1* gene expression according to *rs3753519* genotypes in Peripheral Blood Mononuclear Cells (PBMC) in healthy volunteers.



Supplementary Figure 4: *HSD11B1* gene expression according to *rs846910* and *rs3753519* genotype combinations in Peripheral Blood Mononuclear Cells (PBMC) in healthy volunteers.



Combination of *HSD11B1* *rs846910* and *rs3753519*

Supplementary Table 1: Genomic positions, minor allele frequencies (MAF) and deviation from Hardy-Weinberg equilibrium (HWE) of *HSD11B1* SNPs in the main psychiatric study.

<i>HSD11B1</i> SNP	Alleles W/m	position	MAF	HWE	MAF HapMap
<i>rs12565406</i>	G/T	209861086	0.088	0.33	0.085
<i>rs10863782</i>	G/A	209872590	0.175	0.65	0.164
<i>rs846910</i>	G/A	209875254	0.058	0.23	0.077
<i>rs3753519</i>	G/A	209875515	0.110	0.56	0.097
<i>rs12086634</i>	T/G	209880259	0.178	0.73	0.206
<i>rs4844488</i>	A/G	209885509	0.040	0.77	0.075
<i>rs846906</i>	C/T	209887718	0.151	0.76	0.136

Supplementary Table 2: Genotype frequencies of *HSD11B1* SNPs in the 3 psychiatric samples and the combined sample:

Patients	Total	N (%)			HWE
		GG	GT	TT	
<i>rs12565406</i>					
Psychiatric study Sample	478	396 (82.9)	80 (19.7)	2 (0.4)	0.33
1st replication sample	168	145 (86.3)	23 (13.7)	0 (0)	0.06
2nd replication sample	188	162 (86.2)	26 (13.8)	0 (0)	0.31
Combined sample	834	703 (84.3)	129 (15.5)	2 (0.2)	0.12
<i>rs10863782</i>					
Psychiatric study Sample	478	327 (68.4)	135 (28.2)	16 (3.4)	0.65
1st replication sample	168	118 (70.2)	47 (28.0)	3 (1.8)	0.90
2nd replication sample	188	133 (70.7)	53 (28.2)	2 (1.1)	0.90

Combined sample	834	578 (69.3)	235 (28.2)	21 (2.5)	0.62
rs846910		GG	GA	AA	
Psychiatric study Sample	478	426 (89.1)	49 (10.3)	3 (0.6)	0.23
1st replication sample	168	144 (85.7)	24 (14.3)	0 (0)	0.31
2nd replication sample	179	169 (89.9)	18 (9.6)	1 (0.5)	0.50
Combined sample	834	739 (88.6)	91 (10.9)	4 (0.5)	0.51
rs3753519		GG	GA	AA	
Psychiatric study Sample	478	380 (79.5)	91 (19.0)	7 (1.5)	0.56
1st replication sample	168	133 (79.2)	34 (20.2)	1 (0.6)	0.45
2nd replication sample	188	152 (80.9)	35 (18.6)	1 (0.5)	0.50
Combined sample	834	665 (79.7)	160 (19.2)	9 (1.1)	0.86
rs12086634		TT	TG	GG	
Psychiatric study Sample	478	322 (67.4)	142 (29.7)	14 (2.9)	0.73
1st replication sample	168	117 (69.6)	43 (25.6)	8 (4.8)	0.13
2nd replication sample	188	139 (73.9)	43 (22.9)	6 (3.2)	0.25
Combined sample	834	578 (69.3)	228 (27.3)	28 (3.4)	0.35
rs4844488		AA	AG	GG	
Psychiatric study Sample	478	441 (92.3)	36 (7.5)	1 (0.2)	0.77
1st replication sample	168	155 (92.3)	13 (7.7)	0 (0)	0.60
2nd replication sample	188	176 (93.6)	11 (5.9)	1 (0.5)	0.09
Combined sample	834	772 (92.6)	60 (7.2)	2 (0.2)	0.47
rs846906		CC	CT	TT	
Psychiatric study Sample	478	344 (72.0)	124 (25.9)	10 (2.1)	0.76
1st replication sample	168	123 (73.2)	43 (25.6)	2 (1.2)	0.41
2nd replication sample	188	142 (75.5)	43 (22.9)	3 (1.6)	0.90
Combined sample	834	609 (73.0)	210 (25.2)	15 (1.8)	0.52

HWE: hardy-weinberg equilibrium

Supplementary Table 3: Associations between *HSD11B1* SNPs in a dominant model and systolic blood pressure during follow-up in the main psychiatric study:

