



Supplemental Figure S1. Positive correlation of serum acid sphingomyelinase (S-ASM) with liver enzyme activities GGT, ALT, and AST in the total cohort ($n = 229$, a-c) and the subgroup of male ($n = 30$) but not female ($n = 31$) healthy controls (d-f). GGT gamma-glutamyl transferase, ALT alanine aminotransferase (glutamic-pyruvic transaminase, GPT), AST aspartate aminotransferase (glutamic-oxaloacetic transaminase, GOT).

Supplemental table S1. Sex-specific demographic and laboratory data for females corresponding to Table 1 for the whole groups. See legend of Table 1 for details.

Parameters	PU	PM	PR	HC	p values for group difference			
					PU vs. PM	PU vs. HC	PM vs. HC	PR vs. HC
n at inclusion	36	32	31	28				
n at follow-up	34	28						
age (years)	45 (33–53)	46 (32–55.5)	52 (47–63)	47 (32–60)	0.810	0.642	0.645	0.109
total education years ^a	15 (13–17)	14 (12–17)	14 (12–15)	14 (12–17)	0.216	0.527	0.585	0.792
BMI (kg/m ²)	24.0 (21.3–27.3)	27.3 (22.1–30.6)	25.3 (22.7–29.2)	24.3 (23–26.2)	0.055	0.664	0.124	0.309
BDI-II score at inclusion	29 (21–36)	33 (27–39)	3 (0–5)	1 (0–4)	0.176	<0.001	<0.001	0.368
BDI-II score at follow-up ^c	22 (15–27)	24 (16–36)			0.318			
BDI-II score at relative change ^c	-0.23 (-0.42–0.06)	-0.21 (-0.42–0.01)			0.955			
HAM-D score at inclusion	22 (19–26)	24 (21–27)	2 (1–4)	1 (0–3)	0.095	<0.001	<0.001	0.256
HAMD-D score at follow-up ^c	18 (14–21)	17 (11–22)			0.804			
HAMD-D score at relative change ^c	-0.24 (-0.38–0.05)	-0.24 (-0.44–0.08)			0.471			
MADRS score at inclusion	26 (22–28)	28 (25–35)	1 (0–4)	1 (0–2)	0.046	<0.001	<0.001	0.216
MADRS score at follow-up ^c	21 (18–25)	20 (15–29)			0.755			
MADRS score relative change ^c	-0.18 (-0.30–0.04)	-0.18 (-0.46–0.10)			0.258			
STAI state score at inclusion	47 (40–56)	55 (48–66)	32 (30–35)	29 (26–32)	0.009	<0.001	<0.001	0.034
STAI state score at follow-up ^c	46 (36–51)	49 (45–59)			0.047			
STAI state score relative change ^c	-0.05 (-0.15–0.03)	-0.02 (-0.17–0.09)			0.794			
STAI trait score at inclusion	62 (56–68)	65 (53–67)	36 (28–41)	29 (25–35)	0.830	<0.001	<0.001	0.013
STAI trait score at follow-up ^c	58 (52–62)	58 (53–67)			0.666			
STAI trait score relative change ^c	-0.06 (-0.13–0.02)	-0.04 (-0.12–0.07)			0.497			
SF-12 physical component score ^b	49.6 (37.3–56.8)	50.6 (42.3–55.0)	54.3 (49.2–56.7)	56.3 (55.2–57.5)	0.709	0.003	0.001	0.035
SF-12 mental component score ^b	19.4 (16.6–29.9)	16.5 (12.0–26.9)	52.5 (48.1–57.0)	54.3 (50.8–58.2)	0.094	<0.001	<0.001	0.185
CRP (mg/L)	1.0 (0.6–2.3)	1.8 (0.90–3.4)	1.5 (1.0–2.2)	1.4 (0.8–3.3)	0.057	0.074	0.853	0.627
Triglycerides (mg/dL)	75 (57–108)	106 (84–136)	88 (69–139)	80 (64–111)	0.003	0.396	0.039	0.320
Total cholesterol (mg/dL)	211 (185–268)	226 (189–265)	237 (209–263)	217 (185–255)	0.511	0.970	0.449	0.335
HDL cholesterol (mg/dL)	65 (58–71)	59 (51–71)	62 (55–74)	66 (58–73)	0.180	0.720	0.141	0.366
LDL cholesterol (mg/dL)	140 (118–182)	152 (128–190)	154 (136–177)	134 (112–167)	0.258	0.763	0.167	0.154
HDL/LDL ratio	2.1 (1.7–2.8)	2.6 (1.9–3.1)	2.3 (1.9–3.1)	2 (1.7–2.5)	0.117	0.660	0.037	0.120
GGT (U/L)	18 (13–23)	18 (12–26)	18 (13–24)	18 (14–21)	0.863	0.965	0.896	1.000
ALT (U/L)	17 (14–23)	17 (13–24)	17 (14–23)	18 (16–24)	0.975	0.236	0.295	0.429
AST (U/L)	22 (19–25)	22 (19–25)	23 (19–27)	24 (21–27)	0.693	0.038	0.088	0.403
S-ASM (fmol/h/μL serum) at inclusion	138 (119–178)	151 (112–216)	148 (102–196)	177 (130–224)	0.363	0.090	0.573	0.133
S-ASM (fmol/h/μL serum) at follow-up ^c	133 (96–186)	178 (140–245)			0.015			
S-ASM relative change ^c	0.05 (-0.21–0.21)	0.12 (-0.01–0.28)			0.165			

