Table 1. *Cross-sectional studies presented in chronological order*

Study	Design	Sample: patients evaluated/ treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Dazzan *et al*. 2005	Cross-sectional drug-type	62 short-term treated patients at their first episode of psychosis + 22 drug-free patients (ICD-10)	Typicals (32 patients): mean dose in chlorpromazine equivalents = 269 ± 245 mg/day Atypicals (30 patients): 21 on olanzapine, 14 mg/day, 5 on risperidone, 4 mg/day, 2 on quetiapine, 400 mg/day, 1 on sertindole, 16 mg/day, 1 on amisulpiride, 400 mg/day Drug-free (22 patients)	Automated (VBM)/3	Grey matter	Typical *versus* drug free: putamen ↑ with typicals and ↓ frontal areas, temporal-insular areas and precuneus. ($p \leqslant 0.002$) Atypical *versus* drug free: ↑ thalamus with atypicals ($p = 0.002$) Typical *versus* atypical: ↓ left middle temporal gyrus with typicals ($p = 0.002$)
Narr *et al*. 2005	Cross-sectional drug-type	33 short-term treated (median 8 days, range 1–187) + 39 naive patients (analysed together) at their first episode of schizophrenia + 78 controls	Atypicals (33 patients): either olanzapine or risperidone	ROI/1.5	Mesial cortex	Patients *versus* controls: in patients ↓ cortical thickness within cingulate, occipitals and frontopolar cortices
Chakos *et al*. 2005	Cross-sectional drug-type	34 long-term treated male patients with schizophrenia (duration of illness 12 months) + 14 controls	Typicals (17 patients): haloperidol Atypicals (15 patients): 12 on olanzapine, 3 on risperidone Typicals and atypicals (1 patient): clozapine and molindone Unknown (1 patient)	ROI/1.5	Hippocampus	Atypical *versus* typical: ↑ hippocampal volumes with atypicals ($d = 1.3$, $r = 0.56$)
		22 long-term treated male patients with schizophrenia (duration of illness 20 years) + 14 controls	Typicals (5 patients): 3 on haloperidol, 1 on trifluoperazine, 1 on thiothixene Atypicals (15 patients): 6 on olanzapine, 8 on clozapine, 3 on risperidone	ROI/1.5	Hippocampus	Atypical *versus* typical: = hippocampal volumes ($F = 0.54$, $p = 0.48$)
Deicken *et al*. 2002	Cross-sectional dose-correlation	41 long-term treated male patients with schizophrenia + 39 controls	Mean dose in chlorpromazine equivalents = 613.6 ± 649.7 mg/day	ROI/1.4	Thalamus	No correlation between thalamic volume and current antipsychotic dose

Table 1 (*cont.*)

Study	Design	Sample: patients evaluated/ treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Nopoulos *et al*. 2001	Cross-sectional dose-correlation	5 drug-naive and 45 drug-free males (analysed together) at their first episode of schizophrenia + 50 controls (DSM-III-R)	Cumulative antipsychotic exposure at the time of the MRI as chlorpromazine equivalents = mean dose of 40.59 ± 94.699 mg, range 0–524	ROI/1.5	Brainstem (midbrain)	If ↑ the antipsychotic exposure then ↓ the midbrain area ($r = -0.42$, $p = 0.002$)
Gur *et al*. 2000	Cross-sectional drug-naive *versus* long-term treated	29 naive and 41 long-term treated patients with schizophrenia + 81 controls	Typicals: 24 patients Atypicals: 6 patients Typicals followed by atypicals: 11 patients	ROI/1	Prefrontal cortex	Naive *versus* previously treated patients: = prefrontal cortex volume
Velakoulis *et al*. 1999	Cross-sectional dose-correlation	33 long-term treated patients with chronic schizophrenia (medication doses were calculated for the 30 days prior to MRI scan) and 31 short-term treated patients at their first episode of psychosis (treated on average 30 days before scan) + 140 controls (DSM-III-R)	Total antipsychotic dose in chlorpromazine equivalents: for long-term treated patients: 21018 ± 16153 mg (mean daily dose: 656 ± 431) for short-term treated patients: 5384 ± 7983 mg (mean daily dose: 164 ± 107)	ROI/1.5	Whole-brain volume Hippocampus	Chronic schizophrenia patients *versus* controls: ↓ hippocampal volumes in patients (right side: $r = 0.5$, left side: $r = 0.4$) First-episode psychosis patients *versus* controls: ↓ hippocampal volumes in patients (right side: $r = 0.4$, left side: $r = 0.5$) Chronic schizophrenia patients: no associations between whole-brain volume ($r = 0.08$) or hippocampal volumes (right side: 0.02, left side: 0.09) and medication dosage First-episode psychosis patients: no associations between whole-brain volume ($r = -0.15$) or hippocampal volumes (right side: −0.17, left side: 0.04) and medication dosage