	Main psychiatric sample				Men				Women			
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Systolic Blood pressure												
<i>rs12565406</i>	386				167				219			
GG		ref				ref				ref		
GT/TT		0.49 (-2.13 - 4.23)	0.35 (> 0.05)			-3.12 (-5.49 - 1.15)	0.12 (> 0.05)			2.44 (-2.18 - 6.22)	0.15 (> 0.05)	
<i>rs10863782</i>	386				167				219			
GG		ref				ref				ref		
GA/AA		-0.42 (-2.69 - 2.11)	0.45 (> 0.05)			-2.05 (-4.19 - 2.11)	0.20 (> 0.05)			0.03 (-3.63 - 2.51)	0.42 (> 0.05)	
<i>rs846910</i>	386				167				219			
GG		ref				ref				ref		
GA/AA		-1.62 (-4.15 - 2.42)	0.31 (> 0.05)			-0.78 (-4.28 - 4.18)	0.43 (> 0.05)			-3.01 (-6.89 - 2.05)	0.12 (> 0.05)	
<i>rs3753519</i>	386				167				219			
GG		ref				ref				ref		
GA/AA		-1.30 (-3.54 - 1.67)	0.25 (> 0.05)			-2.31 (-4.85 - 1.38)	0.17 (> 0.05)			-1.32 (-3.41 - 2.09)	0.30 (> 0.05)	
<i>rs12086634</i>	386				167				219			
TT		ref				ref				ref		
TG/GG		1.02 (-1.71 - 3.51)	0.19 (> 0.05)			4.08 (0.48 - 7.43)	0.02 (> 0.05)			-1.74 (-4.71 - 2.19)	0.22 (> 0.05)	
<i>rs4844488</i>	386				167				219			
AA		ref				ref				ref		
AG/GG		1.66 (-2.42 - 5.99)	0.20 (> 0.05)			3.43 (-2.00 - 7.47)	0.14 (> 0.05)			-1.54 (-6.76 - 5.42)	0.43 (> 0.05)	
<i>rs846906</i>	386				167				219			
CC		ref				ref				ref		
CT/TT		-0.89 (-3.44 - 1.72)	0.26 (> 0.05)			1.09 (-2.82 - 5.15)	0.37 (> 0.05)			-2.57 (-5.16 - 0.36)	0.05 (> 0.05)	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and antihypertensive intake. 1000 bootstraps were done for the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, $P_{\text{corrected}}$: Bonferroni corrected p-value.

Supplementary Table 4: Associations between *HSD11B1* SNPs in a dominant model and diastolic blood pressure during follow-up in the main psychiatric study:

	Main psychiatric sample				Men				Women			
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Diastolic blood pressure												
<i>rs12565406</i>	386				167				219			
GG		ref				ref				ref		
GT/TT		-0.47 (-2.27 - 2.09)	0.47 (> 0.05)			-1.76 (-3.71 - 1.94)	0.23 (> 0.05)			-0.30 (-3.49 - 2.82)	0.41 (> 0.05)	
<i>rs10863782</i>	386				167				219			
GG		ref				ref				ref		
GA/AA		-0.58 (-2.32 - 1.86)	0.42 (> 0.05)			-1.52 (-3.29 - 1.69)	0.26 (> 0.05)			-0.49 (-2.73 - 2.38)	0.32 (> 0.05)	
<i>rs846910</i>	386				167				219			
GG		ref				ref				ref		
GA/AA		-3.02 (-5.93 - 0.11)	0.03 (> 0.05)			-1.53 (-4.49 - 2.75)	0.32 (> 0.05)			-4.69 (-8.75 - (-)1.33)	0.004 (0.028)	1.30
<i>rs3753519</i>	386				167				219			
GG		ref				ref				ref		
GA/AA		-2.84 (-4.43 - (-)0.54)	0.005 (0.035)	0.84		-1.79 (-4.01 - 1.44)	0.28 (> 0.05)			-4.21 (-6.15 - (-)1.57)	0.0006[§] (0.004)	1.92
<i>rs12086634</i>	386				167				219			
TT		ref				ref				ref		
TG/GG		-0.83 (-2.49 - 0.91)	0.20 (> 0.05)			1.38 (-1.29 - 4.12)	0.19 (> 0.05)			-2.04 (-4.09 - 0.27)	0.05 (> 0.05)	
<i>rs4844488</i>	386				167				219			
AA		ref				ref				ref		
AG/GG		-3.79 (-7.24 - (-)0.87)	0.01 (> 0.05)			-0.25 (-4.55 - 6.81)	0.56 (> 0.05)			-6.98 (-11.23 - (-)3.32)	0.0002[§] (0.001)	2.19
<i>rs846906</i>	386				167				219			
CC		ref				ref				ref		
CT/ TT		0.13 (-1.79 - 1.69)	0.52 (> 0.05)			1.89 (-1.43 - 5.54)	0.12 (> 0.05)			-1.39 (-3.74 - 0.96)	0.10 (> 0.05)	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and antihypertensive intake.

[§] 10000 bootstraps were used for this analysis. 1000 bootstraps were done for the rest of the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, $P_{\text{corrected}}$: Bonferroni corrected p-value.

Supplementary Table 5: Associations between *HSD11B1* SNPs in a dominant model and fasting blood glucose during follow-up in the main psychiatric study:

