

Plasma β -III Tubulin, Neurofilament Light Chain and Glial Fibrillary Acidic Protein are Associated with Neurodegeneration and Progression in Schizophrenia

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Supplementary table 1: Previous treatments of the clozapine-treated group.

Patient code	Current treatment	First treatment	Second treatment	Illness onset	Duration of illness
E070	Clozapine	Risperidone	Risperidone + Olanzapine	31	14
E079	Clozapine	Aripiprazole	Aripiprazole + Quetiapine	53	6
E102	Clozapine	Amisulpride	Olanzapine	20	9
E117	Clozapine	Risperidone	Risperidone + Haloperidol	25	27
E128	Clozapine	Risperidone	Risperidone + Amisulpride	30	30
E175	Clozapine	Zuclopentixol	Aripiprazole	22	32
E176	Clozapine	Haloperidol	Risperidone	30	11
E178	Clozapine	Aripiprazole	Aripiprazole + Clotiapine	21	3
E179	Clozapine	Risperidone	Risperidone + Quetiapine	23	23

Supplementary table 2: Equivalent amount of proteins (volume - μ l) calculation by the a bicinchoninic acid assay (BCA).

Patient	SZ/Ctrl	Absorbance	Concentration μ g/ml	Volume μ l (10 μ g)
E113	FEP	2,136	4158,9	2
E118	FEP	2,188	4260,8	2
E123	FEP	2,527	4924,8	2
E130	FEP	1,912	3720,1	3
E135	FEP	2,889	6565,4	2
E136	FEP	2,170	4855,8	2
E140	FEP	2,672	6049,5	2
E167	FEP	2,510	5664,3	2
E170	FEP	2,560	5783,1	2
E074	Aripiprazole	2,931	5716,2	2
E075	Aripiprazole	2,419	2645,8	4
E093	Aripiprazole	2,282	2495,7	4
E119	Aripiprazole	2,400	2625,0	4
E122	Aripiprazole	2,289	2503,4	4
E126	Aripiprazole	2,236	2445,3	4
E131	Aripiprazole	2,201	2406,9	4
E134	Aripiprazole	2,056	2248,0	4
E088	Risperidone	2,212	2419,0	4
E114	Risperidone	2,173	2376,2	4
E115	Risperidone	2,085	4059,0	2
E132	Risperidone	1,523	1664,0	6
E141	Risperidone	2,262	2473,8	4
E143	Risperidone	2,108	2305,0	4
E150	Risperidone	2,349	2569,1	4
E163	Risperidone	2,195	2400,4	4
E086	Olanzapine	2,218	4319,5	2
E094	Olanzapine	2,206	2412,4	4
E112	Olanzapine	2,236	2445,3	4
E116	Olanzapine	2,224	2432,1	4
E121	Olanzapine	2,218	2425,6	4
E149	Olanzapine	2,206	2412,4	4
E160	Olanzapine	2,212	2419,0	4
E190	Olanzapine	2,243	2453,0	4
E070	Clozapine	2,138	4162,8	2
E079	Clozapine	2,272	4425,3	2
E102	Clozapine	2,025	3941,5	3
E117	Clozapine	2,648	5161,8	2
E128	Clozapine	2,101	4090,4	2
E175	Clozapine	2,401	5405,1	2
E176	Clozapine	2,310	5188,7	2
E178	Clozapine	2,196	4276,4	2
E179	Clozapine	1,989	3871,0	3
654	Control	2,389	4231,4	2
655	Control	2,466	4231,4	2
656	Control	2,426	4231,4	2
657	Control	2,165	4231,4	2
658	Control	2,757	4231,4	2

659	Control	2,363	4231,4	2
660	Control	2,228	4231,4	2
661	Control	2,574	4231,4	2
662	Control	2,316	4231,4	2
663	Control	2,389	4231,4	2
664	Control	2,125	4231,4	2
665	Control	1,875	4231,4	2
666	Control	2,228	4231,4	2
667	Control	2,015	4231,4	2
668	Control	2,050	4231,4	2
669	Control	2,260	4231,4	2
670	Control	2,101	4231,4	2
671	Control	1,780	4231,4	2
672	Control	2,331	4231,4	2
673	Control	2,247	4231,4	2
674	Control	2,266	4231,4	2
675	Control	2,436	4231,4	2
676	Control	2,426	4231,4	2
677	Control	2,115	4231,4	2
678	Control	2,389	4231,4	2
679	Control	2,115	4231,4	2
680	Control	2,216	4231,4	2
681	Control	2,301	4231,4	2
682	Control	2,280	4231,4	2
683	Control	2,062	4231,4	2
684	Control	1,969	4231,4	2
S254	Control	2,720	2975,7	3
S255	Control	2,739	2996,5	3
S256	Control	2,634	2881,4	3
S259	Control	2,701	2954,8	3
S261	Control	2,683	2935,1	3
S262	Control	2,666	2916,5	3
S264	Control	2,634	2881,4	3
S268	Control	2,619	2865,0	3
S288	Control	2,780	3041,4	3