Table 1 (*cont.*)

Study	Design	Sample: patients evaluated/ treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Gur *et al*. 1998*b*	Cross-sectional dose-correlation for drug type	75 long-term treated and 27 naive patients with schizophrenia + 128 controls	Typicals: 44 patients Typicals + atypicals: 24 patients Mean dose in chlorpromazine equivalent units/day: typicals: 407.1 ± 25.3 atypicals (clozapine and risperidone): 334.1 ± 286.3	ROI/1	Caudate putamen Globus pallidus Thalamus	Long-term treated patients: ↑ putamen ($F = 4.86$, $p = 0.03$) and globus pallidus ($F = 12.58$, $p = 0.0005$) compared with controls and naive patients Patients on typicals: if ↑ dose of typicals then ↑ caudate (left side: $r = 0.38$, $p < 0.01$; right side: $r = 0.34$, $p < 0.05$) and thalamus (left side: $r = 0.55$, $p < 0.01$; right side: $r = 0.36$, $p < 0.05$) and left putamen ($r = 0.36$, $p < 0.01$) Patients on typicals and atypicals: (*a*) if ↑ dose of typicals then ↑ thalamus (left side: $r = 0.75$, $p < 0.01$; right side: $r = 0.62$, $p < 0.01$), left putamen ($r = 0.37$, $p < 0.01$) and left globus pallidus ($r = 0.46$, $p < 0.05$) (*b*) if ↑ dose of atypical then ↑ thalamus (left side: $r = 0.60$, $p < 0.01$, right side: $r = 0.59$, $p < 0.01$)
Zipursky *et al*. 1998	Cross-sectional dose-correlation	26 short-term treated patients at their first episode of a non-affective psychosis + 82 controls (DSM-III-R)	Haloperidol for 4 weeks (haloperidol dose was increased until the 'optimal dose' was reached) 13 patients treated with 2 mg/day ('low-dose group') 13 patients treated with doses of 5, 10 or 20 mg/day ('higher-dose group')	ROI/3	Grey matter (total and cortical)	The low-dose group had more cortical grey matter than the higher-dose group ($t = 2.35$, $p = 0.03$) There was a trend in the same direction for the total grey matter volume ($t = 1.89$, $p = 0.07$)
Shihabuddin *et al*. 1998	Cross-sectional drug-free and drug-naive *versus* controls	7 drug-naive and 11 drug-free patients with schizophrenia or schizo-affective disorder + 24 controls matched for sex and age (comprehensive assessment of symptoms and history)	Antipsychotics (type and dose not known)	ROI/1.2	Caudate putamen	Drug-free patients: ↓ caudate than controls (ventral: $d = 0.8$, $r = 0.37$, dorsal: $d = 0.9$, $r = 0.43$ and combined: $d = 0.8$, $r = 0.39$) and than drug-naive patients (ventral: $d = 0.0$, $r = 0.04$, dorsal: $d = 0.5$, $r = 0.28$ and combined: $d = 0.2$, $r = 0.12$) Drug-free patients: ↑ dorsal putamen than drug-naive patients ($d = 0.3$, $r = 0.16$) and than controls ($d = 0.3$, $r = 0.15$)

MRI, Magnetic resonance imaging; VBM, voxel-based morphometry; ROI, region of interest.