Main psychiatric sample				Men				Women				
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Fasting blood glucose												
<i>rs12565406</i>	294				123				171			
GG		ref				ref				ref		
GT/TT		-0.18 (-0.42 - (-)0.02)	0.03 (> 0.05)			-0.21 (-0.69 - 0.12)	0.11 (> 0.05)			-0.10 (-0.29 - 0.16)	0.18 (> 0.05)	
<i>rs10863782</i>	294				123				171			
GG		ref				ref				ref		
GA/AA		-0.11 (-0.35 - 0.03)	0.09 (> 0.05)			-0.07 (-0.60 - 0.29)	0.37 (> 0.05)			-0.12 (-0.26 - 0.05)	0.08 (> 0.05)	
<i>rs846910</i>	294				123				171			
GG		ref				ref				ref		
GA/AA		0.05 (-0.28 - 0.24)	0.37 (> 0.05)			0.13 (-0.59 - 0.70)	0.33 (> 0.05)			-0.10 (-0.37 - 0.14)	0.20 (> 0.05)	
<i>rs3753519</i>	294				123				171			
GG		ref				ref				ref		
GA/AA		-0.06 (-0.32 - 0.10)	0.17 (> 0.05)			-0.3 (-0.66 - 0.38)	0.43 (> 0.05)			-0.13 (-0.35 - 0.02)	0.08 (> 0.05)	
<i>rs12086634</i>	294				123				171			
TT		ref				ref				ref		
TG/GG		0.03 (-0.21 - 0.36)	0.28 (> 0.05)			0.22 (-0.28 - 0.99)	0.16 (> 0.05)			-0.03 (-0.20 - 0.12)	0.36 (> 0.05)	
<i>rs4844488</i>	294				123				171			
AA		ref				ref				ref		
AG/GG		0.13 (-0.24 - 0.48)	0.29 (> 0.05)			0.245 (-0.50 - 1.05)	0.23 (> 0.05)			-0.07 (-0.33 - 0.27)	0.30 (> 0.05)	
<i>rs846906</i>	294				123				171			
CC		ref				ref				ref		
CT/ TT		0.00 (-0.19 - 0.27)	0.40 (> 0.05)			-0.09 (-0.53 - 0.34)	0.44 (> 0.05)			0.02 (-0.14 - 0.25)	0.30 (> 0.05)	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and antidiabetic drug intake. 1000 bootstraps were done for the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, $P_{\text{corrected}}$: Bonferroni corrected p-value.

Supplementary Table 6: Associations between *HSD11B1* SNPs in a dominant model and triglycerides blood levels during follow-up in the main psychiatric study:

	Main psychiatric sample				Men				Women			
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Triglycerides												
<i>rs12565406</i>	312				128				184			
GG		ref				ref				ref		
GT/TT		0.10 (-0.18 - 0.37)	0.18 (> 0.05)			0.09 (-0.33 - 0.44)	0.31 (> 0.05)			0.09 (-0.15 - 0.46)	0.23 (> 0.05)	
<i>rs10863782</i>	312				128				184			
GG		ref				ref				ref		
GA/AA		0.03 (-0.16 - 0.19)	0.37 (> 0.05)			0.08 (-0.22 - 0.30)	0.28 (> 0.05)			-0.02 (-0.19 - 0.18)	0.47 (> 0.05)	
<i>rs846910</i>	312				128				184			
GG		ref				ref				ref		
GA/AA		0.00 (-0.22 - 0.20)	0.47 (> 0.05)			0.07 (-0.22 - 0.30)	0.41 (> 0.05)			-0.03 (-0.32 - 0.19)	0.37 (> 0.05)	
<i>rs3753519</i>	312				128				184			
GG		ref				ref				ref		
GA/AA		-0.02 (-0.15 - 0.14)	0.47 (> 0.05)			0.02 (-0.25 - 0.30)	0.40 (> 0.05)			-0.05 (-0.33 - 0.15)	0.35 (> 0.05)	
<i>rs12086634</i>	312				128				184			
TT		ref				ref				ref		
TG/GG		-0.13 (-0.27 - 0.02)	0.04 (> 0.05)			-0.09 (-0.35 - 0.12)	0.22 (> 0.05)			-0.16 (-0.34 - 0.02)	0.07 (> 0.05)	
<i>rs4844488</i>	312				128				184			
AA		ref				ref				ref		
AG/GG		0.12 (-0.21 - 0.35)	0.23 (> 0.05)			0.27 (-0.18 - 0.73)	0.15 (> 0.05)			0.06 (-0.28 - 0.52)	0.30 (> 0.05)	
<i>rs846906</i>	312				128				184			
CC		ref				ref				ref		
CT/ TT		0.29 (0.10 - 0.46)	0.001 (0.007)	1.93		0.53 (0.12 - 0.88)	0.004 (0.028)	5.4		0.15 (-0.07 - 0.29)	0.14 (> 0.05)	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and hypolipidemic agents. 1000 bootstraps were done for the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, $P_{\text{corrected}}$: Bonferroni corrected p-value.

Supplementary Table 7: Associations between *HSD11B1* SNPs in a dominant model and HDL-cholesterol blood levels during follow-up in the main psychiatric study:

Main psychiatric sample				Men			Women					
	n	β (95% C.I.)	p-value	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
HDL-cholesterol												
<i>rs12565406</i>					126				185			
GG		NA				ref				ref		
GT/TT						-0.06 (-0.14 - 0.02)	0.07 (> 0.05)			-0.08 (-0.20 - 0.03)	0.06 (> 0.05)	
<i>rs10863782</i>					126				185			
GG		NA				ref				ref		
GA/AA						-0.05 (-0.12 - 0.04)	0.09 (> 0.05)			-0.08 (-0.18 - 0.00)	0.03 (> 0.05)	
<i>rs846910</i>					126				185			
GG		NA				ref				ref		
GA/AA						-0.02 (-0.17 - 0.10)	0.45 (> 0.05)			0.06 (-0.04 - 0.19)	0.13 (> 0.05)	
<i>rs3753519</i>					126				185			
GG		NA				ref				ref		
GA/AA						-0.02 (-0.12 - 0.08)	0.35 (> 0.05)			0.04 (-0.06 - 0.14)	0.22 (> 0.05)	
<i>rs12086634</i>					126				185			
TT		NA				ref				ref		
TG/GG						0.02 (-0.06 - 0.09)	0.28 (> 0.05)			0.02 (-0.08 - 0.12)	0.36 (> 0.05)	
<i>rs4844488</i>					126				185			
AA		NA				ref				ref		
AG/GG						0.01 (-0.11 - 0.15)	0.45 (> 0.05)			0.01 (-0.16 - 0.21)	0.44 (> 0.05)	
<i>rs846906</i>					126				185			
CC		NA				ref				ref		
CT/ TT						-0.14 (-0.21 - (-)0.05)	0.0008[§] (0.006)	3.37		-0.06 (-0.17 - 0.05)	0.13 (> 0.05)	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, smoking status, current psychotropic drug and hypolipidemic agents.

