

Repeated-measured ANOVA: effects of time and treatment and mixed effect of time x treatment

Anthropometric parameters

Repeated measured analysis of variance revealed no significant effects of time (before therapy and 6 weeks after therapy), effect of treatment (monotherapy with fluoxetine and augmentation – fluoxetine in combination with quetiapine) and mixed effects of time × treatment (before therapy and 6 weeks after therapy x monotherapy with fluoxetine and augmentation – fluoxetine in combination with quetiapine) in all anthropometric parameters. Next, post-hoc analysis revealed no significant changes within- and between-groups. These results could indicate that the changes of body composition over 6 weeks were similar in both groups. All results are presented in Table S1.

Table S1. Evaluated anthropometric parameters before and after treatment in both groups

Parameter	(a) ALL before treatment	(b) FLX before treatment	(c) AUG before treatment	(d) ALL after treatment	(e) FLX after treatment	(f) AUG after treatment	F, p, (η^2_p)	pBH- value	F, p, (η^2_p)	pBH- value	F, p, (η^2_p)	pBH- value	(a vs. d) p – value	(b vs. e) p – value	(c vs. f) p – value	(b vs. c) p – value	(e vs. f) p – value
							Effect of time (before vs. after treatment)		Effect of treatment (FLX vs. AUG)		Mixed effect of time and treatment						
Weight (kg)	60.5 ± 15.7	57.2 ± 11.5	68.3 ± 21.8	60.9 ± 15.7	57.5 ± 11.2	68.8 ± 22.1	1.03, 0.322, (0.047)	0.024	2.70, 0.115, (0.114)	0.032	0.08, 0.785, (0.004)	0.044	0.322	0.999	0.999	0.714	0.674
Total body water (L)	31.4 ± 6.3	31.1 ± 6.71	32.2 ± 5.6	31.7 ± 6.1	31.3 ± 6.3	32.8 ± 6.0	2.87, 0.105, (0.120)	0.006	0.21, 0.650, (0.010)	0.050	0.52, 0.477, (0.024)	0.038	0.105	0.999	0.974	0.999	0.999
Total protein (kg)	9.6 ± 5.6	8.3 ± 1.8	9.6 ± 5.6	9.9 ± 6.7	10.3 ± 8.0	8.8 ± 1.7	0.19, 0.665, (0.009)	0.044	0.42, 0.526, (0.019)	0.038	2.15, 0.158, (0.093)	0.015	0.665	0.999	0.999	0.871	0.999
Total minerals (kg)	3.1 ± 0.6	3.1 ± 0.7	3.2 ± 0.6	3.1 ± 0.6	3.0 ± 0.6	3.3 ± 0.6	0.42, 0.522, (0.020)	0.038	0.39, 0.537, (0.018)	0.041	1.18, 0.290, (0.053)	0.021	0.522	0.999	0.999	0.999	0.999
Overall fat mass (kg)	17.6 ± 10.2	14.7 ± 6.2	24.2 ± 14.6	17.5 ± 10.1	14.8 ± 6.1	23.9 ± 14.6	0.40, 0.536, (0.019)	0.041	4.87, 0.039, (0.188)	0.006	1.16, 0.293, (0.052)	0.024	0.536	0.999	0.999	0.208	0.259
Total muscle (kg)	23.4 ± 5.1	23.2 ± 5.5	24.1 ± 4.6	22.4 ± 4.9	23.2 ± 5.1	24.7 ± 4.7	3.50, 0.076,	0.003	0.25, 0.624,	0.047	2.30, 0.144,	0.012	0.076	0.999	0.331	0.999	0.999