Table 2. *Follow-up studies presented in chronological order*

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/ diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Girgis *et al.* 2006	Follow-up (6 weeks) Acute	15 naive patients at their first episode of psychosis +15 controls	Risperidone (mean dose 2.67 mg/day)	Automated (VBM)/1.5	Grey and white brain matter	Patients: ↑ in left superior temporal gyrus and middle temporal gyrus and ↓ in left rectal gyrus and corpus callosum Controls: no changes over time
Khorram *et al.* 2006	Follow-up (1 year) Long-term	20 long-term treated patients with schizophrenia +20 controls Not known how diagnoses were made	Typicals for at least 1 year before the first MRI then atypicals until the second MRI	ROI/4	Thalamus	If ↑ dosage of typical antipsychotics at baseline then ↓ thalamus after switching to olanzapine ($r=0.7$, $p=0.0$)
McClure *et al.* 2006	Follow-up (mean 25±13 days for the withdrawal group and 52±39 days for the stable chronic treatment group) Acute	Long-term treated patients: 11 medication withdrawal patients; 8 chronic stable treatment patients	Placebo *versus* typicals and atypicals	ROI and automated (VBM)/1.5	Whole-brain volume Grey and white matter (total and regional) Lateral ventricles Cerebrospinal fluid volume	Drug-withdrawal group: both with ROI and VBM: no effect of treatment status and antipsychotic type on brain volumes Chronic stable treatment group: both with ROI and VBM: no effect of treatment on brain volumes
Taylor *et al.* 2005	Follow-up (4 weeks) Acute	6 drug-free schizophrenic patients +5 drug-free patients at their first psychotic episode +11 controls	Haloperidol (2 patients), risperidone (7 patients), mean dose 4 mg/day, ziprasidone (2 patients)	ROI/2	Basal ganglia	Patients: ↑ in striatal tissues (left side: $d=0.3$, $r=0.1$; right side: $d=0.3$, $r=0.1$)
Garver *et al.* 2005	Follow-up (4 weeks; T_0, T_4) Acute Partially random design	19 drug-free schizophrenic patients + 7 controls	First 7 patients assigned to risperidone at 4 mg/day Subsequent 12 patients, randomly assigned to: ziprasidone 120 mg/day (6 patients), haloperidol 7 mg/day (6 patients)	Automated (VBM)/2	Cortical grey matter	Patients on atypicals: diffuse ↑cortical grey without differences between ziprasidone ($d=0.3$, $r=0.1$) and risperidone ($d=0.5$, $r=0.2$) Patients on haloperidol: = cortical grey matter ($d=1.1$, $r=0.5$)

Table 2 (*cont.*)

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Lieberman *et al*. 2005	Follow-up (104 weeks; T_0, T_{12}, T_{24}, T_{52}, T_{104}) Long-term Random design	115 short-term treated + 46 naive (analysed together) at their first episode of psychosis who received at least one post-baseline MRI scan + 62 controls matched to patient's demographic characteristics	Haloperidol (79 patients) 2–20 mg/day Olanzapine (82 patients) 5–20 mg/day	ROI/3	Whole-brain grey matter: frontal temporal parietal occipital Caudate	Olanzapine *versus* haloperidol: (*a*) whole-brain grey matter: ↓ in the haloperidol group (week 12: $d=1.6$, $r=0.6$). Frontal grey matter: ↓ in the haloperidol group (week 52: $d=2.6$, $r=0.79$). Temporal and parietal grey matter: ↓ in the haloperidol group (week 52: $d=1.1$, $r=0.5$ and $d=1.2$, $r=0.5$ respectively) (*b*) caudate volumes: ↑ in the haloperidol group (week 24 d = 1.3, $r=0.5$, week 52: $d=2.3$, $r=0.76$; week 104: $d=0.2$, $r=0.13$) Patients *versus* controls: (*a*) whole-brain grey matter: ↓ in the haloperidol group (week 12: $d=3$, $r=0.1$; week 52: $d=2.3$, $r=0.7$) whereas = in the olanzapine group (week 12: $d=3$, $r=0.1$; week 52: $d=0.17$, $r=0.0$) Frontal grey matter. haloperidol group (week 12: $d=2.1$, $r=0.7$; week 52: $d=3.3$, $r=0.8$) Temporal grey matter: ↓ in the haloperidol group (week 52: $d=0.9$, $r=0.4$) Parietal grey matter: ↓ in the haloperidol group (week 52: $d=1.3$, $r=0.5$)
Massana *et al*. 2005	Follow-up (3 months) Acute	11 naive patients at their first episode of psychosis	Risperidone (no fixed dose; mean dose of 6.05 mg/day)	Automated (optimized VBM)/1.5	Caudate putamen Globus pallidus Nucleus accumbens	↑ left nucleus accumbens ($T=4.26$, $p=0.00$) and the left caudate ($T=3.68$, $p=0.02$)

