Localized differences in caudate and hippocampal shape are associated with schizophrenia but not antipsychotic type

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Abstract

Background—Caudate and hippocampal volume differences in patients with schizophrenia are associated with disease and antipsychotic treatment, but local shape alterations have not been thoroughly examined.

Methods—Schizophrenia patients randomly assigned to haloperidol and olanzapine treatment underwent MRI scans at 3, 6, and 12 months. The caudate and hippocampus were represented as medial representations (M-reps); mesh structures derived from automatic segmentations of high resolution MRIs. Two quantitative shape measures were examined: local width and local deformation. A novel nonparametric statistical method adjusted exponentially tilted (ET) likelihood, was used to compare the shape measures across the three groups while controlling for covariates.

Results—Longitudinal shape change was not observed in the hippocampus or caudate when the treatment groups and controls were examined in a global analysis, nor when the three groups were examined individually. Both baseline and repeated measures analysis showed differences in local caudate and hippocampal size between patients and controls, while no consistent differences were shown between treatment groups.

Conclusions—Regionally specific differences in local hippocampal and caudate shape are present in schizophrenic patients. Treatment related longitudinal shape change was not observed within the studied timeframe. Our results provide additional evidence for disrupted cortico-basal ganglia-thalamo-cortical circuits in schizophrenia.

Clinical trial information—This longitudinal study was conducted from March 1, 1997, to July 31, 2001, at 14 academic medical centers (11 in the United States, 1 in Canada, 1 in the Netherlands, and 1 in England). This study was performed prior to the establishment of centralized registries of federally and privately supported clinical trials.

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1. Introduction

Converging trends in the neuroimaging of schizophrenia have led to the research conducted in this study. The first trend is the association of altered caudate volume with antipsychotic treatment. Reduction in caudate volume has been reported in MRI studies of antipsychotic-naïve, first-episode schizophrenia patients (Corson et al. 1999a; Keshavan et al. 1998; Levitt et al. 2002; Shihabuddin et al. 1998), who should not exhibit effects associated with treatment and disease chronicity, however findings are inconsistent (Chakos et al. 1994; Gur et al. 1998a). Cross-sectional MRI studies suggest that treatment of schizophrenia with typical antipsychotic medications can be, but is not always, associated with enlarged caudate. Dose (Chakos et al. 1994) and treatment findings (Corson et al. 1999b; Keshavan et al. 1994; Lieberman et al. 2005; Massana et al. 2005) have been observed over periods of twelve to twenty-four months in longitudinal MRI studies. Treatment of schizophrenia with atypical antipsychotics for extended periods is associated with decreases in caudate volume (Corson et al. 1999b), although studies in rodents are not entirely consistent with the human data (Andersson et al. 2002; Lee et al. 1999).

The second trend is the reduction of volume (McClure and Weinberger, 2001) and deformation of shape (Csernansky et al. 1998, 2002) demonstrated in the hippocampus by cross-sectional MRI studies in schizophrenia. The size of the hippocampus is reduced at onset of the first episode of psychosis, before the effects associated with treatment and disease chronicity should occur (Lieberman et al. 2001; Szeszko et al. 2003; Velakoulis et al. 1999). Longitudinal MRI studies over treatment periods of two to two and a half years have shown hippocampal and temporal lobe volumes decrease (Gur et al. 1998b; Mathalon et al. 2001), though not all studies show such changes (Lieberman et al. 2001). The inconsistent findings should be viewed in the context of the common (Davis et al. 1998; Delisi et al. 1988, 1992, 1995, 1997; Gur et al. 1998b; Jacobsen et al. 1998; Lieberman et al. 2005; Rapport et al. 1997), but not ubiquitous (Garver et al. 2000; Lieberman et al. 2001) observation that regional grey and white matter volumes can decrease while CSF volumes increase in longitudinal schizophrenia studies. There have also been some reports of an association between hippocampal volume and antipsychotic type. In a cross-sectional MRI study, treatment with atypical antipsychotics was associated with larger hippocampal volumes than treatment with haloperidol, but the relationship was observed only in male patients early in the course of their illness (Chakos et al. 2002). In a longitudinal MRI study, first-episode schizophrenic subjects given haloperidol demonstrated more decreases in gray matter volume than those given olanzapine after 24, 52 and 104 weeks of treatment (Lieberman et al. 2005). While it is possible that antipsychotic type is associated with differences in hippocampal volume change, there is not conclusive evidence yet.

