

## Supporting Information

### Profiling of Acylcarnitines in First Episode Psychosis (FEP) before and after Antipsychotic Treatment

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## Table of Contents

<b>Supplementary Tables .....</b>	<b>S3</b>
Table S-1. Identification of Differences in Acylcarnitine Serum Levels ( $\mu$ moles) between First Episode Psychosis (FEP) Patients at Baseline (FEPb) and Control Subjects (CSs).....	S3
Table S-2. Identification of Differences in Acylcarnitine Serum levels ( $\mu$ moles) between FEP Patients at Baseline (FEPb) and FEP Patients after 7 Month Treatment (FEPa) with Antipsychotics	S5
Table S-3. Metabolite Levels in FEP Patients after 7 Month Treatment with Antipsychotics Compared to CSs .....	S7
Table S-4. Comparison of Acylcarnitine, Metabolic and Inflammatory Biomarker Serum Levels between FEP Patients at Baseline (Before Treatment with Antipsychotics) and CSs .....	S9
Table S-5. Effects of 7 Month Treatment with Antipsychotics on Biomarkers Levels in FEP Patients .....	S10
<b>Quality control.....</b>	<b>S11</b>
Metabolite quantitation .....	S11
Limits of detection.....	S11
Table S-6 .....	S11

## Supplementary Tables

Table S-1. Identification of Differences in Acylcarnitine Serum Levels ( $\mu$ moles) between First Episode Psychosis (FEP) Patients at Baseline (FEP<sub>b</sub>) and Control Subjects (CSs)

<i>Biomarkers</i>	CS		FEP <sub>b</sub>		Z-value <sup>a</sup>	p-value <sup>a</sup>	Effect size ( $\eta^2$ )
	Median (min–max) (N=37)	Median (min–max) (N=38)	Median (min–max) (N=37)	Median (min–max) (N=38)			
<b>C0</b> _Carnitine	32.20 (17.30 – 52.70)	33.30 (18.30 – 46.60)			0.17	0.87	0.00
<b>C10</b> _Decanoyl-carnitine	0.28 (0.15 – 0.45)	0.31 (0.17 – 0.87)			- 2.13	0.03	0.06
<b>C10:1</b> _Decenoyl-carnitine	0.13 (0.08 – 0.23)	0.14 (0.06 – 0.30)			- 0.96	0.34	0.01
<b>C10:2</b> _Decadienyl-carnitine	0.06 (0.04 – 0.10)	0.06 (0.04 – 0.09)			0.54	0.59	0.00
<b>C12</b> _Dodecanoyl-carnitine	0.11 (0.06 – 0.18)	0.12 (0.06 – 0.32)			-2.29	0.02	0.07
<b>C12-DC</b> _Dodecanedioyl-carnitine	0.12 (0.11 – 0.14)	0.13 (0.08 – 0.15)			-0.59	0.56	0.01
<b>C12:1</b> _Dodecenoyl-carnitine	0.12 (0.07 – 0.19)	0.13 (0.07 – 0.29)			-2.13	0.03	0.06
<b>C14</b> _Tetradecanoyl-carnitine	0.03 (0.01 – 0.04)	0.03 (0.02 – 0.05)			-2.44	0.02	0.08
<b>C14:1</b> _Tetradecenoyl-carnitine	0.04 (0.02 – 0.11)	0.06 (0.03 – 0.15)			-3.34	<b>0.0008</b>	<b>0.15</b>
<b>C14:1-OH</b> _Hydroxytetradecenoyl-carnitine	0.02 (0.01 – 0.02)	0.02 (0.01 – 0.03)			-2.45	0.01	0.08
<b>C14:2</b> _Tetradecadienyl-carnitine	0.02 (0.01 – 0.05)	0.02 (0.01 – 0.07)			-3.10	0.002	<b>0.13</b>
<b>C14:2-OH</b> _Hydroxytetradecadienyl-carnitine	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.02)			-0.18	0.86	0.00
<b>C16</b> _Hexadecanoyl-carnitine	0.09 (0.04 – 0.12)	0.12 (0.06 – 0.20)			-4.28	<b>0.00002</b>	<b>0.24</b>
<b>C16-OH</b> _Hydroxyhexadecanoyl-carnitine	0.01 (0.01 – 0.03)	0.02 (0.01 – 0.03)			-2.34	0.02	0.07
<b>C16:1</b> _Hexadecenoyl-carnitine	0.02 (0.02 – 0.04)	0.03 (0.02 – 0.06)			-4.51	<b>0.000007</b>	<b>0.27</b>
<b>C16:1-OH</b> _Hydroxyhexadecenoyl-carnitine	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.02)			-3.42	<b>0.0006</b>	<b>0.16</b>
<b>C16:2</b> _Hexadecadienylcarnitine	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.02)			-1.53	0.13	0.03
<b>C16:2-OH</b> _Hydroxyhexadecadienyl-carnitine	0.03 (0.02 – 0.04)	0.03 (0.02 – 0.04)			1.08	0.28	0.02
<b>C18</b> _Octadecanoyl-carnitine	0.04 (0.02 – 0.07)	0.05 (0.03 – 0.09)			-2.92	0.004	0.11
<b>C18:1</b> _Octadecenoyl-carnitine	0.09 (0.05 – 0.15)	0.13 (0.05 – 0.23)			-4.86	<b>0.000001</b>	<b>0.32</b>
<b>C18:1-OH</b> _Hydroxyoctadecenoyl-carnitine	0.02 (0.01 – 0.05)	0.03 (0.02 – 0.05)			-2.02	0.04	0.05
<b>C18:2</b> _Octadecadienyl-carnitine	0.03 (0.01 – 0.05)	0.04 (0.02 – 0.07)			-3.68	<b>0.0002</b>	<b>0.18</b>
<b>C2</b> _Acetylcarnitine	3.96 (1.78 – 5.96)	4.33 (1.73 – 14.00)			-0.67	0.50	0.01