Table 2 (*cont.*)

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/ diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Lang *et al*. 2004	Follow-up (mean length 45.6 weeks) Long-term	37 long-term treated schizophrenic patients +23 controls	Under typicals (10 patients) switched to olanzapine Under risperidone (27 patients): 13 switched to olanzapine; 14 continuing with risperidone	ROI /4	Basal ganglia Caudate putamen Globus pallidus	Patients on typicals (mean chlorpromazine equivalents 360) switched to olanzapine (mean chlorpromazine equivalents 170): At baseline: patients on typicals ↑ basal ganglia than controls (differences were statistically significant for putamen: $d=0.7$, $r=0.3$ and globus pallidus: $d=1.4$, $r=0.5$) At follow-up: basal ganglia volume ↓ in patients (caudate: $d=0.04$, $r=0.02$; putamen: $d=1.2$, $r=0.5$; globus pallidus: $d=1.06$, $r=0.4$) Patients *versus* controls: = basal ganglia (caudate: $d=0.2$, $r=0.1$; putamen: $d=0.1$, $r=0.08$; globus pallidus: $d=0.5$, $r=0.2$) Patients on risperidone: At baseline: risperidone-treated patients subsequently switched to olanzapine (mean chlorpromazine equivalents 132 ± 150) *versus* those continuing risperidone (mean chlorpromazine equivalents 92 ± 84): = basal ganglia volumes (caudate: $d=0.4$, $r=0.2$, putamen: $d=0.08$, $r=0.04$; globus pallidus: $d=0.1$, $r=0.07$) At follow-up: risperidone patients *versus* olanzapine patients: = basal ganglia volumes (caudate: $d=0.00$, $r=0.00$; putamen: $d=0.08$, $r=0.00$; globus pallidus: $d=0.4$, $r=0.2$)
Heitmiller *et al*. 2004	Follow-up (mean length for patients 30.2 months, S.D. = 13.3) Long-term	14 naive at their first episode of schizophrenia +14 controls matched for gender	Atypicals (risperidone: mean dose 3.625 mg/day; olanzapine, quetiapine, clozapine) Mean dose-year at follow-up in chlorpromazine equivalents $=7.38\pm5.53$	Semi-automated/ 1.5	Caudate	Patients *versus* controls: = amount of change caudate ($d=0.00$, $r=0.001$) However, the female patients had a negative correlation between drug exposure and volume change (total volume: $r=-0.6$, $p=0.1$) whereas the male patients had a positive correlation (total volume: $r=-0.5$, $p=0.2$)

Table 2 (*cont.*)

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/ diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Christensen *et al*. 2004	Follow-up (4 weeks) Acute	16 drug-free schizophrenic patients + 8 controls	Risperidone (7 patients): 4 mg/day, ziprasidone (6 patients): 120 mg/day, haloperidol (6 patients): 7 mg/day	ROI /2	White brain matter volume	Risperidone *versus* ziprasidone *versus* haloperidol: = change in white matter (paired t: 1.561, $p = 0.1$)
Cahn *et al*. 2002	Follow-up (1 year) Long-term	24 drug-naive and 10 short-term treated patients at their first episode of schizophrenia (analysed together) +36 controls	Typicals (5 patients) Atypicals (15 patients) Typicals + atypicals (14 patients) Cumulative lifetime dose in haloperidol equivalents: $T_0 = 65.9 \pm 157.6$ mg $T_1 = 2077.5 \pm 962.7$ mg	Automated (VBM)/1.6	Whole-brain volume Grey and white brain matter Lateral ventricles Cerebellum	If ↑ cumulative dose of antipsychotic medication (typical or atypical) between T_0 and T_1 then ↓ in global grey matter volume ($r = -0.45$, $p = 0.00$)
Tauscher-Wisniewski *et al*. 2002	Follow-up (approximately 5 years) Long-term	7 short-term treated and 8 naive patients at their first episode of schizophrenia or schizo-affective disorder + 10 controls	Typicals (4 patients): haloperidol at mean dose of 2 mg/day (2 patients); loxapine at mean dose of 10 mg/day (2 patients) Atypicals (9 patients): clozapine (3 patients) Typicals + clozapine (2 patients)	ROI/1.5	Caudate	At baseline, naive *versus* treated patients: = caudate ($F = 0.18$, $p = 0.68$) At follow-up, controls and patients = caudate ↓ of 9% (controls: $d = 0.6$, $r = 0.3$; patients: $d = 0.5$, $r = 0.2$; clozapine: $d = 0.4$, $r = 0.2$; atypicals: $d = 0.09$, $r = 0.04$; typicals: $d = 2.1$, $r = 0.7$; clozapine + typicals: $d = 0.2$, $r = 0.1$)
Scheepers *et al*. 2001*b*	Follow-up (52 weeks) Long-term	22 long-term treated schizophrenic patients on treatment with typical antipsychotic	Clozapine: mean dose 346 ± 61 mg/day	ROI/1.2	Caudate	↓ left caudate at week 24 if on clozapine (left side: $F = 3.9$, $p < 0.05$; right side: $F = 2.4$, $p = 0.1$)
Scheepers *et al*. 2001*a*	Follow-up (24 weeks) Long-term	26 long-term treated schizophrenic patients under treatment with typical antipsychotic	Clozapine: mean dose 345.57 ± 63.44 mg/day; range 200–600 mg/day	ROI /1.2	Caudate Whole-brain volume	↓ caudate if on clozapine ($d = 0.2$, $r = 0.1$) = whole-brain volume if on clozapine ($F = 3.85$, $p = 0.6$)

