

Supplementary Table 1 Clinical characteristics of the recruited patients and healthy controls

Characteristics	Patients	HC	P-value	FE	2-3 episodes	4-6 episodes	Over 6 episodes	P-value
N	327	159		89	110	80	48	
Male (%)	147 (45.0%)	76 (47.8%)	0.555	44 (49.4%)	47 (42.7%)	31 (38.8%)	25 (52.1%)	0.366
Age (years)	32.70±10.40	32.86±10.09	0.879	28.97±11.22	31.13±8.95	35.17±8.53	39.13±11.04	< 0.001
Range	15-59	15-60	-	15-59	15-57	19-56	16-57	-
BMI (kg/m²)	21.97±3.69	22.10±2.88	0.684	20.59±2.89	21.67±3.53	22.87±3.92	23.49±4.03	< 0.001
Duration of disease (years)	7.8±7.7	-	-	1.5±1.9	6.8±6.3	9.9±5.5	16.8±9.0	< 0.001
Chlorpromazine-equivalent dose	385.4±186.1	-	-	382.0±175.0	419.5±191.6	354.6±189.2	359.0±179.2	0.088
AAPDs (n, %)								
Risperidone	74 (22.63%)	-	-	23 (25.84%)	20 (18.18%)	17 (21.25%)	14 (29.17%)	-
Olanzapine	72 (22.02%)	-	-	26 (29.21%)	28 (25.45%)	12 (15.00%)	6 (12.50%)	-
Aripiprazole	28 (8.56%)	-	-	4 (4.49%)	14 (12.73%)	7 (8.75%)	3 (6.25%)	-
Amisulpride	16 (4.89%)	-	-	8 (8.99%)	4 (3.64%)	3 (3.75%)	1 (2.08%)	-
Clozapine	16 (4.89%)	-	-	1 (1.12%)	2 (1.82%)	9 (11.25%)	4 (8.33%)	-
Others	23 (7.03%)	-	-	6 (6.74%)	12 (10.91%)	4 (5.00%)	1 (2.08%)	-
Combination treatment	98 (29.97%)	-	-	21 (23.60%)	30 (27.27%)	28 (35.00%)	19 (39.58%)	-

Values represent as mean ± standard deviation; HC, healthy controls; FE, first episode; BMI, body mass index.

Supplementary Table 2 Demographic characteristics of patients from each clinical site

Characteristics	A	B	C	p
n	43	228	56	
Male (%)	23 (53.5%)	104 (45.6%)	20 (35.7%)	0.198
Age (years)	25.30±7.94	32.94±10.24	37.41±9.76	<0.001
BMI (kg·m ⁻²)	20.08±2.72	21.91±3.70	23.30±3.70	<0.001
Duration of disease (years)	3.2±4.6	7.5±7.4	12.5±8.7	<0.001
Chlorpromazine-equivalent dose	454.7±181.2	396.8±188.3	281.7±135.6	<0.001
Number of episodes				<0.001
FE	26 (60.5%)	61 (26.8%)	2 (3.6%)	
2-3 episodes	11 (25.6%)	84 (36.8%)	15 (26.8%)	
4-6 episodes	4 (9.3%)	54 (23.7%)	22 (39.3%)	
Over 6 episodes	2 (4.7%)	29 (12.7%)	17 (30.4%)	

A. the Second Xiangya Hospital of Central South University; B. the Second People's Hospital of Hunan Province; C. Changsha Psychiatric Hospital.

Supplementary Table 3 Changes in membrane fatty acid levels of patient subgroups after antipsychotic treatment.