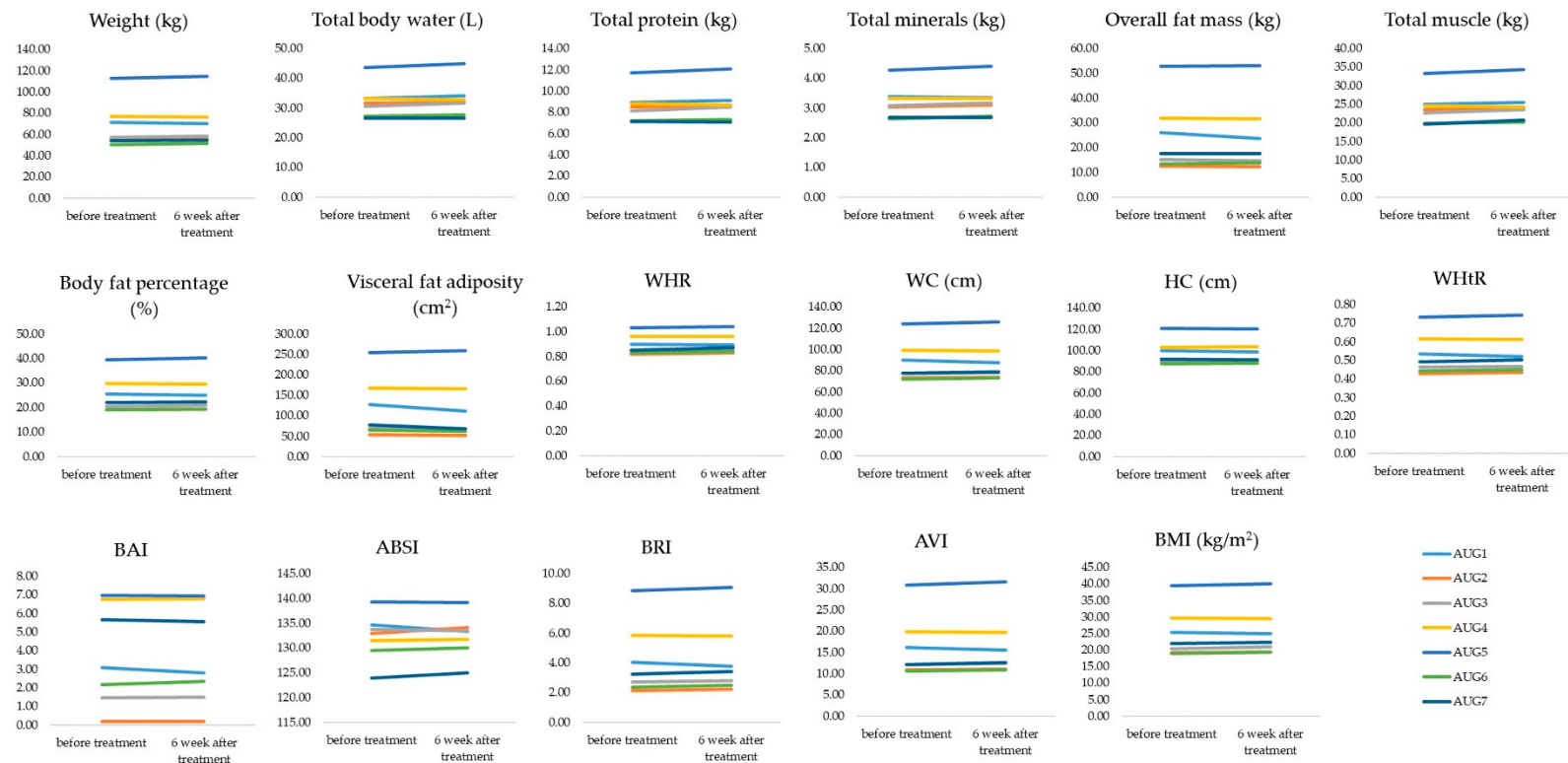
							(0.143)		(0.012)		(0.099)						
Body fat percentage (%)	27.7 ± 9.0	25.3 ± 8.1	33.3 ± 8.9	27.4 ± 8.6	25.3 ± 7.8	32.3 ± 8.9	2.24, 0.150, (0.096)	0.012	4.07, 0.057, (0.162)	0.024	2.92, 0.102, (0.122)	0.009	0.057	0.999	0.411	0.255	0.458
Visceral fat adiposity (cm ²)	81.1 ± 53.9	65.7 ± 36.1	116.0 ± 72.8	80.5 ± 53.6	66.3 ± 34.8	113.0 ± 75.7	1.50, 0.235, (0.085)	0.015	4.67, 0.042, (0.181)	0.012	3.21, 0.087, (0.037)	0.006	0.235	0.999	0.510	0.213	0.305
WHR	0.85 ± 0.06	0.83 ± 0.05	0.89 ± 0.08	0.85 ± 0.07	0.83 ± 0.05	0.90 ± 0.08	2.37, 0.139, (0.101)	0.009	6.24, 0.021, (0.229)	0.003	3.36, 0.081, (0.138)	0.003	0.139	0.999	0.337	0.173	0.092
WC (cm)	79.5 ± 13.5	75.9 ± 9.0	87.6 ± 18.9	79.7 ± 13.5	75.9 ± 8.9	88.2 ± 18.7	0.78, 0.386, (0.036)	0.032	4.41, 0.048, (0.173)	0.018	0.82, 0.375, (0.038)	0.029	0.386	0.999	0.999	0.320	0.262
HC (cm)	93.2 ± 8.4	91.3 ± 6.1	97.6 ± 11.7	93.2 ± 8.2	91.3 ± 5.7	97.4 ± 11.6	0.09, 0.762, (0.004)	0.047	2.93, 0.102, (0.122)	0.029	0.05, 0.822, (0.002)	0.047	0.762	0.999	0.999	0.597	0.632