Table 2 (*cont.*)

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Puri *et al.* 2001	Follow-up (on average 8 months) Long-term	21 short-term treated and three naive patients (analysed together) at their first episode of schizophrenia (diagnosis confirmed after 1 year) +12 controls	Still naive (3 patients) Risperidone (4 patients) Typicals (27 patients) Cumulative medication dose in chlorpromazine equivalents: T_0 = mean 6677.45 (±6994.73) T_1 = mean 68365.96 (±53879.50)	ROI/1.6	Ventricles volumes	Patients *versus* controls: = ventricular volume at baseline ($d=0.4$, $r=0.2$) and follow-up ($d=3.2$, $r=0.8$) and = ventricle brain ratios at baseline ($d=0.5$, $r=0.2$) and follow-up ($d=0.5$, $r=0.2$) No correlations between ventricular size at presentation and cumulative medication dose ($r=-0.2$) or duration of treatment ($r=-0.1$) No correlations between change in ventricular size and total duration of treatment ($r=0.2$) or total cumulative medication dose ($r=0.05$)
Lieberman *et al.* 2001	Follow-up (mean length 2.5 years) Long-term	56 short-term treated patients at their first episode of psychosis +16 controls (Schedule for Affective Disorders and Schizophrenia)	Open therapy with a standardized treatment algorithm composed largely of conventional antipsychotic drugs (used ultimately clozapine for treatment refractory patients)	Semi-automated/3.1	Cortical grey and hemispheric white matter Ventricules Caudate Hippocampus	Patients *versus* controls: ↓ caudate in patients; ↓ anterior hippocampus and cortical volume in controls; = ventricles volumes No association between cumulative dose of antipsychotic treatment in the interscan interval and ventricular, cortical, hippocampal or caudal volumes Association between longer duration of treatment with typicals during the interscan interval and smaller ventricular volumes in patients both at baseline and follow-up scan ($F=5.73$, $p=0.2$)
Lang *et al.* 2001	Follow-up (1 year) Long-term	15 short-term treated patients at their first episode of schizophrenia +17 controls	At baseline patients treated with risperidone (dose range 1–6 mg/day, mean 2.7 mg/day). They took risperidone continuously for ⩾6 months	ROI/4	Basal ganglia: Caudate putamen Globus pallidus	At follow-up, both patients and controls = basal ganglia than at baseline (for all comparisons $p>0.2$)

Table 2 (*cont.*)