Supplemental table S2. Sex-specific demographic and laboratory data for males corresponding to Table 1 for the whole groups. See legend of Table 1 for details.

Parameters	PU	PM	PR	HC	p values for group difference			
					PU vs. PM	PU vs. HC	PM vs. HC	PR vs. HC
n at inclusion	27	34	30	11				
n at follow-up	27	32						
age (years)	49 (35–53)	46 (33–53)	49 (33–53)	36.5 (30–49)	0.642	0.143	0.244	0.407
total education years ^a	16 (13–19)	14 (13–16)	15 (13–17)	16.5 (14–18)	0.073	0.936	0.028	0.413
BMI (kg/m ²)	25.7 (23.3–28.3)	28.5 (26.7–30.2)	25.8 (25.6–27.0)	25.0 (22.9–28.4)	0.003	0.854	0.003	0.424
BDI-II score at inclusion	28 (23–32)	27 (21–32)	1 (0–3)	2 (0–3)	0.810	<0.001	<0.001	0.851
BDI-II score at follow-up ^c	18 (15–22)	17 (10–27)				0.402		
BDI-II score at relative change ^c	-0.34 (-0.41–0.15)	-0.36 (-0.56–0.10)				0.448		
HAM-D score at inclusion	21 (19–23)	22 (20–25)	2 (0–3)	0 (0–1)	0.439	<0.001	<0.001	0.116
HAMD-D score at follow-up ^c	18 (14–20)	13 (9–21)				0.173		
HAMD-D score at relative change ^c	-0.13 (-0.38–0.05)	-0.38 (-0.58–0.24)				0.009		
MADRS score at inclusion	27 (24–29)	27 (23–34)	2 (0–2)	0 (0–1)	0.541	<0.001	<0.001	0.080
MADRS score at follow-up ^c	20 (18–24)	17 (13–23)				0.127		
MADRS score relative change ^c	-0.21 (-0.34–0.09)	-0.34 (-0.49–0.23)				0.032		
STAI state score at inclusion	52 (46–58)	53 (40–62)	26 (22–36)	27 (25–31)	0.839	<0.001	<0.001	0.965
STAI state score at follow-up ^c	48 (42–54)	45 (39–57)				0.639		
STAI state score relative change ^c	-0.08 (-0.14–0.02)	-0.05 (-0.12–0.07)				0.527		
STAI trait score at inclusion	62 (57–67)	58 (52–67)	31 (25–35)	27 (25–32)	0.085	<0.001	<0.001	0.591
STAI trait score at follow-up ^c	59 (54–64)	56 (50–60)				0.216		
STAI trait score relative change ^c	-0.06 (-0.11–0.02)	-0.04 (-0.17–0.01)				0.701		
SF-12 physical component score ^b	51.6 (39.1–57.6)	52.2 (45.2–58.4)	56.2 (50.2–56.5)	55.7 (53.8–56.5)	0.529	0.143	0.416	0.835
SF-12 mental component score ^b	20.0 (16.6–26.3)	20.1 (15.4–26.0)	57.2 (50.8–58.9)	56.9 (52.6–58.9)	0.866	<0.001	<0.001	0.788
CRP (mg/L)	0.9 (0.5–2.1)	1.6 (1.1–2.7)	1.0 (0.8–2.4)	1.2 (0.6–1.9)	0.058	0.761	0.044	0.873
Triglycerides (mg/dL)	108 (79–134)	157 (112–191)	101 (65–127)	90 (60–175)	0.003	0.406	0.010	0.919
Total cholesterol (mg/dL)	224 (189–254)	244 (199–272)	211 (196–235)	198 (172–243)	0.299	0.185	0.019	0.828
HDL cholesterol (mg/dL)	52 (46–59)	45 (41–52)	45 (42–53)	51 (47–61)	0.016	0.879	0.030	0.080
LDL cholesterol (mg/dL)	152 (121–179)	173 (138–197)	148 (139–166)	131 (117–169)	0.144	0.123	0.001	0.315
HDL/LDL ratio	2.9 (2.3–3.7)	3.7 (2.8–4.5)	3.2 (2.5–3.7)	2.6 (2.0–3.3)	0.007	0.133	<0.001	0.174
GGT (U/L)	24 (18–43)	39 (23–53)	25 (17–32)	22 (15–33)	0.023	0.263	0.003	0.761
ALT (U/L)	26 (19–36)	33 (27–50)	23 (19–33)	29 (19–33)	0.020	0.955	0.032	0.942
AST (U/L)	25 (21–34)	28 (22–35)	27 (20–37)	30 (23–35)	0.227	0.128	0.471	0.344
S-ASM (fmol/h/μL serum) at inclusion	161 (129–242)	185 (157–240)	158 (90–177)	160 (126–210)	0.504	0.774	0.294	0.359
S-ASM (fmol/h/μL serum) at follow-up ^c	167 (126–223)	193 (159–211)				0.475		
S-ASM relative change ^c	0.00 (-0.17–0.28)	0.04 (-0.14–0.24)				0.704		