Fatty acids	FE				2-3 episodes					4-6 episodes				Over 6 episodes						
	SZ-0w	SZ-4w	Z	p	SZ-0w	SZ-4w	Z	p	SZ-0w	SZ-4w	Z	p	SZ-0w	SZ-4w	Z	p				
C16:0	472.85±22.09	652.3±32.11	-7.38	<0.001	↑	485.04±19.62	597.96±24.49	-6.041	<0.001	↑	593.09±32.16	539.73±29.89	-2.168	0.030	↓	611.40±45.52	473.85±32.18	-3.908	<0.001	↓
C18:0	244.7±12.14	341.14±16.43	-7.64	<0.001	↑	242.18±9.95	286.25±11.67	-4.943	<0.001	↑	285.51±14.9	260.32±14.38	-2.628	0.009	↓	297.92±19.8	237.97±17.82	-3.313	<0.001	↓
C18:1n9c	289.54±12.83	429.66±22.47	-7.51	<0.001	↑	297.45±13.16	360.81±15.45	-5.259	<0.001	↑	369.03±22.25	338.93±19.44	-1.573	0.116	ns	371.03±28.53	277.61±22.64	-3.846	<0.001	↓
C18:2n6c	288.67±15.14	458.88±25.94	-7.12	<0.001	↑	302.28±15.12	382.69±17.51	-4.854	<0.001	↑	390.59±22.4	373.07±20.55	-0.321	0.748	ns	390.12±38.51	317.28±29.48	-2.585	0.010	↓
C20:3n6	10.42±0.65	19.99±1.28	-7.58	<0.001	↑	12.04±0.85	15.11±0.99	-4.138	<0.001	↑	15.16±1.29	15.15±1.14	-0.377	0.707	ns	16.35±1.76	12.98±1.42	-2.831	0.005	↓
C20:4n6	170.17±8.44	246.43±12.17	-7.42	<0.001	↑	179.47±8.52	209.55±9.02	-3.814	<0.001	↑	239.66±13.78	188.33±10.14	-5.079	<0.001	↓	231.84±18.36	172.77±14.83	-4.400	<0.001	↓
C20:5n3	2.59±0.34	6.45±0.56	-7.98	<0.001	↑	2.65±0.18	3.36±0.28	-3.434	<0.001	↑	4.94±0.76	3.27±0.37	-4.048	<0.001	↓	4.41±0.40	2.95±0.33	-4.677	<0.001	↓
C22:4n6	25.42±1.41	41.04±1.99	-7.96	<0.001	↑	27.43±1.57	30.81±1.53	-3.276	0.001	↑	37.51±2.65	28.69±1.93	-5.621	<0.001	↓	38.25±3.20	27.45±2.81	-4.041	<0.001	↓
C22:5n3	18.53±1.54	31.17±2.17	-7.99	<0.001	↑	20.42±1.52	24.34±2.03	-4.213	<0.001	↑	26.96±2.95	20.81±2.01	-4.441	<0.001	↓	24.12±2.69	17.81±1.93	-4.339	<0.001	↓
C22:6n3	29.52±1.65	48.70±2.12	-8.03	<0.001	↑	32.73±1.59	37.39±1.75	-3.440	<0.001	↑	45.34±3.49	33.09±2.45	-5.756	<0.001	↓	42.26±3.81	29.63±2.93	-4.810	<0.001	↓

Mean±SEM; FE, first episode; Wilcoxon Signed Ranks Test.

Supplementary Table 4 Clinical characteristics of patients in more-responsive and less-responsive subgroups

Characteristics	More-responsive				Less-responsive			
	0-5 yr(s)	5-10 yrs	>10 yrs	Total	0-5 yr(s)	5-10 yrs	>10 yrs	Total
N	141	37	21	199	18	45	65	128
Male (%)	69 (48.9%)	15 (40.5%)	7(33.3%)	91 (45.7%)	9 (50.0%)	17(37.8%)	30 (46.2%)	56 (43.8%)
Age (years)	28.49±9.68	29.59±7.29	42.38±8.58	30.16±10.06	28.89±7.71	32.87±6.88	41.43±9.39	36.66±9.70
Range	15-59	20-53	29-57	15-59	16-46	19-49	18-57	16-57
BMI (kg/m ²)	20.88±3.02	22.10±4.12	21.61±3.20	21.20±3.30	22.02±3.74	24.09±4.87	23.10±4.25	23.29±4.43
Duration of disease (years)	1.84±1.58	8.14±1.50	18.39±8.07	4.76±6.06	3.70±1.34	7.76±1.31	18.26±6.79	12.52±7.75
Chlorpromazine-equivalent dose	395.0±179.7	423.4±187.6	420.1±219.4	403.1±185.0	369.1±251.5	344.7±151.8	360.0±197.7	356.2±184.9