[§] 10000 bootstraps were used for this analysis. 1000 bootstraps were done for the rest of the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, P_{corrected}: Bonferroni corrected p-value, NA: non-applicable.

Supplementary Table 8: Associations between *HSD11B1* SNPs in a dominant model and BMI in the replication samples:

	n	β (95% C.I.)	p-value ($P_{\text{corrected}}$)	E. Var.	Men				Women			
					n	β (95% C.I.)	p-value ($P_{\text{corrected}}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{\text{corrected}}$)	E. Var.
1st replication sample												
<i>rs846910</i>	168				89				79			
GG		ref				ref				ref		
GA/AA		0.17 (-1.42 - 0.87)	0.42			0.71 (-1.45 - 2.74)	0.37			-0.38 (-2.67 - 2.32)	0.37	
<i>rs3753519</i>	168				89				79			
GG		ref				ref				ref		
GA/AA		-0.87 (-2.17 - 0.48)	0.08			-0.25 (-2.07 - 1.52)	0.38			-1.66 (-3.79 - 0.38)	0.06	
<i>rs4844488</i>	168				89				79			
AA		ref				UD				ref		
AG/GG		2.48 (-0.42 - 5.19)	0.05							2.87 (-1.35 - 7.03)	0.12	
2nd replication sample												
<i>rs846910</i>	184				114				70			
GG		ref				ref				ref		
GA/AA		-0.89 (-2.28 - 0.58)	0.12			-1.02 (-2.94 - 0.72)	0.14			-1.36 (-3.91 - 1.34)	0.15	
<i>rs3753519</i>	184				114				70			
GG		ref				ref				ref		
GA/AA		-1.34 (-2.28 - (-)0.31)	0.01			-1.79 (-3.23 - (-)0.61)	0.004	2.91		-1.67 (-3.90 - 0.49)	0.07	
<i>rs4844488</i>	184				114				70			
AA		ref				UD				ref		
AG/GG		0.44 (-1.64 - 2.65)	0.33							0.22 (-3.77 - 4.27)	0.49	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and comedications possibly causing weight-gain. 1000 bootstraps were done for the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for significant tests.
ref: reference, UD: unable to perform GAMM analyses for this group

Supplementary Table 9: Associations between the combination of *HSD11B1* rs846910G>A and rs3753519G>A SNPs and BMI and MetS components during follow-up in the main psychiatric study sample and the 3 combined samples:

	main psychiatric sample				Men				Women			
	n	β (95% C.I.)	p-value	E. Var.	n	β (95% C.I.)	p-value	E. Var.	n	β (95% C.I.)	p-value	E. Var.
BMI	450				193				257			
GG/GG		ref				ref				ref		
GG/GA-AA		-2.02 (-3.17 - (-)1.17)	<0.0001[§]			-1.68 (-2.73 - (-)0.65)	0.007			-2.33 (-3.69 - (-)0.83)	0.002	
GA-AA/GA-AA		-2.50 (-3.59 - (-)1.38)	<0.0001[§]	2.94		-0.43 (-1.88 - 1.00)	0.31			-4.21 (-6.04 - (-)2.97)	<0.0001[§]	5.05
Waist circumference					204				255			
GG/GG		NA				ref				ref		
GG/GA-AA						-3.34 (-6.15 - 2.44)	0.11			-7.04 (-11.81 - (-)1.69)	0.007	
GA-AA/GA-AA						-2.72 (-6.99 - 2.95)	0.22			-9.04 (-12.41 - (-)5.31)	<0.0001[§]	5.09
Systolic pressure	386				167				219			
GG/GG		ref				ref				ref		
GG/GA-AA		-0.86 (-3.31 - 2.29)	0.33			-3.12 (-9.13 - 2.59)	0.17			0.22 (-3.55 - 3.78)	0.35	
GA-AA/GA-AA		-1.72 (-4.40 - 2.37)	0.29			-0.49 (-3.99 - 3.76)	0.49			-2.99 (-6.60 - 2.18)	0.12	
Diastolic pressure	386				167				219			
GG/GG		ref				ref				ref		
GG/GA-AA		-2.37 (-4.10 - 0.80)	0.07			-1.20 (-4.99 - 3.31)	0.39			-3.45 (-5.45 - 0.08)	0.028	
GA-AA/GA-AA		-3.28 (-5.90 - 0.74)	0.05			-1.01 (-3.96 - 2.79)	0.46			-5.05 (-9.06 - (-)1.71)	0.002	2.02
Fasting glucose	294				123				171			
GG/GG		ref				ref				ref		
GG/GA-AA		-0.17 (-0.47 - (-)0.01)	0.02			-0.22 (-0.83 - 0.22)	0.22			-0.15 (-0.36 - 0.01)	0.06	
GA-AA/GA-AA		0.03 (-0.30 - 0.21)	0.42			0.11 (-0.64 - 0.69)	0.33			-0.11 (-0.40 - 0.10)	0.19	
Triglycerides	312				128				184			
GG/GG		ref				ref				ref		
GG/GA-AA		-0.05 (-0.28 - 0.22)	0.45			-0.03 (-0.56 - 0.52)	0.57			-0.07 (-0.44 - 0.35)	0.39	
GA-AA/GA-AA		0.00 (-0.22 - 0.20)	0.46			0.06 (-0.19 - 0.29)	0.38			0.04 (-0.34 - 0.20)	0.34	
HDL-cholesterol					126				185			
GG/GG		NA				ref				ref		
GG/GA-AA						-0.01 (-0.14 - 0.10)	0.40			0.02 (-0.13 - 0.17)	0.42	
GA-AA/GA-AA						-0.03 (-0.17 - 0.10)	0.41			0.06 (-0.03 - 0.21)	0.15	