WHtR	0.48 ± 0.08	0.46 ± 0.05	0.53 ± 0.11	0.48 ± 0.08	0.46 ± 0.05	0.53 ± 0.11	0.86, 0.365, (0.039)	0.026	4.63, 0.043, (0.181)	0.015	0.69, 0.417, (0.032)	0.035	0.365	0.999	0.999	0.288	0.236
BAI	3.2 ± 3.4	2.9 ± 3.6	3.8 ± 2.7	3.2 ± 3.5	3.0 ± 3.9	3.7 ± 2.7	0.0003, 0.987, (0.00001)	0.050	0.26, 0.614, (0.012)	0.044	0.19, 0.665, (0.009)	0.041	0.987	0.999	0.999	0.999	0.999
ABSI	129.0 ± 7.9	128.0 ± 8.8	132.0 ± 4.8	129.0 ± 8.0	127.0 ± 8.9	132.0 ± 4.4	0.55, 0.469, (0.025)	0.035	1.67, 0.211, (0.074)	0.035	1.62, 0.217, (0.072)	0.018	0.469	0.496	0.999	0.999	0.999
BRI	3.2 ± 1.6	2.7 ± 0.9	4.2 ± 2.4	3.2 ± 1.6	2.7 ± 0.9	4.2 ± 2.4	1.07, 0.312, (0.049)	0.021	4.75, 0.041, (0.184)	0.009	0.78, 0.387, (0.036)	0.032	0.312	0.999	0.999	0.270	0.224
AVI	13.1 ± 4.8	11.9 ± 2.6	16.1 ± 7.3	13.2 ± 4.9	11.9 ± 2.6	16.2 ± 7.4	0.85, 0.367, (0.039)	0.029	4.43, 0.048, (0.174)	0.021	0.96, 0.338, (0.044)	0.026	0.367	0.999	0.999	0.314	0.261
BMI (kg/m ²)	22.2 ± 4.9	21.0 ± 2.9	25.0 ± 7.4	22.4 ± 4.9	21.1 ± 2.8	25.2 ± 7.5	1.41, 0.248, (0.063)	0.018	3.71, 0.068, (0.150)	0.026	0.02, 0.885, (0.001)	0.050	0.248	0.999	0.999	0.418	0.402