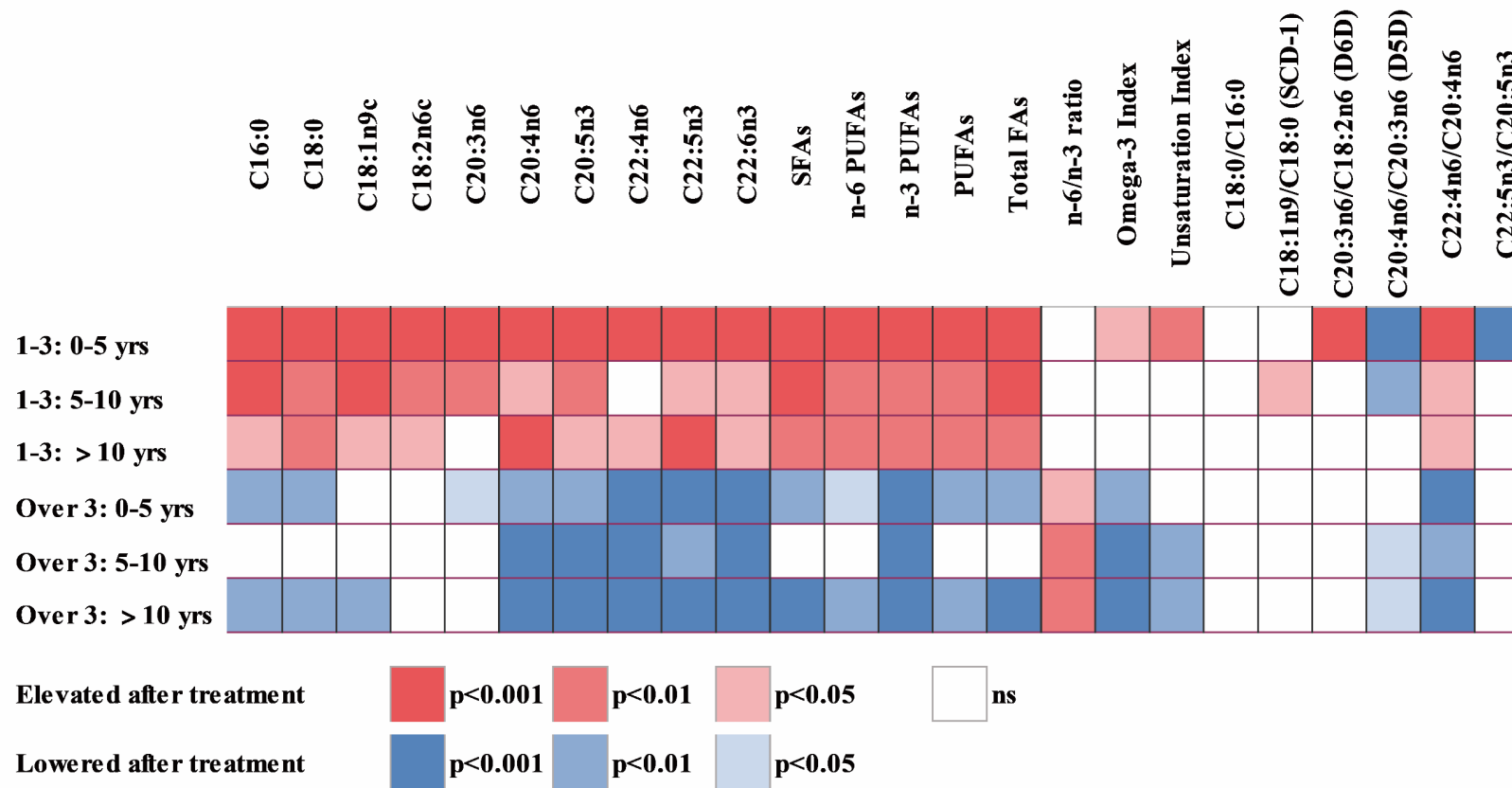
Values represent as mean ± standard deviation; More responsive subgroup consists of patients on 1-3 episode(s) and less-responsive subgroup consists of patients on over 3 episodes. BMI, body mass index; yr(s), year(s).