Supplemental table S3. Comparison of activities of secretory acid sphingomyelinase (S-ASM) in the serum of patients and controls depending on specific medications. Except for the first three lines, activities and the number of individuals (*n*) is provided for those taking the indicated drug. Mann–Whitney U-test for the comparison of activities with drug versus without drug with nominal *p* < 0.05 in bold. Groups: PU unmedicated depressive patients, PM medicated depressive patients, HC healthy controls, PR patients with remitted major depressive disorder; FIASMA - functional inhibitor of acid sphingomyelinase (less than 50% residual activity in a cell culture modell). Please note, that these drugs have been tested at higher concentrations than present in patients' blood. Class refers to the classification of psychotropic substances as indicated in the first lines. Reference: Kornhuber, J.; Tripal, P.; Gulbins, E.; Muehlbacher, M. Functional Inhibitors of Acid Sphingomyelinase (FIASMAS) in E. Gulbins and I. Petrache (eds.), Sphingolipids: Basic Science and Drug Development, Handbook of Experimental Pharmacology 215, DOI 10.1007/978-3-7091-1368-4_9, # Springer-Verlag Wien 2013.

Drugs	class	FIASMA	median S-ASM activity (pmol/h/μL)										<i>p</i> values (with vs. without drug)				
			all	<i>n</i>	UP	<i>n</i>	MP	<i>n</i>	RP	<i>n</i>	HC	<i>n</i>	all	UP	MP	RP	HC
all			161.8	229	150.5	63	175.7	66	150.4	39	173.2	61					
no drugs			151.8	101	148.6	41		0	144.8	17	152.4	43					
any drug			175.7	128	150.9	22	175.7	66	154.4	22	202.4	18	0.018	0.594		0.380	0.006
anti-epileptic drug (AED)	1		156.4	10	216.3	2	156.4	6	144.0	2	.	0	0.281	0.969	0.075		
antipsychotic	2		173.7	33	219.7	3	170.0	29	177.2	1	.	0	0.291	0.322	0.713	0.183	
benzodiazepine	3		137.8	14	219.7	3	137.7	11	.	0	.	0	0.909	0.655			
monoamine oxidase inhibitor (MAOI)	4		262.8	3	.	0	262.8	3	.	0	.	0	0.649	0.662			
noradrenergic and specific serotonergic antidepressant	5		185.7	23	91.5	1	190.7	22	.	0	.	0	0.698	0.705	0.183		
norepinephrine and dopamine reuptake inhibitor	6		164.5	7	.	0	160.2	6	177.2	1	.	0	0.137	0.305	0.425		
selective serotonin reuptake inhibitor (SSRI)	7		181.9	36	216.3	2	184.1	28	129.5	6	.	0	0.813	0.574	0.656		
serotonin and norepinephrine reuptake inhibitor	8		141.3	18	.	0	141.3	16	138.3	2	.	0	0.269	0.358			
stimulant	9		276.7	1	.	0	276.7	1	.	0	.	0	0.215	0.520	0.374		
tricyclic antidepressant (TCA)	10		137.9	11	.	0	131.3	10	186.0	1	.	0	0.211	0.463	0.790		
different psychotropic drug	11		205.4	12	91.5	1	206.4	11	.	0	.	0	0.452	0.187	0.348		
Acetylsalicylic acid	-	-	254.2	2	223.3	1		0		0	285.1	1	0.081	0.296	0.173		
Aconit pain relieving plant oil	-		187.1	1		0	187.1	1		0		0	0.535	0.694			