Abbreviations: ALL – total study population, FLX – fluoxetine monotherapy group, AUG – low dose quetiapine augmentation group, WHR – waist to hip ratio, WC – waist circumference, HC – hip circumference, BAI – body adiposity index, ABSI – a body shape index, BRI – body roundness index, AVI – abdominal volume index, BMI – body mass index, a – ALL before treatment, b – FLX before treatment, c – AUG before treatment, d – ALL 6 weeks after treatment, e – FLX 6 weeks after treatment, and f – AUG 6 weeks after treatment. Degree of freedom (df) for between groups comparisons as well as df for within group comparisons was 1. Effect of time provided are F value and p-value and effect size

was assessed by partial eta-squared (η_p^2), with large effect sizes (>0.14). Data are considered as statistically significant different as the following conditions are met at the same time: $p < 0.05$, $pBH < 0.05$, and $p < pBH$. A p-value < 0.05 (post-hoc; in bold) indicates statistically significant differences between time (i.e. before and 6 weeks after therapy).

Additionally, to better visualize individual changes within the AUG group (N=7), spaghetti plots have been included.

Figure S1. Spaghetti plots illustrating individual trajectories of anthropometric measures before and 6-weeks after treatment for patients in the AUG group.



AUG – low dose quetiapine augmentation group, WHR – waist to hip ratio, WC – waist circumference, HC – hip circumference, BAI – body adiposity index, ABSI – a body shape index, BRI – body roundness index, AVI – abdominal volume index, BMI – body mass index

Depressive symptomatology

Item-level MADRS analyses showed robust effect of time (before therapy and 6 weeks after therapy) for most items: MADRS no. 1 – apartness sadness ($F = 25.35$, $p < 0.001$, $pBH = 0.006$), MADRS no. 2 – reported sadness ($F = 118.9$, $p < 0.001$, $pBH = 0.009$), MADRS no. 3 – inner tension ($F = 31.59$, $p < 0.001$, $pBH = 0.012$), MADRS no. 4 – reduced sleep ($F = 7.55$, $p = 0.012$, $pBH = 0.044$), MADRS no. 5 – reduced appetite ($F = 9.70$, $p = 0.005$, $pBH = 0.038$), MADRS no. 7 – lassitude ($F = 16.38$, $p < 0.001$, $pBH = 0.015$), MADRS no. 9 – pessimistic thoughts ($F = 25.38$, $p < 0.001$, $pBH = 0.018$), and MADRS no. 10 – suicidal thoughts ($F = 52.86$, $p < 0.001$, $pBH = 0.021$). Similarly, analysis of CDI subjective scale pointed on significant effect of time (before therapy and 6 weeks after therapy) for following items: CDI A – negative mood ($F = 157.78$, $p < 0.001$, $pBH = 0.026$), CDI B – interpersonal problems ($F = 41.43$, $p < 0.001$, $pBH = 0.029$), CDI C – ineffectiveness ($F = 8.03$, $p = 0.010$, $pBH = 0.041$), CDI D – anhedonia ($F = 24.06$, $p < 0.001$, $pBH = 0.032$), and CDI E – negative self-esteem ($F = 85.83$, $p < 0.001$, $pBH = 0.035$). Next, no significant effect of treatment (monotherapy with fluoxetine and augmentation – fluoxetine in combination with quetiapine), and mixed time $\times$ treatment interaction (before therapy and 6 weeks after therapy $\times$ monotherapy with fluoxetine and augmentation – fluoxetine in combination with quetiapine) were detected. All results are presented in Table S2.

Post-hoc analysis

In whole group, almost all MADRS items and all CDI items were significantly decreased after treatment compared to baseline state before treatment (MADRS total score: $p < 0.001$, MADRS no. 1: $p < 0.001$, MADRS no. 2: $p < 0.001$, MADRS no. 3: $p < 0.001$, MADRS no. 4: $p = 0.012$, MADRS no. 5: $p = 0.005$, MADRS no. 7: $p < 0.001$, MADRS no. 9: $p < 0.001$, MADRS no. 10: $p < 0.001$, CDI total score: $p < 0.001$, CDI A: $p < 0.001$, CDI B: $p < 0.001$, CDI C: $p = 0.010$, CDI D: $p < 0.001$, and CDI E: $p < 0.001$).

In FLX group, the MADRS total score ($31.1 \rightarrow 20.2$, $p < 0.001$), MADRS no. 1 ($p < 0.001$), MADRS no. 2 ($p < 0.001$), MADRS no. 3 ($p < 0.001$), MADRS no. 7 ($p < 0.001$), MADRS no. 9 ($p < 0.001$), MADRS no. 10 ($p < 0.001$), CDI total score ($p < 0.001$), CDI A ($p < 0.001$), CDI B ($p < 0.001$), CDI D ($p = 0.003$), and CDI E ($p < 0.001$) were significantly decreased after treatment compared to before treatment.

In AUG group, the MADRS total score ($p < 0.001$), MADRS no. 2 ($p < 0.001$), MADRS no. 3 ($p = 0.008$), MADRS no. 10 ($p = 0.003$), CDI total score ($p < 0.001$), CDI A ($p < 0.001$), CDI B ($p = 0.002$), and CDI E ($p < 0.001$) were significantly decreased after treatment compared to before treatment. Additionally, no significant differences were found before and after treatment in whole group, and separately in FLX and AUG groups. All results are presented in Table S2.