<b>C3</b> _Propionyl-carnitine	0.31 (0.13 – 0.61)	0.23 (0.14 – 0.49)	3.72	<b>0.0002</b>	<b>0.19</b>
<b>C3-DC(C4-OH)</b> _Malonyl-carnitine (Hydroxy-butyrylcarnitine)	0.04 (0.03 – 0.07)	0.05 (0.03 – 0.25)	-2.95	0.003	0.12
<b>C5-OH(C3-DC-M)</b> _Hydroxyvaleryl-carnitine (Methyl-malonylcarnitine)	0.06 (0.04 – 0.09)	0.06 (0.04 – 0.11)	-0.29	0.78	0.00
<b>C3-OH</b> _Hydroxy-propionyl-carnitine	0.04 (0.03 – 0.05)	0.04 (0.03 – 0.07)	0.88	0.38	0.01
<b>C3:1</b> _Propenoyl-carnitine	0.03 (0.02 – 0.04)	0.03 (0.02 – 0.05)	-0.80	0.42	0.01
<b>C4</b> _Butyryl-carnitine	0.18 (0.12 – 0.30)	0.17 (0.10 – 0.32)	2.63	0.008	0.09
<b>C4:1</b> _Butenylcarnitine	0.05 (0.03 – 0.06)	0.05 (0.03 – 0.06)	-1.71	0.09	0.04
<b>C6(C4:1-DC)</b> _Hexanoylcarnitine (Fumaryl-carnitine)	0.03 (0.02 – 0.04)	0.03 (0.02 – 0.05)	-3.43	<b>0.0006</b>	<b>0.16</b>
<b>C5</b> _Valeryl-carnitine	0.17 (0.10 – 0.29)	0.14 (0.10 – 0.31)	2.73	0.006	0.10
<b>C5-DC(C6-OH)</b> _Glutaryl-carnitine (Hydroxyhexanoyl-carnitine)	0.02 (0.01 – 0.04)	0.03 (0.02 – 0.04)	-2.11	0.04	0.06
<b>C5-M-DC</b> _Methylglutaryl-carnitine	0.04 (0.03 – 0.06)	0.04 (0.03 – 0.06)	-0.44	0.66	0.00
<b>C5:1</b> _Tiglylcarnitine	0.08 (0.05 – 0.12)	0.08 (0.05 – 0.11)	-0.17	0.87	0.00
<b>C5:1-DC</b> _Glutaconyl-carnitine	0.03 (0.02 – 0.04)	0.03 (0.02 – 0.03)	-2.23	0.03	0.07
<b>C6:1</b> _Hexenoyl-carnitine	0.009 (0.006 – 0.01)	0.01 (0.007 – 0.01)	-1.27	0.21	0.02
<b>C7-DC</b> _Pimelylcarnitine	0.03 (0.02 – 0.04)	0.03 (0.02 – 0.06)	-1.75	0.08	0.04
<b>C8</b> _Octanoylcarnitine	0.13 (0.09 – 0.20)	0.14 (0.10 – 0.33)	-1.48	0.14	0.03
<b>C9</b> _Nonaylcarnitine	0.06 (0.03 – 0.12)	0.05 (0.03 – 0.08)	2.88	0.004	0.11
<b>H1</b> _Hexose	3907.00 (2335– 5533)	4291.50 (2802– 5918)	-2.59	0.01	0.09