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Corson *et al.* 1999	Follow-up (2 years) Long-term	4 naive and 19 short-term treated (analysed together) male patients with schizophrenia spectrum disorders	Typicals: 13 patients: 8 treated only with typicals and 5 minimally exposed also to atypicals Mean dose years for typicals = 9.05 ± 6.89 Atypicals: 10 patients: 6 treated only with atypicals and 4 minimally exposed also to typicals Mean dose years for atypicals = 10.96 ± 9.14	ROI/1	Caudate putamen Globus pallidus	Patients on typicals: ↑ basal ganglia ($t = 2.93$, $p < 0.02$) Patients on atypicals: ↓ basal ganglia ($t = 1.98$, $p < 0.04$)
Gur *et al.* 1998*a*	Follow-up (2 years) Long-term	20 naive and 20 drug-free patients +17 controls	Mainly typicals + atypicals Follow-up daily dose in chlorpromazine equivalents: drug-naive: mean dose 259.9 ± 165.6 drug-free: mean dose 515.3 ± 224.0	ROI/5	Frontal and temporal lobes	Drug-naive *versus* drug-free patients: in drug-naive patients more ↓ in left hemispheric frontal lobes ($T = 0.17$, $p = 0.02$) and in temporal lobes bilaterally ($T = 0.12$, $p = 0.05$) Drug-free patients: if ↑ medication dose then ↓ in frontal and temporal volumes ($r = -0.75$ and -0.66 respectively; $p < 0.001$) Drug-naive patients: no association between medication dose and ↓ in frontal and temporal volumes ($r = 0.03$ and 0.16 respectively)
Frazier *et al.* 1996	Follow-up (2 years) Long-term	8 long-term treated patients with treatment refractory schizophrenia +8 controls matched for age, sex, handedness (DSM-III-R)	Patients were under typicals for about 2 years before the first MRI All patients were under clozapine at the time of the second MRI (mean dose 400 ± 128.9 mg/day)	ROI/1.5, 2	Caudate putamen Globus pallidus Ventricles volume	Caudate: ↓ in patients ($F = 4.96$, $p = 0.02$) Putamen: ↓ in patients ($F = 2.32$, $p = 0.08$) Globus pallidus: ↓ equally in patients and controls ($F = 21.74$, $p = 0.00$) Lateral ventricles; ↑ in patients ($F = 2.38$, $p = 0.07$)

Table 2 (*cont.*)

Study	Design (duration) Acute: ⩽16 weeks Long-term: >16 weeks	Sample (patients evaluated/treatment/diagnosis (DSM-IV, unless specified otherwise)	Antipsychotic (type, dose)	Method of MRI analysis/slice thickness (mm)	Region/s evaluated	Main findings
Chakos *et al*. 1995	Follow-up (mean length for patients switched to clozapine: 54.6 weeks, S.D. = 35) Long-term	8 long-term treated male patients with schizophrenia 7 long-term treated patients with schizophrenia Not known how diagnoses were made	Patients were under typicals before the first MRI, then switched to clozapine before the second MRI Patients were under typicals at the time of the first and the second MRI	ROI/3.1	Caudate	Patients on clozapine: caudate ↓ 10% at second scan ($d = 0.9$, $r = 0.4$) Patients on typicals: caudate ↑ 8% at second scan ($d = 0.5$, $r = 0.2$)
Chakos *et al*. 1994	Follow-up (18 months) Long-term	21 naive and 8 short-term treated* patients (analysed together) at their first episode of psychosis +10 controls * short-term treated patients had <12 weeks of lifetime exposure to antipsychotics and at least 2 weeks wash-out period before entering the study (DSM-III-R)	Standardized typical antipsychotics regimens (fluphenazine up to 20 mg/day for 6 weeks. If not improved, patients progressed through the treatment algorithm receiving full trials of up to three different typical antipsychotics)	ROI/3.1	Cortical grey and hemispheric white matter Lateral ventricle volume Caudate	Patients: caudate ↑ 5.7% ($d = 0.3$, $r = 0.1$) Controls: caudate ↓ 1.6% ($d = 0.09$, $r = 0.04$) A higher daily dose received prior to the first MRI was associated with larger ↑ in caudate ($r = 0.4$, $p < 0.02$)
Keshavan *et al*. 1994	Follow-up (305 days, S.D. = 218) Long-term	11 naive patients at their first episode of psychosis Not known how diagnoses were made	Typicals: mean maintenance dose in haloperidol equivalents 2.24 ± 1.2 mg/day	Semi-automated	Caudate Prefrontal cortex Brain volumes	↑ in right ($d = 1$, $r = 0.44$), left ($d = 0.68$, $r = 0.32$) and total caudate ($d = 0.86$, $r = 0.39$) None of the other MRI parameters changed

MRI, Magnetic resonance imaging; S.D., standard deviation.