Supplementary Table 5 Demographic characteristics of male and female patients

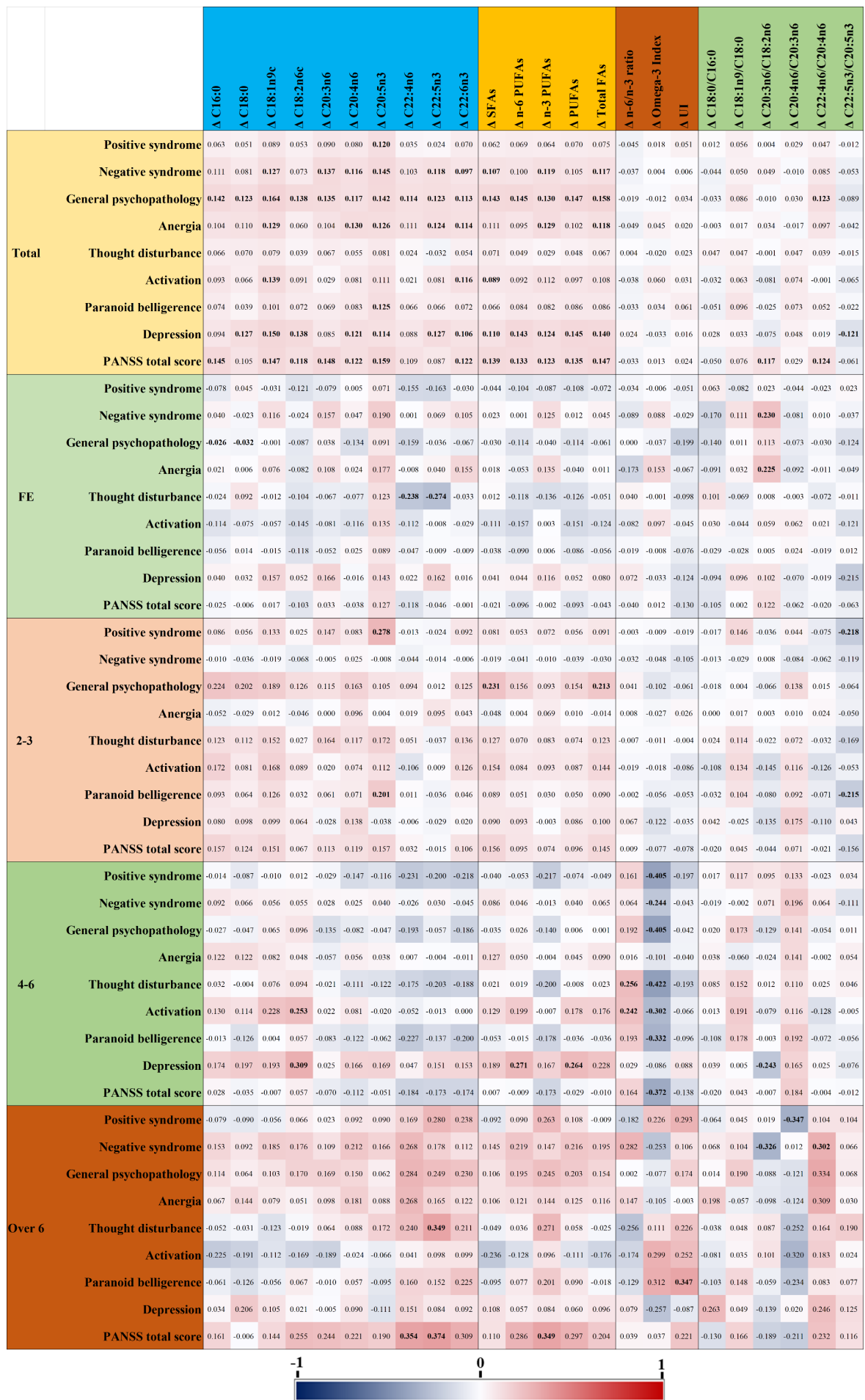
	Male	Female	p
n	147	180	
Age (years)	30.89±10.02	34.18±10.50	0.004
BMI (kg/m2)	22.40 ±3.47	21.61 ±3.84	0.066
Duration of disease (years)	7.24 ±6.89	8.26 ±8.37	0.237
Chlorpromazine-equivalent dose	406.55 ±190.93	366.88 ±180.25	0.062
Number of episodes			0.366
FE	44 (29.9%)	45 (25.0%)	
2-3 episodes	47 (32.0%)	63 (35.0%)	
4-6 episodes	31 (21.1%)	49 (27.2%)	
Over 6 episodes	25 (17.0%)	23 (12.8%)	

Supplementary Table 6 Meal composition for patients

Meal	Composition	Caloric Value (kcal)	Protein (g)	Fat (g)	Carbohydrate (g)
Breakfast	Egg 50g, meat bun 100g, steamed roll 90g, rice porridge 250g	608	22.7	16.2	97.4
Lunch	Rice 200g, vegetables 250g, meat 200g, oil 33g	806	48	36	76.2
Dinner	Rice 200g, vegetables 375g, meat 75g, oil 18g	611	24.8	22.5	81.6



Supplementary Figure 1 Changes in membrane fatty acid levels and ratios of patients with different durations of illness disease in more-responsive (1-3 episodes) and less-responsive (over 3 episodes) subgroups after antipsychotic treatment. ns, not significant; yrs, years.



Supplementary Figure 2 Heatmap of correlation coefficients between fatty acid level and ratio changes and symptom improvement in schizophrenia patients after ant