Z-adjusted values according to Mann-Whitney *U*-test (FEP<sub>b</sub> compared to CSs).

p-values less than or equal to 0.001 after Bonferroni correction (bolded) were considered statistically significant. Effect sizes were interpreted as small, moderate, and large, with corresponding eta-squared ranging from 0.01 – 0.05, 0.06 – 0.13, and  $\geq 0.14$ , respectively.

**Table S-2. Identification of Differences in Acylcarnitine Serum levels ( $\mu$ moles) between FEP Patients at Baseline (FEPb) and FEP Patients after 7 Month Treatment (FEPa) with Antipsychotics**

<i>Biomarkers</i>	FEP <sub>b</sub>	FEP <sub>a</sub>	Z-value <sup>b</sup>	p-value <sup>b</sup>	Effect size ( $\eta^2$ )
	Median (min–max) (N=36)	Median (min– max) (N=36)			
<b>C0_Carnitine</b>	33.30 (18.30 – 46.60)	30.35 (15.80 – 58.40)	0.32	0.75	0.00
<b>C10_</b> Decanoyl-carnitine	0.31 (0.17 – 0.87)	0.22 (0.12 – 1.08)	1.43	0.15	0.03
<b>C10:1_</b> Decenoyl-carnitine	0.14 (0.06 – 0.30)	0.13 (0.06 – 0.31)	0.80	0.42	0.01
<b>C10:2_</b> Decadienyl-carnitine	0.06 (0.04 – 0.09)	0.05 (0.04 – 0.10)	0.72	0.47	0.01
<b>C12_</b> Dodecanoyl-carnitine	0.12 (0.06 – 0.32)	0.09 (0.04 – 0.28)	1.71	0.09	0.04
<b>C12-DC_</b> Dodecanedioyl- carnitine	0,13 (0.08 – 0.15)	0.12 (0.10 – 0.16)	0.45	0.65	0.00
<b>C12:1_</b> Dodecenoyl-carnitine	0.13 (0.07 – 0.29)	0.12 (0.05 – 0.27)	1.63	0.10	0.04
<b>C14_</b> Tetradecanoyl-carnitine	0.03 (0.02 – 0.05)	0.02 (0.01 – 0.04)	2.59	0.01	0.09
<b>C14:1_</b> Tetradecenoyl- carnitine	0.06 (0.03 – 0.15)	0.04 (0.02 – 0.16)	2.53	0.01	0.09
<b>C14:1-OH_</b> Hydroxytetra- decenoyl-carnitine	0.02 (0.01 – 0.03)	0.01 (0.01 – 0.03)	2.29	0.02	0.07
<b>C14:2_</b> Tetradecadienyl- carnitine	0.02 (0.01 – 0.07)	0.02 (0.01 – 0.04)	2.75	0.006	0.11
<b>C14:2-OH_</b> Hydroxytetra- decadienyl-carnitine	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.02)	1.65	0.10	0.04
<b>C16_</b> Hexadecanoyl-carnitine	0.12 (0.06 – 0.20)	0.08 (0.04 – 0.15)	3.40	<b>0.0007</b>	<b>0.16</b>
<b>C16-OH_</b> Hydroxyhexa- decanoyl-carnitine	0.02 (0.01 – 0.03)	0.01 (0.01 – 0.03)	1.76	0.08	0.04
<b>C16:1_</b> Hexa-decenoyl- carnitine	0.03 (0.02 – 0.06)	0.02 (0.01 – 0.05)	3.05	0.002	<b>0.13</b>
<b>C16:1-OH_</b> Hydroxyhexa- decenoyl-carnitine	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.02)	2.62	0.009	0.10
<b>C16:2_</b> Hexadeca- dienylcarnitine	0.01 (0.01 – 0.02)	0.01 (0.01 – 0.02)	2.47	0.01	0.09
<b>C16:2-OH_</b> Hydroxyhexa- decadienyl-carnitine	0.03 (0.02 – 0.04)	0.03 (0.02 – 0.04)	0.70	0.48	0.01
<b>C18_</b> Octadecanoyl-carnitine	0.05 (0.03 – 0.09)	0.04 (0.02 – 0.06)	2.70	0.007	0.10
<b>C18:1_</b> Octadecenoyl- carnitine	0.13 (0.05 – 0.23)	0.08 (0.04 – 0.17)	4.13	<b>0.00004</b>	<b>0.24</b>
<b>C18:1-OH_</b> Hydroxyocta- decenoyl-carnitine	0.03 (0.02 – 0.05)	0.02 (0.01 – 0.05)	1.38	0.17	0.03
<b>C18:2_</b> Octadecadienyl- carnitine	0.04 (0.02 – 0.07)	0.03 (0.02 – 0.05)	3.86	<b>0.0001</b>	<b>0.21</b>
<b>C2_</b> Acetylcarnitine	4.33	4.11	0.66	0.51	0.01