Table S2. Evaluated MADRS and CDI scores before treatment and six weeks after treatment in monotherapy and augmentation groups

Parameter	(a) ALL before treatm ent	(b) FLX before treatm ent	(c) AUG before treatm ent	(d) ALL after treatm ent	(e) FLX after treatm ent	(f) AUG after treat ment	F, p, η^2_{pv}	pBH - valu e	F, p, η^2_{pv}	pB H- valu e	F, p, η^2_{pv}	pB H- valu e	(a vs . d) p – valu e	(b vs. e) p – valu e	(c vs. f) p – valu e	(b vs. c) p – valu e	(e vs. f) p – valu e
							Effect of time (before vs. after treatment)		Effect of treatment (FLX vs. AUG)		Mixed effect of time and treatment						
MADRS total score	31.3 ± 5.0	31.1 ± 5.5	32.0 ± 4.1	20.8 ± 5.4	20.2 ± 4.9	22.1 ± 6.7	80.41, <0.001, (0.793)	0.003	0.47, 0.500, (0.022)	0.02 6	0.19, 0.664, (0.009)	0.03 5	<0.00 1	<0.00 1	<0.00 1	0.99 9	0.99 9
MADRS no. 1 (apparent sadness)	3.4 ± 1.2	3.7 ± 1.1	2.9 ± 1.1	2.1 ± 1.1	2.1 ± 1.1	2.3 ± 1.0	25.35, <0.001, (0.547)	0.006	0.46, 0.505, (0.021)	0.02 9	5.83, 0.025, (0.217)	0.00 3	<0.00 1	<0.00 1	0.788	0.63 3	0.99 9
MADRS no. 2 (reported sadness)	4.2 ± 1.1	4.4 ± 1.1	3.9 ± 1.2	2.2 ± 0.9	2.2 ± 0.9	2.3 ± 1.0	118.9, <0.001, (0.850)	0.009	0.23, 0.633, (0.011)	0.03 8	3.19, 0.088, (0.132)	0.00 6	<0.00 1	<0.00 1	<0.00 1	0.99 9	0.99 9
MADRS no. 3 (inner tension)	4.0 ± 1.1	4.0 ± 1.1	4.0 ± 1.3	2.7 ± 1.2	2.8 ± 0.9	2.6 ± 1.8	31.59, <0.001, (0.601)	0.012	0.06, 0.808, (0.003)	0.04 7	0.27, 0.610, (0.013)	0.02 6	<0.00 1	<0.00 1	0.008	0.99 9	0.99 9
MADRS no. 4 (reduced sleep)	2.8 ± 1.4	2.7 ± 1.5	3.1 ± 1.1	2.0 ± 1.1	2.1 ± 1.3	1.6 ± 0.5	7.55, 0.012, (0.265)	0.044	0.01, 0.907, (0.001)	0.05 0	1.69, 0.208, (0.074)	0.01 5	0.012	0.999	0.146	0.99 9	0.99 9
MADRS no. 5 (reduced appetite)	2.3 ± 1.8	2.4 ± 2.1	2.1 ± 1.2	1.1 ± 1.3	1.4 ± 1.4	0.6 ± 0.8	9.70, 0.005, (0.316)	0.038	0.77, 0.390, (0.035)	0.02 1	0.48, 0.496, (0.022)	0.02 1	0.005	0.237	0.198	0.99 9	0.99 9
MADRS no. 6 (concentratio n difficulties)	2.1 ± 1.0	1.9 ± 1.0	2.7 ± 1.0	2.2 ± 1.0	2.0 ± 0.9	2.7 ± 1.0	0.07, 0.789, (0.003)	0.047	4.80, 0.040, (0.186)	0.00 9	0.07, 0.789, (0.003)	0.05 0	0.789	0.999	0.999	0.33 0	0.60 0
MADRS no. 7 (lassitude)	3.0 ± 1.3	2.8 ± 1.3	3.7 ± 1.0	2.0 ± 1.4	1.5 ± 1.3	3.1 ± 0.9	16.38, <0.001, (0.438)	0.015	6.82, 0.016, (0.245)	0.00 3	2.27, 0.147, (0.098)	0.01 2	<0.00 1	<0.00 1	0.857	0.53 2	0.05 3