The third trend is the emergence of medial representations (M-reps); a shape analysis method providing information on a rich set of features not accessible by conventional volume-based morphometry (Fletcher et al. 2003; Han et al. 2005; Pizer et al. 2005). MRI studies performed at the UNC Neuro Image Research and Analysis Laboratory using these high-dimensional statistical descriptions of shape in lateral ventricles (Styner et al. 2003, 2005) and hippocampi (Styner et al. 2004), have demonstrated effects of genetic relatedness and schizophrenia, as well as a main effect of antipsychotic type in hippocampal shape of male schizophrenia patients (Chakos et al. 2002).

This investigation examined caudate and hippocampal shape in schizophrenia patients randomly assigned to treatment with haloperidol or olanzapine. The specific purpose of the study was to determine if shape differences in the caudate and hippocampus of schizophrenia patients emerge following treatment. The specific outcome measures were two quantitative shape measurements: radius and position. These two shape measurements for the caudate and hippocampus were defined through M-reps with the **_radius_** measurement quantifying the **_local width_** at an M-rep node(represented in Figure 1 by the length of a thin rod projecting from a sphere) and the **_position_** measurement quantifying **_local deformation_** at an M-rep node (represented in Figure 1 by the location of a sphere).

The following questions were addressed: do haloperidol-, olanzapine-treated patients, and healthy control groups—globally (3-group comparison) or individually (comparisons between each group)—differ at baseline or in a repeated measures analysis (considering data from all time points but not longitudinal changes)? Over time, does shape change emerge globally among or individually between, the three groups? According to the *a priori* hypotheses, the following results were expected for shape measures in the hippocampus and caudate: (1) at baseline, an effect of diagnosis between schizophrenia patients and controls; (2) in the repeated measures analysis, an effect of diagnosis between schizophrenia patients and controls; (3) at baseline as well as in the repeated-measures analysis, no effect of antipsychotic type between schizophrenia patients in the two treatment groups; (4) in the global and individual group comparisons, differences will emerge over time.

2. Materials and Methods

Subjects were enrolled in a randomized, multi-site, double-blind study (Lieberman et al. 2005) that was conducted from March 1, 1997 to July 31, 2001 at 14 academic medical centers (11 in the United States, 1 in Canada, 1 in the Netherlands, and 1 in England).

In this study, 238 first-episode schizophrenia patients were enrolled. After random allocation at baseline, 123 patients were selected to receive the conventional antipsychotic haloperidol (2–20 mg/d), and 115 were selected to receive the atypical antipsychotic olanzapine (5–20 mg/d). Patients were treated and followed for up to 47 months. Fifty-six psychiatrically healthy subjects were matched to the patients' demographic characteristics and enrolled as control subjects (see Table 1 and Table 2). High resolution MRI (multi-site SPGR T1 weighted imaging on 1.5 Tesla scanners at $0.9375 \times 0.9375 \times 1.5mm$ resolution) was performed at baseline and after 3, 6, and 12 months (Lieberman et al. 2005). A small set of scans were performed after 24 months which were not considered in this study. Standardized geometric phantoms were scanned twice per month to ensure geometric acuity and minimize scanner bias across the 14 medical centers.

Prior to structural segmentation, the baseline MRI scans were rigidly aligned (mutual information based registration) to a standard coordinate space and follow up MRI scans were globally, affinely aligned to their baseline data. This setup minimizes inherent effects due to changes over time in MR field-of-view (FOV) size or MR field inhomogeneity. In particular, we analyzed FOV variation across time by studying changes in scale-factors computed with affine co-registration of longitudinally paired geometric phantom acquisitions. These scale-factor measurements allowed us to estimate that within-site FOV size varied by as much as 3% over time, both within-slice-plane as well as out-of-plane, necessitating an affine alignment to correct for these FOV distortions. Not surprisingly these FOV variations varied across site, and thus affine alignment also reduces this site-specific bias.