	(1.73 – 14.00)	(2.24 – 7.72)			
<b>C3</b> _Propionyl-carnitine	0.23 (0.14 – 0.49)	0.30 (0.14 – 0.62)	3.22	<b>0.001</b>	<b>0.15</b>
<b>C3-DC(C4-OH)</b> _Malonyl-carnitine (Hydroxy-butyrylcarnitine)	0.05 (0.03 – 0.25)	0.04 (0.03 – 0.07)	2.69	0.007	0.10
<b>C5-OH(C3-DC-M)</b> _Hydroxyvaleryl-carnitine (Methyl-malonylcarnitine)	0.06 (0.04 – 0.11)	0.06 (0.05 – 0.12)	1.11	0.27	0.02
<b>C3-OH</b> _Hydroxy-propionyl-carnitine	0.04 (0.03 – 0.07)	0.04 (0.03 – 0.07)	0.05	0.96	0.00
<b>C3:1</b> _Propenoyl-carnitine	0.03 (0.02 – 0.05)	0.03 (0.02 – 0.06)	1.02	0.31	0.02
<b>C4</b> _Butyryl-carnitine	0.17 (0.10 – 0.32)	0.17 (0.10 – 0.31)	0.78	0.44	0.01
<b>C4:1</b> _Butenylcarnitine	0.05 (0.03 – 0.06)	0.05 (0.03 – 0.07)	0.86	0.39	0.01
<b>C6(C4:1-DC)</b> _Hexanoylcarnitine (Fumaryl-carnitine)	0.03 (0.02 – 0.05)	0.02 (0.01 – 0.06)	2.22	0.03	0.07
<b>C5</b> _Valeryl-carnitine	0.14 (0.10 – 0.31)	0.16 (0.10 – 0.39)	2.51	0.01	0.09
<b>C5-DC(C6-OH)</b> _Glutaryl-carnitine (Hydroxyhexanoyl-carnitine)	0.03 (0.02 – 0.04)	0.02 (0.01 – 0.04)	2.37	0.02	0.09
<b>C5-M-DC</b> _Methylglutaryl-carnitine	0.04 (0.03 – 0.06)	0.04 (0.02 – 0.05)	1.00	0.32	0.01
<b>C5:1</b> _Tiglylcarnitine	0.08 (0.05 – 0.11)	0.07 (0.04 – 0.12)	1.05	0.30	0.02
<b>C5:1-DC</b> _Glutaconyl-carnitine	0.03 (0.02 – 0.03)	0.02 (0.01 – 0.04)	0.92	0.36	0.01
<b>C6:1</b> _Hexenoyl-carnitine	0.01 (0.007 – 0.01)	0.009 (0.006 – 0.01)	1.43	0.15	0.03
<b>C7-DC</b> _Pimelylcarnitine	0.03 (0.02 – 0.06)	0.03 (0.01 – 0.05)	2.16	0.03	0.07
<b>C8</b> _Octanoylcarnitine	0.14 (0.10 – 0.33)	0.12 (0.07 – 0.42)	1.18	0.24	0.02
<b>C9</b> _Nonanoylcarnitine	0.05 (0.03 – 0.08)	0.06 (0.04 – 0.09)	1.83	0.07	0.05
<b>H1</b> _Hexose	4291.50 (2802– 5918)	4054.50 (2846 – 7189)	0.93	0.35	0.01

Z-values according to Wilcoxon matched pairs test (FEP<sub>b</sub> compared to FEP<sub>a</sub>).

p-values less than or equal to 0.001 after Bonferroni correction (bolded) were considered statistically significant. Effect sizes were interpreted as small, moderate, and large, with corresponding eta-squared ranging from 0.01 – 0.05, 0.06 – 0.13, and  $\geq 0.14$ , respectively.