Agomelatine	11		187.2	3		0	187.2	3		0		0	0.362	0.569			
Allopurinol	-		207.3	2		0	101.3	1		0	313.3	1	0.780	0.198	0.125		
Alprazolam	3		87.0	1	87.0	1		0		0		0	0.151	0.138			
Amiloride	-		224.4	2	135.5	1		0		0	313.3	1	0.493	0.700	0.125		
Amisulpride	2		211.6	1		0	211.6	1		0		0	0.364	0.416			
Amitriptyline	10	+	137.7	1		0	137.7	1		0		0	0.586	0.416			
Amlodipine	-	+	313.3	1		0		0		0	313.3	1	0.123		0.120		
Aripiprazole	2		114.0	3		0	114.0	3		0		0	0.528	0.380			
Asenapine	2		164.5	1		0	164.5	1		0		0	0.928	0.813			
asthma spray	-		184.8	1		0		0		0	184.8	1	0.576		0.650		

Atorvastatin	-	155.8	2	0	101.3	1	210.4	1	0	0.855	0.198	0.248
Bisoprolol	-	151.3	3	246.2	2	0	103.1	1	0	0.888	0.240	0.424
Bisphosphonate	-	345.3	1	0	0	0	0	345.3	1	0.102		0.100
Budesonide	-	151.3	1	151.3	1	0	0	0	0	0.809	0.956	
Bupropion	6	-	174.5	7	0	174.1	6	219.2	1	0	0.698	0.705
Candesartan	-	118.8	5	0	118.8	3	162.6	2	0	0.785	0.678	0.610
Carbamazepine	1	-	174.5	3	0	174.5	3	0	0	0.986	0.747	
Carvedilol	-	276.7	1	0	276.7	1	0	0	0	0.155	0.135	
Cetirizine	-	241.6	2	0	241.6	2	0	0	0	0.108	0.108	
Citalopram	7	-	162.5	12	0	155.8	9	206.1	3	0	0.785	0.336
Clomipramine	10	+	118.8	1	0	118.8	1	0	0	0.364	0.331	
Clozapine	2	-	100.0	1	0	100.0	1	0	0	0.232	0.181	
Diazepam	3	-	145.4	1	0	145.4	1	0	0	0.717	0.582	
Duloxetine	8	-	170.2	8	0	176.9	7	112.8	1	0	0.888	0.763
Enalapril	-	187.2	3	0	187.2	3	0	0	0	0.629	0.914	
Escitalopram	7	-	211.6	9	0	211.6	9	0	0	0.240	0.317	
Ezetimibe	-	61.3	1	61.3	1	0	0	0	0	0.096	0.099	
Flurazepam	3	-	211.6	1	0	211.6	1	0	0	0.364	0.416	
Fluticasone/Salmeterol	-	-	101.3	1	0	101.3	1	0	0	0.250	0.198	
Homeopathic drugs	-	-	205.5	2	205.5	2	0	0	0	0.966	0.969	
Hormonal contraceptive	-	-	184.5	13	112.5	2	375.9	1	141.0	2	187.7	0.626
Hydrochlorothiazide	-	-	165.6	6	188.8	2	157.3	2	112.8	1	313.3	0.196
Ibuprofen	-	-	104.5	1	0	104.5	1	0	0	0.263	0.217	
Insulin	-	-	150.5	3	150.5	1	179.6	2	0	0	1.000	1.000
Iodine	-	-	155.4	5	162.8	2	14.1	1	163.3	2	0	0.433
Irbesartan	-	-	313.3	1	0	0	0	313.3	1	0.123		0.125
Lamotrigine	1	-	173.3	4	0	145.4	3	210.4	1	0	0.790	0.633
Lercanidipine	-	-	153.0	2	0	153.0	2	0	0	0.847	0.708	
Levodopa/benserazide	11	-	246.2	1	0	246.2	1	0	0	0.244	0.306	
Lisinopril	-	-	242.1	1	242.1	1	0	0	0	0.257	0.248	
Lithium	11	-	170.7	6	0	183.0	5	158.4	1	0	0.774	0.913
Loratadine	-	+	187.8	2	187.8	2	0	0	0	0.676	0.530	
Lorazepam	3	-	177.4	12	230.9	2	144.4	10	0	0	0.757	0.126
Losartan	-	-	389.2	1	389.2	1	0	0	0	0.090	0.088	
L-Thyroxin	-	-	180.4	34	147.0	6	183.0	13	194.0	10	223.8	0.195
Macrogol	-	-	100.0	1	0	100.0	1	0	0	0.232	0.181	
Magnesium	-	-	150.4	1	0	0	0	150.4	1	0	0.785	1.000
Metformin	-	-	169.0	2	0	118.8	1	219.2	1	0	0.966	0.331
Metoprolol	-	-	212.0	2	0	211.6	1	212.5	1	0	0.195	0.416
Mirtazapine	5	-	176.9	23	0	176.9	23	0	0	0	0.649	0.662