Caudate and hippocampus structures were then segmented from the aligned MRI scans with an automated atlas based segmentation tool developed in-house called AutoSeg (Gouttard et al. 2007). Caudate and hippocampus shape were next represented as a medial mesh of sampled nodes via a statistically-constrained based fit of a prior medial mesh model into the binary segmentations (Pizer et al. 2009; Styner et al. 2003).

Figure 1 illustrates the medial mesh for both structures with the associated medial node labeling used in the result section. Shape was captured as local width (medial width/radius) and local deformation (medial deformation) as proposed by Carracso et al. (2000). While local size is independent of pose, appropriate local deformation analysis necessitates a prior alignment. Alignment was performed for the caudate and hippocampus independently, via an extension of the standard rigid Procrustes alignment to medial structures (Gorczowski et al. 2010).

The aim of our study was to investigate differences in medial width and deformation of the hippocampus and caudate across the three groups (haloperidol-treated, olanzapine-treated, and controls) while controlling for other covariates of interest. We utilized a novel nonparametric method called adjusted exponentially tilted (ET) likelihood, along with a likelihood ratio test for hypothesis testing (Zhu et al. 2009). Assuming only a set of estimating equations, the adjusted ET likelihood is a nonparametric extension of general linear mixed models and generalized estimating equations. This extension of the ET method as a nonparametric method is particularly desirable for the analysis of brain morphometry because the distribution of the morphometric measures often deviates from the Gaussian distribution. For this study, the Shapiro-Wilk normality test was applied to check this parametric assumption at each atom for both left and right hippocampi and caudate using the residuals. It turned out that the Shapiro-Wilk test rejected the normality assumption at many atoms of both structures on each side; therefore our nonparametric adjusted ET method is preferred for the analysis of this data.

We first tested the a priori hypothesis at baseline. We used the adjusted ET likelihood to calculate regression parameter estimates and then tested for group differences (Zhu et al. 2009). Specifically, at each atom, we considered the moment model based on the 28×1 estimating function. The dependent variables were local width and local deformation, determined at 24 hippocampal nodes and 21 caudate nodes using M-reps (see Figure 1). Covariates of interest were WBV (whole brain volume = CSF, white matter and gray matter), ethnicity, age, gender, group (the two schizophrenia groups and the healthy control group), and time. The adjusted ET likelihood ratio statistic is used to test hypothesis of interest. Please see Zhu et al. (2009) for detailed analysis.

The false discovery rate approach was then used to correct for multiple comparisons in all atoms for each structure (Benjamini and Hochberg, 1995). Secondly, we performed longitudinal data analyses (Liang and Zeger, 1986). Again, we used the adjusted ET likelihood coupled with the generalized estimating equations for longitudinal data to estimate the regression parameters and then tested for specific group differences. In the longitudinal analysis, we used the similar set of estimating equations as those in the baseline analysis. Based on our previous analysis in Shi et al. (2011), we treated WBV as type II covariate and adjusted the estimating equations slightly. Please see Shi et al. (2011) for detailed analysis.

3. Results

3.1 Hippocampal Shape: Local Width and Local Deformation(See Fig 2)

The longitudinal analysis did not reveal significant changes in either local width or deformation in the hippocampus (see Tables 3 and 4). The longitudinal global comparison demonstrated a Group × Time interaction of width at nodes M8, C2, C3, and L6 in the left hippocampus (see Figure 1), but only marginally reached statistical significance (Table 3). Longitudinal analysis of the individual groups demonstrated no effect of time for local width in any region of the left hippocampus (Table 3). Neither the global nor the individual group comparisons, demonstrated an interaction of Group × Time or an effect of Time with respect to local deformation of the left hippocampus longitudinally (see Table 4). Longitudinal analysis also failed to show any Group × Time interaction or an effect of Time with respect to local width or deformation in the right hippocampus (see Tables 3 and 4).

At baseline and in repeated measures analysis (using measurements from all the time points), patients demonstrated significantly reduced node width (meaning a significantly reduced local volume near the node location) when compared to controls (see Tables 5, 6, 7, and 8). Significant baseline differences in width were observed in comparison of the haloperidol-treated patients and controls, localized to node M8, C3, C4, and C5 in the left hippocampus. The repeated measures analysis of haloperidol-treated patients compared to controls revealed significant differences in width at nodes M8, C3 and C4 in the left hippocampus. Significant differences in width were observed in the baseline analysis comparison of olanzapine-treated patients to controls, located at nodes C4 and C5 of the left hippocampus. Repeated-measures analysis of olanzapine-treated patients compared to controls did not show significant differences in width at any left or right hippocampal region. As expected, neither the baseline nor the repeated-measures analysis showed any significant differences in width between haloperidol and olanzapine-treated patients for the left hippocampus.