**Table S-3. Metabolite Levels in FEP Patients after 7 Month Treatment with Antipsychotics Compared to CSs**

<i>Biomarkers</i>	$\beta$	$\beta$ (95 % CI)	t-value	p-value
<b>C0</b> _Carnitine	-0.11	-0.34, 0.13	-0.93	0.36
<b>C10</b> _Decanoylcarnitine	-0.03	-0.27, 0.20	-0.29	0.77
<b>C10:1</b> _Decenoylcarnitine	-0.03	-0.26, 0.21	-0.22	0.83
<b>C10:2</b> _Decadienylcarnitine	-0.16	-0.39, 0.08	-1.35	0.18
<b>C12</b> _Dodecanoylcarnitine	-0.10	-0.33, 0.13	-0.84	0.40
<b>C12-DC</b> _Dodecanedioylcarnitine	-0.02	-0.26, 0.23	-0.14	0.89
<b>C12:1</b> _Dodecenoylcarnitine	-0.05	-0.29, 0.19	-0.40	0.69
<b>C14</b> _Tetradecanoylcarnitine	-0.16	-0.39, 0.08	-1.31	0.20
<b>C14:1</b> _Tetradecenoylcarnitine	-0.10	-0.33, 0.13	-0.89	0.38
<b>C14:1-OH</b> _Hydroxytetradecenoylcarnitine	-0.11	-0.34, 0.13	-0.92	0.36
<b>C14:2</b> _Tetradecadienylcarnitine	-0.16	-0.38, 0.07	-1.40	0.17
<b>C14:2-OH</b> _Hydroxytetradecadienylcarnitine	-0.22	-0.45, 0.02	-1.86	0.07
<b>C16</b> _Hexadecanoylcarnitine	-0.03	-0.27, 0.20	-0.28	0.79
<b>C16-OH</b> _Hydroxyhexadecanoylcarnitine	0.07	-0.17, 0.31	0.59	0.56
<b>C16:1</b> _Hexadecenoylcarnitine	0.003	-0.24, 0.24	0.02	0.98
<b>C16:1-OH</b> _Hydroxyhexadecenoylcarnitine	0.06	-0.19, 0.30	0.45	0.65
<b>C16:2</b> _Hexadecadienylcarnitine	-0.18	-0.42, 0.05	-1.59	0.12
<b>C16:2-OH</b> _Hydroxyhexadecadienylcarnitine	-0.08	-0.31, 0.16	-0.63	0.53
<b>C18</b> _Octadecanoylcarnitine	0.001	-0.24, 0.24	0.01	0.99
<b>C18:1</b> _Octadecenoylcarnitine	-0.07	-0.31, 0.17	-0.61	0.54
<b>C18:1-OH</b> _Hydroxyoctadecenoylcarnitine	-0.03	-0.26, 0.21	-0.23	0.82
<b>C18:2</b> _Octadecadienylcarnitine	-0.08	-0.31, 0.14	-0.74	0.46
<b>C2</b> _Acetylcarnitine	0.13	-0.10, 0.36	1.11	0.27
<b>C3</b> _Propionylcarnitine	-0.08	-0.31, 0.16	-0.64	0.53
<b>C3-DC(C4-OH)</b> _Malonylcarnitine (Hydroxybutyrylcarnitine)	-0.01	-0.24, 0.23	-0.04	0.97
<b>C5-OH(C3-DC-M)</b> _Hydroxyvalerylcarnitine (Methylmalonylcarnitine)	0.07	-0.17, 0.30	0.58	0.56
<b>C3-OH</b> _Hydroxypropionylcarnitine	-0.02	-0.26, 0.22	0.20	0.84
<b>C3:1</b> _Propenoylcarnitine	0.02	-0.21, 0.25	0.17	0.86
<b>C4</b> _Butyrylcarnitine	-0.22	-0.45, 0.02	-1.84	0.07
<b>C4:1</b> _Butenylcarnitine	0.12	-0.11, 0.35	1.02	0.31
<b>C6(C4:1-DC)</b> _Hexanoylcarnitine (Fumaryl carnitine)	-0.01	-0.25, 0.23	-0.10	0.92
<b>C5</b> _Valerylcarnitine	-0.01	-0.24, 0.23	-0.06	0.95
<b>C5-DC(C6-OH)</b> _Glutaryl carnitine (Hydroxyhexanoylcarnitine)	-0.09	-0.32, 0.14	-0.76	0.45
<b>C5-M-DC</b> _Methylglutaryl carnitine	-0.09	-0.33, 0.15	-0.74	0.46
<b>C5:1</b> _Tiglylcarnitine	-0.08	-0.32, 0.16	-0.68	0.50
<b>C5:1-DC</b> _Glutaconyl carnitine	0.02	-0.22, 0.26	0.15	0.88
<b>C6:1</b> _Hexenoylcarnitine	-0.04	-0.27, 0.20	-0.31	0.76
<b>C7-DC</b> _Pimelylcarnitine	-0.17	-0.40, 0.06	-1.45	0.15
<b>C8</b> _Octanoylcarnitine	-0.02	-0.26, 0.22	-0.15	0.88
<b>C9</b> _Nonaylcarnitine	-0.13	-0.37, 0.11	-1.08	0.28
<b>H1</b> _Hexose	0.20	-0.03, 0.43	1.72	0.09