	Combined psychiatric sample			Men		Women		
BMI	802			396		406		
GG/GG		ref			ref		ref	
GG/GA-AA		-2.16 (-2.92 - (-)1.45)	<0.0001[§]		-1.93 (-2.97 - (-)1.26)	<0.0001[§]	-2.39 (-3.27 - (-)1.32)	0.0001
GA-AA/GA-AA		-1.65 (-2.34 - (-)0.65)	0.0002	1.97	-0.46 (-1.41 - 0.43)	0.25	-2.69 (-3.79 - (-)1.58)	<0.0001[§]

Genotype combinations: *GG/GG*: wild-type genotype for both SNPs (*rs846910* and *rs3753519*), *GG/GA-AA*: wild-type for *rs846910* and carriers of the variant allele of *rs3753519*, *GA-AA/GA-AA*: carriers of the variant allele of both SNPs (*rs846910* and *rs3753519*)

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and comedications possibly causing weight-gain for BMI and waist circumference analyses, antihypertensive intake for blood pressure analyses, antidiabetic agent for fasting glucose analyses and hypolipidemic agents for triglycerides and HDL-cholesterol analyses.

[§] 10000 bootstraps were used for this analysis. 1000 bootstraps were done for the rest of the rest of the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for significant tests

ref: reference, NA: non-applicable.

Supplementary Table 10: Associations between *HSD11B1* SNPs in a dominant model and BMI and metabolic syndrome components during follow-up in a subgroup from the main psychiatric study sample newly diagnosed with psychiatric disease:

	Main psychiatric sample				Men				Women			
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
BMI												
<i>rs12565406</i>	178				77				101			
GG		ref				ref				ref		
GT/TT		-1.1 (-2.27 - (-)0.13)	0.01 (> 0.05)	0.84		-0.94 (-2.19 - 0.25)	0.11 (> 0.05)			-1.17 (-2.75 - (-)0.12)	0.02 (> 0.05)	0.52
<i>rs10863782</i>	178				77				101			
GG		ref				ref				ref		
GA/AA		-1.45 (-2.57 - (-)0.34)	0.005 (0.035)	2.16		-0.73 (-1.98 - 0.35)	0.09 (> 0.05)			-2.05 (-3.66 - (-)0.28)	0.007 (0.049)	3.11
<i>rs846910</i>	178				77				101			
GG		ref				UD				ref		
GA/AA		-4.28 (-5.88 - (-)2.68)	<0.001 (0.007)	7.91						-5.31 (-6.98 - (-)3.50)	<0.001 (0.007)	10.35
<i>rs3753519</i>	178				77				101			
GG		ref				ref				ref		
GA/AA		-2.83 (-3.98 - (-)1.72)	<0.001 (0.007)	6.28		-1.69 (-3.26 - (-)0.56)	0.01 (0.07)	2.91		-3.19 (-4.81 - (-)1.62)	<0.001 (0.007)	6.76
<i>rs12086634</i>	178				77				101			
TT		ref				ref				ref		
TG/GG		0.45 (-0.59 - 1.55)	0.26 (> 0.05)			0.44 (-0.95 - 1.87)	0.33 (> 0.05)			0.38 (-1.45 - 2.35)	0.36 (> 0.05)	
<i>rs4844488</i>	178				77				101			
AA		ref				UD				ref		
AG/GG		-2.63 (-4.77 - (-)1.03)	0.01 (> 0.05)	2.04						-3.64 (-6.46 - (-)0.08)	0.03 (> 0.05)	2.55
<i>rs846906</i>	178				77				101			
CC		ref				ref				ref		
CT/ TT		1.22 (-0.08 - 2.19)	0.03 (> 0.05)	1.17		0.69 (-0.87 - 2.39)	0.20 (> 0.05)			1.83 (-0.02 - 3.54)	0.04 (> 0.05)	1.99