In both the baseline and the repeated-measures analysis, each patient group showed local differences in hippocampal deformation at the medial nodes compared to controls (see Tables 7 and 8). Haloperidol-treated patients compared to controls, showed differences in local deformation throughout medial, central, and lateral regions of the left hippocampus in both the baseline and repeated-measures analyses. In the baseline analysis only, the olanzapine-treated patients showed differences from controls in local deformation in medial, central, and lateral nodes for the left hippocampus, overlapping with the nodes showing differences in the comparison of haloperidol-treated patients to controls. However in the repeated-measures analysis, olanzapine-treated patients compared to controls showed differences in local deformation in only a few left hippocampal nodes (M8, C1, and L4).

No significant differences in local deformation of the left hippocampus were observed between haloperidol- or olanzapine-treated patients in the baseline or repeated-measures analyses (Tables 7 and 8). In the right hippocampus, differences in local deformation were observed in the repeated measures analysis between haloperidol-treated patients and controls at nodes M1, M7, M8, C1, C3, C6, C7, L2, and L7, but no differences in local deformation were noted in the right hippocampus between either the olanzapine-treated patients and controls or the olanzapine and haloperidol-treated patients.

3.2 Caudate Shape: Local Width and Local Deformation (See Fig 3)

There was little evidence for significant longitudinal caudate shape change in local width or deformation (see Tables 9 and 10). Global comparison of the three groups in the longitudinal analysis demonstrated a Group × Time interaction in local width of the left caudate at nodes S5 and I1 (see Fig 1), but these findings only marginally reached statistical significance. No

effect of Time was observed in local width at any node in the individual group analysis. In the right caudate, the longitudinal global comparison demonstrated a Group × Time interaction in local width at nodes S1, S4 and I2, but again no effect of Time was observed in the individual group analysis. Longitudinal analysis of deformation did not show significant effects in either left or right caudate and no Group × Time interaction was observed.

The baseline and repeated measures analyses of left and right caudate width showed highly similar results with respect to regional specificity (Tables 11, 12). While no left caudate width differences were observed between any groups, haloperidol-treated patients compared to controls showed significant differences in right caudate width for nodes S4 and I7 at baseline. The repeated measures analysis also showed right caudate width differences at node I7. Similarly, olanzapine-treated patients compared to controls had significant right caudate width differences at node S4 at baseline, but not in the repeated measures analysis. No significant differences in the right caudate were observed between treatment groups.

The repeated measures analyses of local deformation in patient groups compared to controls showed widespread differences in the caudate (Tables 13 and 14). In the baseline analysis, haloperidol-treated patients showed differences from controls in deformation of the left caudate at nodes S2–8, C1, C3, C4, and I1–I6, which was also reflected in the repeated measures analysis where they showed significant differences in deformation of nodes S2, S5, S6, C3, I1, I2 and I6. Compared to controls, olanzapine-treated patients displayed differences in deformation in left caudate nodes S2–5, C1, C4, I1–4, I6, and I7. One superior node in the left caudate (S2) showed differences in deformation when the haloperidol-treated and the olanzapine-treated patients were compared (Table 14), but this finding was regionally isolated and no difference in width was observed. Repeated measures analysis of right caudate deformation demonstrated similar differences between treatment groups and controls. Differences in local deformation were observed in haloperidol-treated patients at nodes S2–6, C1, C5, I1–6 and in olanzapine-treated patients at nodes S1–5, C1 and C2, C5, I1–I4, I6 and I7. No differences in deformation were noted in the right caudate between treatment groups (Table 14).