$\beta$  – regression coefficients, CI – confidence intervals,

p-values (derived from GLM analysis) – significance values of  $\log_{10}$ -transformed acylcarnitines levels in first-episode patients group after seven-month treatment with antipsychotics compared to control subjects, adjusted for gender, age and smoking status.

**Table S-4. Comparison of Acylcarnitine, Metabolic and Inflammatory Biomarker Serum Levels between FEP Patients at Baseline (Before Treatment with Antipsychotics) and CSs**

<i>Biomarkers</i>	$\beta$	$\beta$ (95 % CI)	t-value	p-value
<i>Inflammatory markers</i>				
Interleukin (IL)-4	0.38	0.15, 0.61	3.36	0.001
<b>IL-6</b>	0.40	0.18, 0.63	3.53	0.0008
<b>IL-1<math>\beta</math></b>	-0.29	-0.52, -0.07	-2.60	0.01
Epidermal growth factor (EGF)	0.77	0.61, 0.93	9.75	<0.00000001
<b>Ferritin</b>	0.29	0.11, 0.48	3.14	0.003
Plasminogen activator inhibitor-1 ( <b>PAI-1</b> )	0.28	0.06, 0.49	2.53	0.01
<i>Metabolic markers</i>				
<b>Resistin</b>	0.30	0.07, 0.54	2.55	0.01
<b>Leptin</b>	-0.29	-0.51, -0.07	-2.65	0.01
<i>Acylcarnitines</i>				
<b>C10</b> _Decanoylcarnitine	0.34	0.11, 0.57	2.96	0.004
<b>C12</b> _Dodecanoylcarnitine	0.33	0.09, 0.56	2.79	0.007
<b>C12:1</b> _Dodecenoylcarnitine	0.30	0.07, 0.53	2.60	0.01
<b>C14</b> _Tetradecanoylcarnitine	0.34	0.11, 0.57	2.99	0.004
<b>C14:1</b> _Tetradecenoylcarnitine	0.47	0.25, 0.68	4.37	0.00005
<b>C14:1-OH</b> _Hydroxytetradecenoylcarnitine	0.34	0.10, 0.57	2.87	0.006
<b>C14:2</b> _Tetradecadienylcarnitine	0.44	0.22, 0.66	3.95	0.0002
<b>C16</b> _Hexadecanoylcarnitine	0.49	0.28, 0.71	4.65	0.00002
<b>C16:1</b> _Hexadecenoylcarnitine	0.56	0.36, 0.75	5.73	0.0000003
<b>C16:1-OH</b> _Hydroxyhexadecenoylcarnitine	0.46	0.24, 0.67	4.27	0.00007
<b>C18</b> _Octadecanoylcarnitine	0.34	0.11, 0.57	2.90	0.005
<b>C18:1</b> _Octadecenoylcarnitine	0.56	0.36, 0.76	5.56	0.000001
<b>C18:2</b> _Octadecadienylcarnitine	0.44	0.23, 0.66	4.08	0.0001
<b>C2</b> _Acetylcarnitine	0.25	0.03, 0.47	2.23	0.03
<b>C3</b> _Propionylcarnitine	-0.43	-0.64, -0.21	-4.00	0.0002
<b>C3-DC(C4-OH)</b> _Malonylcarnitine(Hydroxybutyrylcarnitine)	0.36	0.14, 0.59	3.20	0.002
<b>C4</b> _Butyrylcarnitine	-0.31	-0.53, -0.09	-2.75	0.008
<b>C6(C4:1-DC)</b> _Hexanoylcarnitine(Fumaryl carnitine)	0.45	0.23, 0.67	4.02	0.0002
<b>C5</b> _Valeryl carnitine	-0.25	-0.48, -0.02	-2.18	0.03
<b>C5-DC(C6-OH)</b> _Glutaryl carnitine(Hydroxyhexanoylcarnitine)	0.23	0.003, 0.46	2.02	0.047
<b>C7-DC</b> _Pimelylcarnitine	0.26	0.02, 0.49	2.18	0.03
<b>C8</b> _Octanoylcarnitine	0.25	0.01, 0.49	2.10	0.04
<b>C9</b> _Nonaylcarnitine	-0.35	-0.58, -0.12	-3.00	0.004
<b>H1</b> _Hexose	0.27	0.05, 0.50	2.41	0.02