Main psychiatric sample				Men				Women			
n	β (95% C.I.)	p-value	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Waist circumference											
<i>rs12565406</i>											
	NA			76	ref			96	ref		
GG					-3.81	0.02	2.26		-0.13	0.51	
GT/TT					(-7.48 - (-)0.55)	(> 0.05)			(-5.29 - 4.04)	(> 0.05)	
<i>rs10863782</i>											
	NA			76	ref			96	ref		
GG					-2.49	0.09			-4.59	0.01	2.32
GA/AA					(-6.37 - 0.70)	(> 0.05)			(-9.22 - (-)0.43)	(> 0.05)	
<i>rs846910</i>											
	NA			76	ref			96	ref		
GG					-4.95	<0.01	1.12		-9.75	0.001	4.99
GA/AA					(-11.22 - (-)1.13)	(<0.07)			(-16.16 - (-)3.63)	(0.007)	
<i>rs3753519</i>											
	NA			76	ref			96	ref		
GG					-3.97	0.03	2.02		-6.02	0.002	3.5
GA/AA					(-7.96 - 0.17)	(> 0.05)			(-9.93 - (-)2.07)	(0.014)	
<i>rs12086634</i>											
	NA			76	ref			96	ref		
TT					2.59	0.09			1.37	0.35	
TG/GG					(-0.72 - 5.72)	(> 0.05)			(-2.25 - 5.68)	(> 0.05)	
<i>rs4844488</i>											
	NA			76	UD			96	ref		
AA									-2.54	0.15	
AG/GG									(-8.69 - 3.92)	(> 0.05)	
<i>rs846906</i>											
	NA			76	ref			96	ref		
CC					2.91	0.10			2.57	0.08	
CT/ TT					(-1.30 - 6.62)	(> 0.05)			(-1.87 - 7.45)	(> 0.05)	

Main psychiatric sample				Men				Women				
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Systolic Blood pressure												
rs12565406	140				60				80			
GG		ref				ref				ref		
GT/TT		-1.25 (-6.34 - 4.02)	0.30 (> 0.05)			-3.64 (-8.52 - 2.99)	0.25 (> 0.05)			0.55 (-4.42 - 6.81)	0.35 (> 0.05)	
rs10863782	140				60				80			
GG		ref				UD				ref		
GA/AA		-1.48 (-5.37 - 3.09)	0.27 (> 0.05)							-0.48 (-5.51 - 5.17)	0.46 (> 0.05)	
rs846910	140				60				80			
GG		ref				UD				ref		
GA/AA		-4.96 (-10.10 - 1.97)	0.12 (> 0.05)							-6.25 (-13.89 - 3.15)	0.11 (> 0.05)	
rs3753519	140				60				80			
GG		ref				ref				ref		
GA/AA		-3.54 (-9.19 - 2.24)	0.11 (> 0.05)			-5.57 (-11.0 - 5.48)	0.16 (> 0.05)			-2.21 (-6.77 - 3.27)	0.24 (> 0.05)	
rs12086634	140				60				80			
TT		ref				UD				ref		
TG/GG		2.31 (-1.62 - 6.04)	0.16 (> 0.05)							-0.96 (-6.13 - 5.20)	0.43 (> 0.05)	
rs4844488	140				60				80			
AA		ref				UD				UD		
AG/GG		0.16 (-7.08 - 9.48)	0.37 (> 0.05)									
rs846906	140				60				80			
CC		ref				ref				ref		
CT/ TT		-1.14 (-5.52 - 3.86)	0.47 (> 0.05)			0.50 (-6.12 - 9.29)	0.37 (> 0.05)			-2.77 (-8.46 - 4.33)	0.19 (> 0.05)	

Main psychiatric sample				Men			Women					
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Diastolic blood pressure												
rs12565406	140				60				80			
GG		ref				UD				ref		
GT/TT		1.66 (-2.19 - 6.31)	0.08 (> 0.05)							2.50 (-0.11 - 7.34)	0.05 (> 0.05)	
rs10863782	140				60				80			
GG		ref				UD				ref		
GA/AA		0.75 (-2.54 - 3.26)	0.30 (> 0.05)							0.61 (-2.26 - 4.66)	0.35 (> 0.05)	
rs846910	140				60				80			
GG		ref				UD				ref		
GA/AA		-6.11 (-11.51 - (-)1.53)	0.01 (> 0.05)	2.14						-9.633 (-15.61 - (-)3.76)	0.002 (0.014)	6.7
rs3753519	140				60				80			
GG		ref				ref				ref		
GA/AA		-2.77 (-6.07 - (-)0.09)	0.02 (> 0.05)	0.89		0.01 (-4.95 - 7.39)	0.38 (> 0.05)			-4.06 (-7.74 - (-)0.03)	0.03 (> 0.05)	2.35
rs12086634	140				60				80			
TT		ref				ref				ref		
TG/GG		-0.91 (-4.62 - 1.94)	0.27 (> 0.05)			2.41 (-1.06 - 7.83)	0.09 (> 0.05)			-4.00 (-7.47 - (-)0.64)	0.01 (> 0.05)	2.56
rs4844488	140				60				80			
AA		ref				UD				UD		
AG/GG		-7.63 (-13.39 - (-)2.06)	0.02 (> 0.05)	2.5								
rs846906	140				60				80			
CC		ref				ref				ref		
CT/ TT		1.12 (-1.84 - 4.02)	0.21 (> 0.05)			2.91 (-1.35 - 9.79)	0.07 (> 0.05)			-0.81 (-5.82 - 2.93)	0.30 (> 0.05)	