Moclobemide	4		128.1	2	0	128.1	2	0	0	0.379	0.246
Modafinil	9		240.3	1	0	240.3	1	0	0	0.269	0.358
Nifedipine	-		273.9	1	0	273.9	1	0	0	0.164	0.149
Nitrendipine	-		183.5	1	0	183.5	1	0	0	0.628	0.854
Nortriptyline	10	+	165.6	2	0	165.6	2	0	0	0.881	0.881
Olanzapine	2		164.5	5	0	164.5	5	0	0	0.865	0.490
Opipramol	10	-	229.8	4	0	273.6	3	186.0	1	0	0.103
Oxcarbazepine	1		196.3	1	0	196.3	1	0	0	0.468	0.582
Pancreatin	-		225.6	1	0	0	225.6	1	0	0.304	0.155
Pantoprazol	-		118.8	5	135.3	2	100.0	3	0	0	0.040 0.505 0.030
Paroxetine	7	+	273.9	1	0	273.9	1	0	0	0.164	0.149
Pipamperone	2	-	185.4	6	219.7	1	183.5	5	0	0	0.635 0.322 0.837
Pregabalin	1		196.9	4	0	174.5	3	219.2	1	0	0.311 0.794 0.183
Propranolol	-	-	163.6	1	0	163.6	1	0	0	0.988	0.733
Quetiapine	2	-	164.5	11	0	164.5	11	0	0	0.453	0.763
Ramipril	-		179.0	12	150.3	3	179.0	6	161.1	2	285.1 0.540 0.698 0.702 0.173
Risperidone	2		177.9	6	0	170.0	5	219.2	1	0	0.382 0.990 0.183
Salbutamol	-		212.5	3	0	187.6	2	212.5	1	0	0.499 0.911 0.214
Selen	-		155.3	1	0	0	0	155.3	1	0.892	0.776
Sertraline	7	+	184.7	11	0	184.7	9	165.0	2	0	0.218 0.355 0.610
Simvastatin	-		220.0	2	0	0	126.7	1	313.3	1	0.555 0.790 0.125
Sitagliptin	-		242.1	1	242.1	1	0	0	0	0.257	0.248
St John's wort	11		187.1	1	0	187.1	1	0	0	0.535	0.694
Statins	-		137.7	1	0	137.7	1	0	0	0.586	0.416
Sumatriptan	-		164.6	2	164.6	2	0	0	0	0.829	0.811
Tamoxifen	-	+	264.1	1	0	264.1	1	0	0	0.180	0.198
Tamsulosin	-		389.2	1	389.2	1	0	0	0	0.090	0.088
Tianeptine	10		225.9	2	0	225.9	2	0	0	0.154	0.217
Tranylcypromine	4		227.6	1	0	227.6	1	0	0	0.297	0.386
Trimipramine	10	+	163.6	1	0	163.6	1	0	0	0.988	0.733
Urapidil	-		118.8	1	0	118.8	1	0	0	0.364	0.331
Valproic Acid	1		164.5	1	0	164.5	1	0	0	0.940	0.773
Valsartan	-		135.7	2	0	101.3	1	0	170.2	1	0.486 0.198 0.955
Venlafaxine	8	-	184.1	12	0	183.5	11	210.4	1	0	0.677 0.673 0.248
Vitamine B4	-		73.5	1	0	0	73.5	1	0	0.166	0.131
Vitamine B6	-		112.0	2	0	0	112.0	2	0	0.972	0.279
Vitamine D	-		114.8	6	0	91.8	3	139.8	2	213.8	1 0.162 0.024 0.750 0.394
Zinc	-		105.9	2	61.3	1	0	150.4	1	0	0.170 0.099 1.000
Ziprasidone	2		174.5	1	0	174.5	1	0	0	0.809	0.979