4. Discussion

Longitudinal changes in local width and deformation were not observed globally or when the haloperidol-treated, olanzapine-treated, and control groups were examined individually. While no differences were found between the treatment groups for the caudate or hippocampus, both treatment groups showed significant differences from controls. The baseline analysis demonstrated differences in local width of the left hippocampus at central-middle areas between both treatment groups and controls with the repeated measures analysis showing the same result for only the haloperidol-treated patients. Differences in local deformation between each treatment group and controls were observed at baseline in the left hippocampus at anterior, middle, and posterior nodes. Furthermore, at baseline haloperidol-treated patients and controls also showed differences in local deformation for anterior and posterior nodes of the right hippocampus. These baseline hippocampal shape differences are expected as previous studies have found differential hippocampal volumes for first episode schizophrenic patients (Lieberman et al. 2001; Velakoulis et al. 1999) with Szeszko et al. (2003) specifically finding reduced volume for the anterior hippocampus. A previous study by Styner et al. (2004) in chronic schizophrenia patients reported significant deformation differences in a few posterior (tail) nodes after normalization for hippocampal size differences.

Baseline and repeated measures analyses demonstrated differences in local deformation between patients and controls at several superior and inferior nodes of both the right and left caudate, with considerable regional overlap between the treatment groups. These broad deformation differences were expected as other studies have shown similar differences to be present in anti-psychotic naïve schizophrenics (Ballmaier et al. 2008) and even in the unaffected siblings of schizophrenia patients (Mamah et al. 2008). Local width differences between patients and controls were seen at baseline only for the right caudate and only in isolated superior (S4) and head (I7) regions. This finding is particularly consistent with those of Levitt et al (2009) which showed a very similar pattern of significant isolated local shape differences for males with schizotypal personality disorder that appeared only in the right caudate using a surface based shape analysis. While such a surface based analysis can provide a higher degree of locality, it cannot separate changes in local width (growth or shrinkage) from changes in local deformation as our M-Rep method can. See Styner et al. (2004) for a more detailed comparison of these two methods of shape analysis.

Surprisingly, significant differences in shape change were not observed over time between haloperidol- and olanzapine-treated patients. There are several potential explanations for why our primary hypothesis was not supported. First, the results could be false-negative, and while significant shape differences did emerge between the treatment groups, our methods did not detect them. This is possible but unlikely, given that shape differences were observed at baseline between controls and schizophrenics, with considerable regional overlap between the two treatment groups. Second, it is possible our results are true negative. The structural changes in the caudate associated with antipsychotic treatment are small in size and not seen in every study (Mamah et al. 2007; Tauscher-Wisniewski et al. 2002). Third, although shape measures are thought to be more sensitive than volume measures, the shape change associated with antipsychotic treatment may be smaller than volume changes, and undetectable using the M-reps method. Fourth, unidentified confounding factors may have masked the effects of antipsychotic treatment. Confounding factors certainly could have masked actual shape change, since it is not possible to match subjects on every factor that may alter brain structure. Several factors may have altered the brain structures measured with MRI in this population: disease progression (McClure and Lieberman, 2003); external environmental events associated with schizophrenia such as changes in tissue perfusion, fat content, and water content; changes in the neuronal and non-neuronal tissue compartments in the brain (Weinberger and McClure, 2002). Other potentially confounding factors not controlled for in this study include hydration status, body weight, illness severity, and previous treatment with antipsychotic medication.

This study is the first large-scale analysis that specifically examines longitudinal changes in local width and deformation in schizophrenia patients treated with typical and atypical antipsychotics using the M-reps method. The absence of shape differences at baseline between schizophrenia patients randomized into treatment groups indicates that our execution of the M-reps method was stable and reliable. Differences in the shape of the hippocampus and caudate between schizophrenic patients and controls using these methods is a novel finding, though not unexpected. There is extensive evidence of anatomical specificity in connections between the basal ganglia, hippocampus, and cerebral cortex (Draganski et al. 2008). There is also evidence from functional neuroimaging studies suggesting the presence of dysfunctional prefrontal-hippocampal (Callicott et al. 2003) and prefrontal-basal ganglia (Morey et al. 2008) circuits in schizophrenia. Demonstrating a direct relationship between dysfunction of specific circuits and altered morphometry of the caudate and hippocampus would provide additional evidence for the disruption of those circuits in schizophrenia.