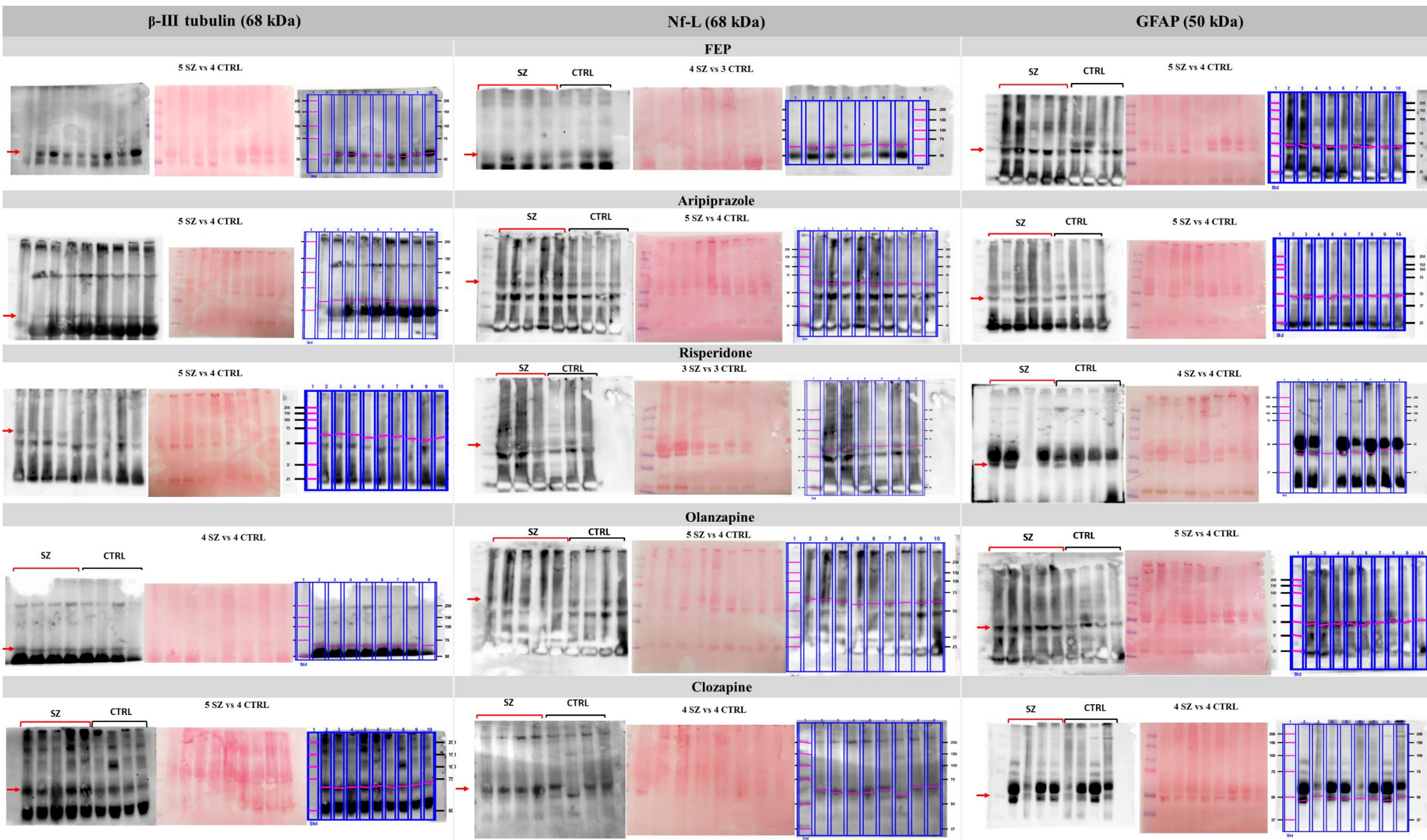
Legend: SZ – schizophrenia; Ctrl - Control; FEP - first-episode psychosis.

Supplementary table 3: Summary One-way ANOVA and Bonferroni's multiple comparisons tests results.

