Supplementary Online Content

Voineskos AN, Mulsant BH, Dickie EW, et al. Effects of antipsychotic medication on brain structure in patients with major depressive disorder and psychotic features: neuroimaging findings in the context of a randomized placebo-controlled clinical trial. *JAMA Psychiatry*. Published online February 26, 2020. doi:10.1001/jamapsychiatry.2020.0036

This supplementary material has been provided by the authors to give readers additional information about their work.

Supplementary Table S1. Magnetic Resonance Imaging acquisition parameters for T1-weighted scans.

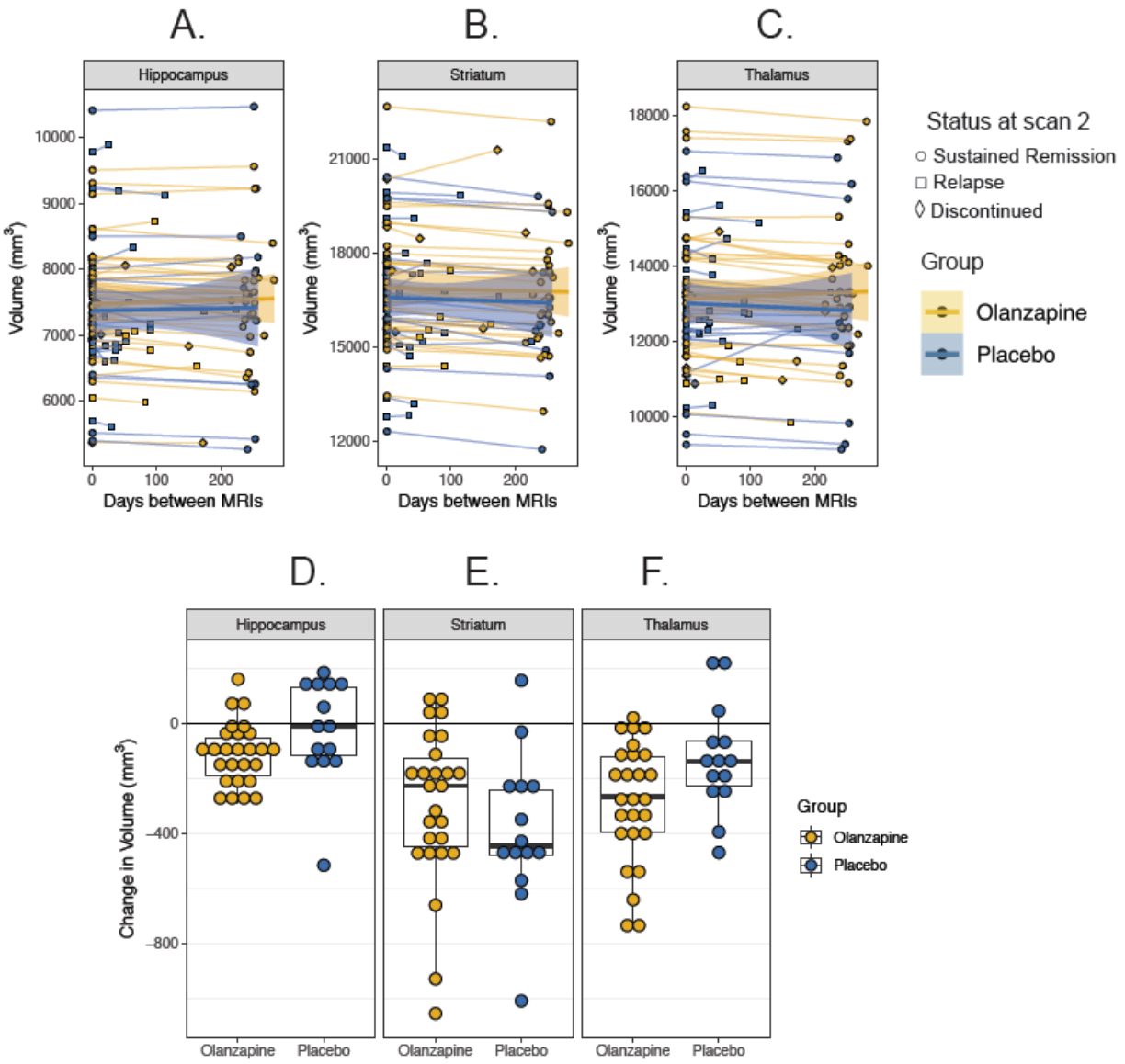
Site	Repetition Time (TR;ms)	Echo Time (TE;ms)	Flip angle	Matrix	Slice thickness (mm)	Number of slices
Toronto	6.7	3·0	8°	256 x 256	0·9	200
Cornell/NKI	2500	3·5	8°	256 x 256	1·0	192
UPMC	2300	3·0	8°	256 x 232	0·9	208
UMass	6.7	3·0	8°	240 x 240	1·0	181

Supplementary Table S2. Magnetic Resonance Imaging acquisition parameters for DTI scans.