$\beta$  – regression coefficients, CI – confidence intervals, p-values (derived from GLM analysis) – significance values of  $\log_{10}$ -transformed biomarkers serum levels with disease, adjusted for gender, age and smoking status.

**Table S-5. Effects of 7 Month Treatment with Antipsychotics on Biomarkers Levels in FEP Patients**

<i>Biomarkers</i>	$\beta$	$\beta$ (95 % CI)	t-value	p-value
<i>Inflammatory markers</i>				
Interleukin (IL)-2	0.68	0.41, 0.94	5.14	0.000003
IL-4	0.44	0.13, 0.74	2.89	0.005
Interferon- $\gamma$ (INF- $\gamma$ )	0.35	0.04, 0.66	2.23	0.03
Epidermal growth factor (EGF)	0.75	0.55, 0.96	7.37	<0.00000001
<i>Metabolic markers</i>				
<b>C-peptide</b>	-0.31	-0.63, 0.00	-2.01	0.048
<b>Leptin</b>	-0.34	-0.62, -0.05	-2.36	0.02
<b>Body mass index (BMI)</b>	-0.52	-0.83, -0.21	-3.36	0.001
<i>Acylcarnitines</i>				
<b>C14</b> _Tetradecanoylcarnitine	0.39	0.08, 0.71	2.51	0.01
<b>C14:1</b> _Tetradecanoylcarnitine	0.42	0.12, 0.72	2.81	0.007
<b>C14:1-OH</b> _Hydroxytetradecenoylcarnitine	0.38	0.06, 0.70	2.38	0.02
<b>C14:2</b> _Tetradecadienylcarnitine	0.45	0.15, 0.75	2.98	0.004
<b>C16</b> _Hexadecanoylcarnitine	0.47	0.18, 0.77	3.19	0.002
<b>C16:1</b> _Hexadecenoylcarnitine	0.46	0.18, 0.74	3.25	0.002
<b>C16:1-OH</b> _Hydroxyhexadecenoylcarnitine	0.42	0.11, 0.72	2.73	0.008
<b>C18</b> _Octadecanoylcarnitine	0.41	0.08, 0.73	2.52	0.01
<b>C18:1</b> _Octadecenoylcarnitine	0.54	0.27, 0.81	3.98	0.0002
<b>C18:1-OH</b> _Hydroxyoctadecenoylcarnitine	0.36	0.04, 0.68	2.26	0.03
<b>C18:2</b> _Octadecadienylcarnitine	0.45	0.16, 0.74	3.13	0.003
<b>C3</b> _Propionylcarnitine	-0.39	-0.70, -0.07	-2.44	0.02
<b>C3-DC(C4-OH)</b> _Malonylcarnitine(Hydroxybutyrylcarnitine)	0.41	0.12, 0.70	2.81	0.007

$\beta$  – regression coefficients, CI – confidence intervals, p-values (derived from GLM repeated measure) – significance values of log<sub>10</sub>-transformed biomarkers serum levels in patients group before treatment compared to biomarkers values measured after seven-month treatment with antipsychotics, adjusted for gender, and smoking status.