Main psychiatric sample				Men				Women				
	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
Triglycerides												
rs12565406	116								70			
GG		ref				UD				ref		
GT/TT		0.04 (-0.27 - 0.34)	0.41 (> 0.05)							0.15 (-0.23 - 0.65)	0.12 (> 0.05)	
rs10863782	116								70			
GG		ref				UD				ref		
GA/AA		0.05 (-0.18 - 0.26)	0.35 (> 0.05)							0.14 (-0.04 - 0.48)	0.08 (> 0.05)	
rs846910	116								70			
GG		ref				UD				ref		
GA/AA		0.19 (-0.16 - 0.75)	0.17 (> 0.05)							0.19 (-0.32 - 0.67)	0.18 (> 0.05)	
rs3753519	116								70			
GG		ref				UD				ref		
GA/AA		0.03 (-0.27 - 0.30)	0.39 (> 0.05)							0.18 (-0.03 - 0.67)	0.05 (> 0.05)	
rs12086634	116								70			
TT		ref				UD				ref		
TG/GG		0.02 (-0.16 - 0.24)	0.37 (> 0.05)							-0.06 (-0.27 - 0.11)	0.26 (> 0.05)	
rs4844488	116											
AA		ref				UD				UD		
AG/GG		0.76 (0.09 - 1.78)	0.02 (> 0.05)									
rs846906	116								70			
CC		ref				UD				ref		
CT/ TT		0.31 (0.07 - 0.56)	0.01 (> 0.05)							0.28 (0.04 - 0.64)	0.02 (> 0.05)	

Main psychiatric sample				Men				Women			
n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.	n	β (95% C.I.)	p-value ($P_{corrected}$)	E. Var.
HDL-cholesterol											
<i>rs12565406</i>											
	NA				UD			70	ref		
GG									0.02	0.39	
GT/TT									(-0.22 - 0.20)	(> 0.05)	
<i>rs10863782</i>											
	NA				UD			70	ref		
GG									-0.05	0.21	
GA/AA									(-0.26 - 0.07)	(> 0.05)	
<i>rs846910</i>											
	NA				UD			70	ref		
GG									0.08	0.30	
GA/AA									(-0.14 - 0.33)	(> 0.05)	
<i>rs3753519</i>											
	NA				UD			70	ref		
GG									0.04	0.41	
GA/AA									(-0.15 - 0.17)	(> 0.05)	
<i>rs12086634</i>											
	NA				UD			70	ref		
TT									-0.09	0.28	
TG/GG									(-0.27 - 0.11)	(> 0.05)	
<i>rs4844488</i>											
	NA				UD			70	UD		
AA											
AG/GG											
<i>rs846906</i>											
	NA				UD			70	ref		
CC									-0.04	0.29	
CT/ TT									(-0.21 - 0.12)	(> 0.05)	

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and comedications possibly causing weight-gain for BMI and waist circumference analyses, antihypertensive intake for blood pressure analyses and hypolipidemic agents for triglycerides and HDL-cholesterol analyses. We were not able to analyze fasting glucose due to the small sample size. 1000 bootstraps were done for the analyses.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, $P_{\text{corrected}}$: Bonferroni corrected p-value, UD: unable to perform GAMM analyses for this group, NA: non-applicable

Supplementary Table 11: Associations between the combination of *HSD11B1* rs846910G>A and rs3753519G>A SNPs and BMI and MetS components during follow-up in a subgroup from the main psychiatric study sample newly diagnosed with psychotropic disease:

	main psychiatric sample				Men				Women			
	n	β (95% C.I.)	p-value	E. Var.	n	β (95% C.I.)	p-value	E. Var.	n	β (95% C.I.)	p-value	E. Var.
BMI	178								101			
GG/GG		ref				UD				ref		
GG/GA-AA		-1.44 (-2.69 - (-)0.26)	0.01							1.21 (-2.99 - 0.17)	0.07	
GA-AA/GA-AA		-4.65 (-6.58 - (-)3.13)	<0.01	8.98						-5.50 (-7.23 - (-)3.66)	<0.01	10.93
Waist circumference					76				96			
GG/GG		NA				ref				ref		
GG/GA-AA						-3.22 (-7.91 - 2.97)	0.09			-2.54 (-9.19 - 2.50)	0.21	
GA-AA/GA-AA						-5.24 (-11.55 - (-)1.35)	0.01	2.15		-10.18 (-16.63 - (-)3.74)	<0.01	5.31
Systolic pressure	140								80			
GG/GG		ref				UD				ref		
GG/GA-AA		-2.41 (-10.26 - 4.12)	0.23							0.29 (-4.14 - 7.79)	0.47	
GA-AA/GA-AA		-5.38 (-10.36 - 1.65)	0.13							-6.19 (-14.02 - 3.55)	0.11	
Diastolic pressure	140								80			
GG/GG		ref				UD				ref		
GG/GA-AA		-0.62 (-4.65 - 2.66)	0.43							-0.57 (-4.66 - 3.68)	0.34	
GA-AA/GA-AA		-6.21 (-11.79 - (-)1.64)	0.01	2.16						-9.76 (-17.23 - (-)1.74)	0.002	6.73
Triglycerides	116								70			
GG/GG		ref				UD				ref		
GG/GA-AA		-0.10 (-0.46 - 0.26)	0.32							0.15 (-0.28 - 0.71)	0.20	
GA-AA/GA-AA		0.17 (-0.20 - 0.54)	0.17							0.21 (-0.27 - 0.70)	0.16	
HDL-cholesterol									70			
GG/GG		NA				UD				ref		
GG/GA-AA										0.01 (-0.23 - 0.22)	0.44	
GA-AA/GA-AA										0.08 (-0.17 - 0.31)	0.32	

Genotype combinations: GG/GG: wild-type genotype for both SNPs (*rs846910* and *rs3753519*), GG/GA-AA: wild-type for *rs846910* and carriers of the variant allele of *rs3753519*, GA-AA/GA-AA: carriers of the variant allele of both SNPs (*rs846910* and *rs3753519*).