Site	Repetition Time (TR; ms)	Echo Time (TE; ms)	Matrix	Slice thickness (mm)	B-factor	Directions	B=0 images
Toronto	8800	"minimum"	128 x 128	2·9	1000	60	5
Cornell/NKI	5700	79	128 x 128	2·9	1000	60	5
UPMC	8800	79	128 x 128	2·9	1000	60	6
UMass	9190	66	96 x 96	2·5	1000	60	1

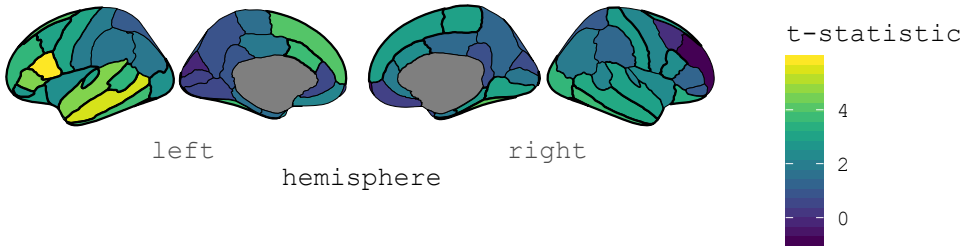
Supplementary Figure S1. In the top panel (A-C), results from modeling the treatment group x time interaction in hippocampus, striatum, and thalamus. The interaction was not significant in in

hippocampus (t=1.4, p=0.1), striatum (t=-0.2 p=0.8), or thalamus (t=2.7, p=0.01) following correction for multiple testing. In the bottom panel (D-F) changes in hippocampal, striatal, and thalamic volume in patients in the olanzapine arm compared to patients in the placebo arm over 36 weeks in the bottom panel (D-F). No association was found in the hippocampus (ß=97.3, Std. Error=48.1, df=36.0, t=2.0, p=0.05), thalamus (ß=156.2, Std. Error=69.4, df=36.0, t=2.3, p=0.03), or striatum (ß=-80.5, Std. Error=96.8, df=36.0, t=-0.8, p=0.4) following correction for multiiple testing. The directionality of difference in hippocampus and thalamus was consistent with cortical thickness and surface area. Striatal change was in the opposite direction, consistent with literature suggesting antipsychotics may cause striatal volume increase due to dopamine D2 receptor binding and density change.



Supplementary Figure S2. Mapping the effect of olanzapine vs placebo on cortical thinning over 36 weeks in participants who sustained remission. The color scale represents the t-statistic

for the effect of treatment (Placebo vs Olanzapine) where brighter colors represents greater cortical thinning. Areas outlined in black are those where the treatment effects was significant after correction for multiple comparisons (across 68 brain regions) using False Discovery Rate. A clear fronto-temporal pattern is evident, where effect sizes are largest. The specific regions that survive FDR correction are listed in Supplementary Table 3.



Supplementary Table S3. Post-hoc analyses for cortical thickness brain regions of interest

and white matter tracts that survive multiple comparison correction in the olanzapine vs. placebo comparison in those who sustained remission over 36 weeks. The table shows the beta estimate, test statistic value, and FDR corrected p value in each column.

A. Cortical Thickness ROIs Post-Hoc Analysis

ROI	estimate	std.error	statistic	p_FDR
L_parsopercularis	0.069304846	0.011915701	5.816262353	1.13E-04
L_middletemporal	0.069323028	0.012830936	5.402803644	1.91E-04
L_superiortemporal	0.059160446	0.012992278	4.55350826	0.001190834
L_parstriangularis	0.059546629	0.013101865	4.544897309	0.001190834
R_fusiform	0.070413872	0.016852936	4.178136771	0.002752208
L_superiorfrontal	0.05426188	0.013441863	4.036782715	0.003434686
L_inferiortemporal	0.070179812	0.018565751	3.780068513	0.005217111
L_fusiform	0.05993735	0.015900236	3.76958875	0.005217111
L_caudalanteriorcingulate	0.076617616	0.020635121	3.712971448	0.005217111
R_inferiortemporal	0.057980972	0.015642398	3.706655039	0.005217111
R_lateraloccipital	0.049416286	0.013893451	3.556804391	0.007002683
L_rostralmiddlefrontal	0.039609445	0.011208632	3.533834002	0.007002683
L_bankssts	0.055941564	0.016061014	3.483065512	0.007424925
R_lateralorbitofrontal	0.052057851	0.015753156	3.304598275	0.011158954
R_middletemporal	0.043890205	0.013810427	3.17804845	0.014568782
L_transversetemporal	0.096483854	0.03136487	3.076175831	0.016975219
L_precentral	0.064788029	0.021092008	3.07168613	0.016975219
R_lingual	0.051992718	0.017185979	3.025298531	0.018057116
L_caudalmiddlefrontal	0.04403988	0.014656848	3.00473067	0.018057116
R_paracentral	0.059291139	0.020080921	2.952610557	0.018945319
L_lateralorbitofrontal	0.056630038	0.019216756	2.946909425	0.018945319
R_superiortemporal	0.050717026	0.017337182	2.925332794	0.019105633
R_superiorfrontal	0.042643848	0.014741172	2.892839753	0.019844827
R_postcentral	0.030375194	0.010962331	2.770870048	0.025817261
R_parahippocampal	0.08526206	0.031047462	2.746184548	0.026346949
L_parsorbitalis	0.052034418	0.019433819	2.677518906	0.029989085
L_lateraloccipital	0.038100306	0.014982574	2.542974642	0.03995339
L_insula	0.05822025	0.023925825	2.433364362	0.048597449
R_parsopercularis	0.036710472	0.015182283	2.417980954	0.048597449
R_caudalanteriorcingulate	0.071639495	0.02966502	2.414948477	0.048597449
R_insula	0.051200941	0.021929728	2.33477322	0.056566227

B. Mean Diffusivity White Matter ROIs Post-Hoc Analysis

ROI	estimate	std.error	statistic	p_FDR
Sagittal Stratum	-5.41E-05	1.67E-05	-3.2478442	0.0418925
Fornix/Stria Terminalis	-5.64E-05	1.86E-05	-3.0347758	0.0418925
External Capsule	-5.26-05	1.76E-05	-2.9902545	0.0418925
SLF	-2.84E-05	1.02E-05	-2.7888879	0.0474893
Right Limb Internal Capsule	-5.37E-05	1.96E-05	-2.7376128	0.0474893

SLF = Superior Longitudinal Fasciculus.