## Quality control

### Metabolite quantitation

Biocrates Absolute/DQ™ p180 kit (Biocrates Life Sciences AG, Innsbruck, Austria) enables the measurement of 188 endogenous metabolites and 45 metabolite ratios using a combination of flow injection analysis and liquid chromatograph tandem mass spectrometry technique. The assay allows simultaneous quantification of 188 metabolites, including 40 acylcarnitines, 21 amino acids, 21 biogenic amines, level of hexoses, 15 sphingolipids and 90 glycerophospholipids. The kit has been validated according to FDA guidelines and Biocrates company holds a ISO 9001:2008 certification of quality. Stable isotope standards are used for the quantification of biogenic amines and amino acids, using 7-point calibration curve. Acylcarnitines, phospho- and sphingolipids, and hexose were quantified by their relative intensity over the chosen isotopically labeled internal standard. In addition, 3 quality control standards are measured to ensure the normalization of signal intensities during inter-plate measurements. The metabolite concentrations were calculated linearly using a combination of Analyst (ABSciex, Framingham, USA) and MetIDQ (Biocrates Life Sciences AG, Innsbruck, Austria) software. This is done for amino acids and biogenic amines in the LC mode. Due to lack of isotopic standards for lipids and acylcarnitines in the FIA mode the results are classified as semi-quantitative.

### Limits of detection

The absolute minimum limit of detection (LOD) for a metabolite is largely dependent on the sensitivity of the mass-spectrometer and the ionization of a metabolite. LODs, lower limit of quantification (LLOQ) and upper limit of quantification (ULOQ) for selected metabolites are given in table S6.

**Table S-6**

Analyte		Quality Type (FIA)		Evaluated Quantification		
MetIDQ Short Name	Biochemical Name	Valid	Semi	LOD (µM)	LLOQ (µM)	ULOQ (µM)
C0	Carnitine	X		4	5	120
C10	Decanoyl-carnitine	X		0.16	0.3	6
C10:1	Decenoyl-carnitine		X	0.12		

C10:2	Decadienyl-carnitine		X	0.04		
C12	Dodecanoyl-carnitine	X		0.057	0.4	12
C12-DC	Dodecanedioyl-carnitine		X	0.2		
C12:1	Dodecenoyl-carnitine		X	0.2		
C14	Tetradecanoyl-carnitine	X		0.03	0.4	6
C14:1	Tetradecenoyl-carnitine		X	0.015		
C14:1-OH	Hydroxytetra-decenoyl-carnitine		X	0.015		
C14:2	Tetradecadienyl-carnitine		X	0.012		
C14:2-OH	Hydroxytetra-decadienyl-carnitine		X	0.015		
C16	Hexadecanoyl-carnitine	X		0.018	0.4	12
C16-OH	Hydroxyhexa-decanoyl-carnitine		X	0.015		
C16:1	Hexa-decenoyl-carnitine		X	0.06		
C16:1-OH	Hydroxyhexa-decenoyl-carnitine		X	0.02		
C16:2	Hexadeca-dienylcarnitine		X	0.008		
C16:2-OH	Hydroxyhexa-decadienyl-carnitine		X	0.03		
C18	Octadecanoyl-carnitine	X		0.02	0.4	6
C18:1	Octadecenoyl-carnitine		X	0.04		
C18:1-OH	Hydroxyocta-decenoyl-carnitine		X	0.023		
C18:2	Octadecadienyl-carnitine		X	0.009		
C2	Acetylcarnitine	X		0.15	0.4	35
C3	Propionyl-carnitine	X		0.08	0.4	15
C3-DC(C4-OH)	Malonyl-carnitine (Hydroxy-butyrilcarnitine)		X	0.09		
C5-OH(C3-DC-M)	Hydroxyvaleryl-carnitine (Methyl-malonylcarnitine)		X	0.1		
C3-OH	Hydroxy-propionyl-carnitine		X	0.05		
C3:1	Propenoyl-carnitine		X	0.03		

C4	Butyryl-carnitine	X		0.03	0.4	12
C4:1	Butenylcarnitine		X	0.03		
C6(C4:1-DC)	Hexanoylcarnitine (Fumaryl-carnitine)	X		0.08	0.2	6
C5	Valeryl-carnitine	X		0.04	0.4	12
C5-DC(C6-OH)	Glutaryl-carnitine (Hydroxyhexanoyl-carnitine)		X	0.035		
C5-M-DC	Methylglutaryl-carnitine		X	0.06		
C5:1	Tiglylcarnitine		X	0.04		
C5:1-DC	Glutaconyl-carnitine		X	0.015		
C6:1	Hexenoyl-carnitine		X	0.035		
C7-DC	Pimelylcarnitine		X	0.035		
C8	Octanoylcarnitine	X		0.17	0.2	8
C9	Nonaylcarnitine		X	0.04		