MADRS no. 8 (inability to feel)	1.9 ± 1.6	1.9 ± 1.7	2.0 ± 1.3	1.9 ± 1.4	1.8 ± 1.3	2.1 ± 1.6	0.021, 0.887, (0.001)	0.050	0.13, 0.718, (0.006)	0.04 1	0.14, 0.716, (0.006)	0.03 8	0.887	0.999	0.999	0.99 9	0.99 9
MADRS no. 9 (pessimistic thoughts)	3.7 ± 0.9	3.8 ± 0.9	3.6 ± 1.1	2.4 ± 0.9	2.4 ± 1.0	2.4 ± 0.8	25.38, <0.001, (0.547)	0.018	0.07, 0.788, (0.004)	0.04 4	0.12, 0.731, (0.006)	0.04 1	<0.00 1	<0.00 1	0.063	0.99 9	0.99 9
MADRS no. 10 (suicidal thoughts)	3.8 ± 1.4	3.7 ± 1.7	4.0 ± 0.6	2.0 ± 1.2	1.9 ± 1.2	2.4 ± 1.1	52.86, <0.001, (0.716)	0.021	0.62, 0.440, (0.029)	0.02 4	0.27, 0.610, (0.013)	0.02 9	<0.00 1	<0.00 1	0.003	0.99 9	0.99 9
CDI total score	26.0 ± 5.5	25.2 ± 5.8	27.9 ± 4.6	17.1 ± 3.6	16.6 ± 3.6	18.1 ± 3.5	91.49, <0.001, (0.813)	0.024	1.24, 0.277, (0.056)	0.01 5	0.36, 0.553, (0.017)	0.02 4	<0.00 1	<0.00 1	<0.00 1	0.99 9	0.99 9
CDI A (negative mood)	7.0 ± 1.8	6.4 ± 1.5	8.3 ± 2.0	4.7 ± 1.3	4.3 ± 0.9	5.6 ± 1.7	157.78, <0.001, (0.883)	0.026	6.10, 0.022, (0.225)	0.00 6	2.34, 0.141, (0.100)	0.00 9	<0.00 1	<0.00 1	<0.00 1	0.05 7	0.40 3
CDI B (interperson al problems)	4.4 ± 1.7	4.5 ± 1.8	4.3 ± 1.5	2.9 ± 1.3	3.1 ± 1.3	2.4 ± 1.0	41.43, <0.001, (0.664)	0.029	0.45, 0.512, (0.021)	0.03 2	0.67, 0.422, (0.031)	0.01 8	<0.00 1	<0.00 1	0.002	0.99 9	0.99 9
CDI C (ineffectiven ess)	3.2 ± 1.6	2.9 ± 1.7	3.7 ± 1.5	2.3 ± 0.9	1.9 ± 0.8	3.0 ± 0.8	8.03, 0.010 , (0.277)	0.041	3.42, 0.079, (0.140)	0.01 2	0.22, 0.642, (0.011)	0.03 2	0.010	0.051	0.999	0.99 9	0.46 0
CDI D (anhedonia)	6.0 ± 2.9	6.1 ± 3.0	5.7 ± 2.7	4.0 ± 1.7	4.3 ± 1.8	3.6 ± 1.7	24.06, <0.001, (0.534)	0.032	0.29, 0.596, (0.014)	0- 035	0.11, 0.747, (0.005)	0.04 7	<0.00 1	0.003	0.052	0.99 9	0.99 9
CDI E (neg. self- esteem)	5.4 ± 1.5	5.2 ± 1.6	5.9 ± 1.1	3.2 ± 1.2	3.1 ± 1.3	3.6 ± 1.0	85.83, <0.001, (0.803)	0.035	1.10, 0.305, (0.050)	0.01 8	0.11, 0.739, (0.005)	0.04 4	<0.00 1	<0.00 1	<0.00 1	0.99 9	0.99 9

Abbreviations: ALL – total study population, FLX – fluoxetine monotherapy group, AUG – low dose quetiapine augmentation group, MADRS – the Montgomery-Åsberg Depression Rating Scale, CDI – the self-report Children's Depression Inventory, a – ALL before treatment, b – FLX before treatment, c – AUG before treatment, d – ALL 6 weeks after treatment, e – FLX 6 weeks after treatment, and f – AUG 6 weeks after treatment. Degree of freedom (df) for between groups comparisons as well as df for within group comparisons was 1. A p-value < 0.05 (in bold) indicates statistically significant differences between groups. Effect of time, treatment and mixed effect values provided are F value and p-value and effect size was assessed by partial eta-squared (η^2_p), with large effect sizes (> 0.14). Data are considered as statistically significant different as the following conditions are met at the same time: $p < 0.05$, $p_{BH} < 0.05$, and $p < p_{BH}$ (in bold). A p-value < 0.05 (post-hoc; in bold) indicates statistically significant differences between time (i.e. before and 6 weeks after therapy).