Supplemental table S4. Comparison of activities of secretory acid sphingomyelinase (S-ASM) in the serum of patients and controls depending on comorbidities and smoking status. Comorbidities were assessed according to the structured clinical interview for DSM-IV. Groups: PU unmedicated depressive patients, PM medicated depressive patients, HC healthy controls, PR patients with remitted major depressive disorder; Mann–Whitney U-test and Kruskal-Wallis test with nominal $p < 0.05$ in bold. The following categories were completely absent in our cohort: schizophrenia, schizophreniform disorder, substance abuse (alcohol or other drugs), obsessive-compulsive disorder, posttraumatic stress disorder, somatization disorder.

Comorbidities	median S-ASM activity (fmol/h/μL)												<i>p</i> value			
	all	<i>n</i>	PU	<i>n</i>	PM	<i>n</i>	PR	<i>n</i>	HC	<i>n</i>	all	PU	PM	PR	HC	
Smoking status	smoker	189.1	56	153.2	16	187.2	23	212.5	7	192.2	10	0.011	0.950	0.163	0.036	0.224
	ex-smoker	155.3	49	143.4	14	146.0	9	111.8	10	176.4	16					
	nonsmoker	153.7	124	150.5	33	165.4	34	151.8	22	152.4	35					
Bipolar I	yes	164.5	11	157.2	4	164.5	7	.	0	.	0	0.978	0.800	0.860		
	no	161.2	218	150.5	59	180.8	59	150.4	39	173.2	61					
Bipolar II	yes	206.1	4	135.5	3	276.7	1	.	0	.	0	0.433	0.897	0.135		
	no	161.8	225	150.9	60	174.5	65	150.4	39	173.2	61					
Panic disorder	yes	151.3	15	151.3	9	153.8	6	.	0	.	0	0.672	0.844	0.365		
	no	163.6	213	150.4	54	180.8	59	150.4	39	173.2	61					
Agoraphobia, social phobia, specific phobia, generalized anxiety disorder	yes	179.3	33	178.3	14	184.7	15	154.3	3	163.7	1	0.066	0.120	0.134	0.685	0.865
	no	155.5	193	148.6	49	170.0	49	144.8	35	173.6	60					

Supplemental table S5. Correlation between S-ASM activity and change of the 20 sub-item scores of the STAI trait inventory between inclusion and follow-up (approximately three weeks) in medicated female depressed patients ($n = 32$, rho and p values from Spearman correlations, nominal $p < 0.05$ in bold).

item #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
reversed	x				x	x		x		x		x		x		x		x		
rho	0.474	-0.088	-0.081	-0.073	0.110	0.434	0.575	0.058	0.119	0.497	0.159	0.126	0.409	0.208	0.038	0.540	0.242	0.100	0.450	0.105
<i>p</i>	0.006	0.631	0.658	0.693	0.550	0.013	0.001	0.751	0.515	0.004	0.383	0.493	0.020	0.254	0.837	0.001	0.183	0.587	0.010	0.567