Results were obtained by fitting Generalized Additive Mixed Models for patients, controlling for age, sex (whenever appropriate), smoking status, current psychotropic drug and comedications possibly causing weight-gain for BMI and waist circumference analyses, antihypertensive intake for blood pressure analyses and hypolipidemic agents for triglycerides and HDL-cholesterol analyses. We were not able to analyze fasting glucose due to the small sample size.

E. Var.: explained variance by the polymorphism (%), only calculated for tests that survived Bonferroni correction.

ref: reference, UD: unable to perform GAMM analyses for this group, NA: non-applicable

Supplementary Table 12: Associations between *HSD11B1* SNPs and BMI and MetS components in the population-based samples:

	BMI β	P- Value	Fat mass β	P- Value	WC β	P- Value	SBP β	P- Value	DBP β	P- Value	Glucose β	P- Value	Triglycerides β	P- Value	HDL-C β	P- Value
CoLaus																
<i>rs846910</i>																
Total	-0.008	0.86	-0.010	0.98	NA		-0.134	0.85	-0.213	0.65	-0.062	0.22	-0.002	0.96	NA	
Men	-0.021	0.75	0.085	0.86	-0.031	0.64	-1.319	0.22	-0.746	0.31	-0.034	0.68	-0.071	0.47	0.047	0.04
Women	0.002	0.98	-0.083	0.88	-0.011	0.85	0.758	0.44	0.189	0.76	-0.052	0.39	0.050	0.16	-0.012	0.60
<i>rs3753519</i>																
Total	0.012	0.73	-0.013	0.96	NA		0.341	0.58	0.144	0.72	0.001	0.98	0.015	0.71	NA	
Men	0.029	0.59	0.233	0.55	0.033	0.55	0.027	0.98	0.054	0.93	0.003	0.97	-0.011	0.89	0.021	0.26
Women	-0.001	0.98	-0.215	0.64	-0.027	0.58	0.596	0.48	0.217	0.68	0.026	0.61	0.036	0.24	0.015	0.43
<i>rs4844488</i>																
Total	0.019	0.69	0.359	0.34	NA		-0.28	0.72	-0.186	0.71	0.014	0.80	0.014	0.79	NA	
Men	0.042	0.54	0.820	0.09	0.037	0.59	-1.117	0.31	-0.079	0.92	0.091	0.28	-0.022	0.83	0.014	0.56
Women	-0.001	0.98	-0.033	0.96	-0.003	0.96	0.420	0.70	-0.275	0.68	-0.044	0.51	0.043	0.26	-0.016	0.51
<i>rs846906</i>																
Total	0.005	0.86	0.245	0.27	NA		-0.440	0.33	-0.206	0.48	0.001	0.96	0.002	0.93	NA	
Men	0.004	0.92	0.341	0.22	0.040	0.31	-0.770	0.23	-0.226	0.60	-0.003	0.96	0.031	0.60	0.022	0.10
Women	0.005	0.88	0.161	0.64	0.016	0.66	-0.146	0.82	-0.189	0.64	0.011	0.77	-0.022	0.34	-0.012	0.40

Results were analyzed by using multivariate linear regression with allele dosage in which potential confounding factors such as age, sex and smoking status

BMI: Body mass index, WC: waist circumference, SBP: systolic blood pressure, DBP: diastolic blood pressure, HDL-C: HDL- Cholesterol, NA: non-applicable

Supplementary Table 13: Associations between *HSD11B1* SNPs and BMI and MetS components in the population-based samples:

	BMI [§] β	P- Value	WHR [§] β	P- Value	WC [§] β	P- Value	Triglycerides [§] β	P- Value	HDL-C [§] β	P- Value
<i>rs846910</i>										
Total	-0.009	0.36	-0.013	0.29	NA		-0.006	0.05	0.003	0.32
Men					-0.024	0.14				
Women					0.01	0.50				
<i>rs3753519</i>										
Total	-0.003	0.65	-0.007	0.47	NA		-0.004	0.17	0.002	0.59
Men					-0.001	0.91				
Women					-0.001	0.87				
<i>rs4844488</i>										
Total	0.002	0.85	0.005	0.71	NA		0.005	0.17	-0.005	0.15
Men					-0.061	0.17				
Women					0.037	0.60				
<i>rs846906</i>										
Total	0.001	0.82	-0.013	0.10	NA		0.004	0.23	-0.003	0.32
Men					0.001	0.95				
Women					0.004	0.76				

[§]This clinical variable was analyzed in GIANT study

[§]This clinical variable was analyzed in the “Genome Wide Associations Scans for Total Cholesterol, HDL-C, LDL-C and triglycerides”

BMI: Body mass index, WC: waist-to hip ratio, WC: waist circumference, HDL-C: HDL- Cholesterol, NA: non-applicable

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