Duration of illness					
ANOVA Summary				F= 0.1973	P=0.8974
Bonferroni's multiple comparison test	Mean Diff.	95% CI of diff.	Significance	Summary	Adjusted P Value
Aripiprazole vs. Risperidone	-0.6250	-14.77 to 13.52	No	ns	>0.9999
Aripiprazole vs. Olanzapine	-1.500	-15.64 to 12.64	No	ns	>0.9999
Aripiprazole vs. Clozapine	-3.472	-17.22 to 10.27	No	ns	>0.9999
Risperidone vs. Olanzapine	-0.8750	-15.02 to 13.27	No	ns	>0.9999
Risperidone vs. Clozapine	-2.847	-16.59 to 10.90	No	ns	>0.9999
Olanzapine vs. Clozapine	-1.972	-15.72 to 11.77	No	ns	>0.9999
Dose equivalencies					
ANOVA Summary				F= 2.413	P=0.0870
Bonferroni's multiple comparison test	Mean Diff.	95% CI of diff.	Significance	Summary	Adjusted P Value
Aripiprazole vs. Risperidone	-101.7	-300.8 to 97.49	No	ns	0.9543
Aripiprazole vs. Olanzapine	85.83	-113.3 to 285.0	No	ns	>0.9999
Aripiprazole vs. Clozapine	-23.89	-217.4 to 169.7	No	ns	>0.9999
Risperidone vs. Olanzapine	187.5	-11.66 to 386.7	No	ns	0.0745
Risperidone vs. Clozapine	77.78	-115.8 to 217.3	No	ns	>0.9999
Olanzapine vs. Clozapine	-109.7	-303.3 to 83.83	No	ns	0.7157
Illness onset					
ANOVA Summary				F=2.857	P=0.0556
Bonferroni's multiple comparison test	Mean Diff.	95% CI of diff.	Significance	Summary	Adjusted P Value
Aripiprazole vs. Risperidone	-13.00	-26.97 to 0.9662	No	ns	0.0798
Aripiprazole vs. Olanzapine	-1.446	-14.97 to 12.08	No	ns	>0.9999
Aripiprazole vs. Clozapine	-4.905	-18.07 to 8.263	No	ns	>0.9999
Risperidone vs. Olanzapine	11.55	-1.969 to 25.08	No	ns	0.1315
Risperidone vs. Clozapine	8.095	-5.072 to 21.26	No	ns	0.5486
Olanzapine vs. Clozapine	-3.458	-16.15 to 9.236	No	ns	>0.9999

Legend: One-way ANOVA followed by Bonferroni post-hoc test: comparison between patients treated with antipsychotics *Statistical significance: $P \leq 0.05$.

Supplementary figure 1: Original western blots.

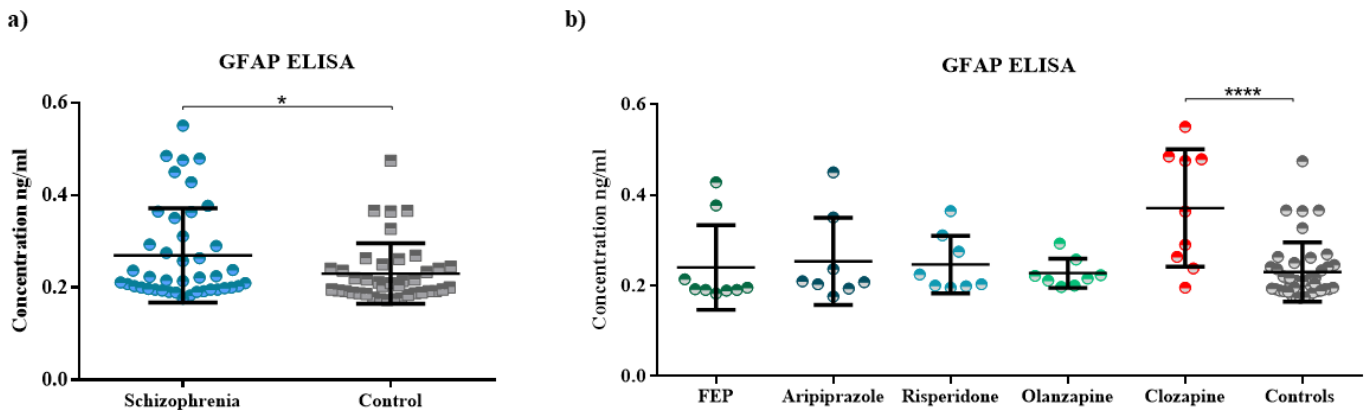


Supplementary table 4: Summary One-way ANOVA and Bonferroni's multiple comparisons tests results for GFAP ELISA.

GFAP					
ANOVA Summary				F= 4.950	P=0.0006
Bonferroni's multiple comparison test	Mean Diff.	95% CI of diff.	Significance	Summary	Adjusted P Value
FEP vs. Controls	-0,009998	-0,08676 to 0,06676	No	ns	> 0.9999
Aripiprazole vs. Controls	-0,02356	-0,1041 to 0,05702	No	ns	> 0.9999
Risperidone vs. Controls	-0,01657	-0,09715 to 0,06401	No	ns	> 0.9999
Olanzapine vs. Controls	0,002630	-0,07795 to 0,08321	No	ns	> 0.9999
Clozapine vs. Controls	-0,1412	-0,2180 to -0,06448	Yes	****	< 0.0001

Legend: One-way ANOVA followed by Bonferroni post-hoc test: comparison between patients treated with antipsychotics and controls *Statistical significance: $P \leq 0.05$.

Supplementary figure 2: Plasma levels of GFAP measured by ELISA.



Legend: Scatterplots showing the plasma levels of GFAP. a) Scatterplot of levels of GFAP that reveals statistical significance between patients with schizophrenia and the control group using unpaired two-tailed T-test ($P=0.0407$). b) Scatterplot of levels of GFAP that showing a significant result between clozapine-treated patients and the control group using one-way ANOVA multiple comparison ($P < 0.0001$).