Acknowledgments

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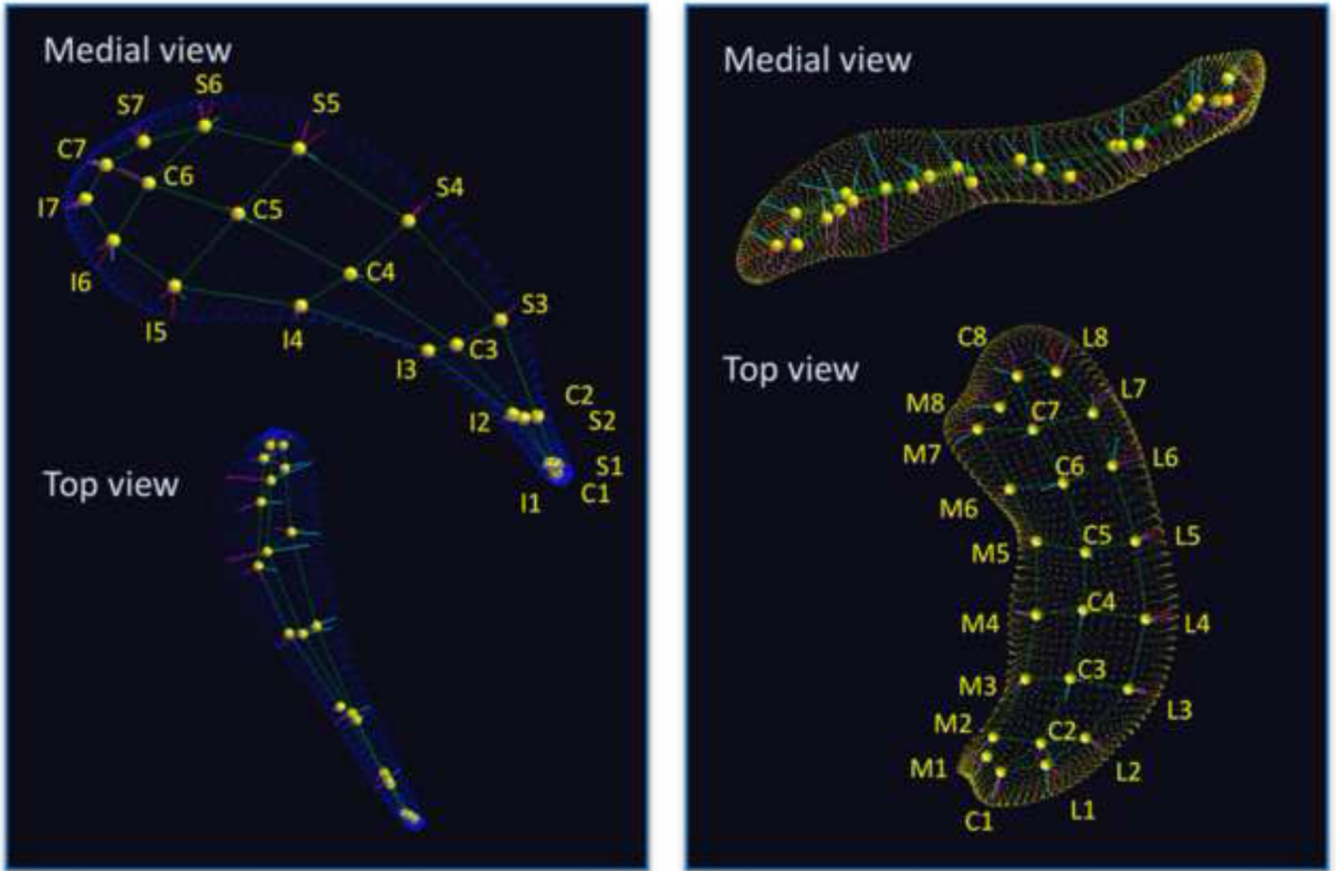
Figure 1.
Visualization of the medial representation grid and node labeling for right caudate (left, labeled from a medial view) and hippocampus (right, labeled from the top view). Labels: S = Superior, C = Central, I = Inferior, M = Medial, L = Lateral. Increasing numerical value means going from a posterior to an anterior location. Local *radius* is represented by the length of the thin rods projecting from the node points, the node *width*. Local *position* is represented by the location of the node points measuring local *deformation*.
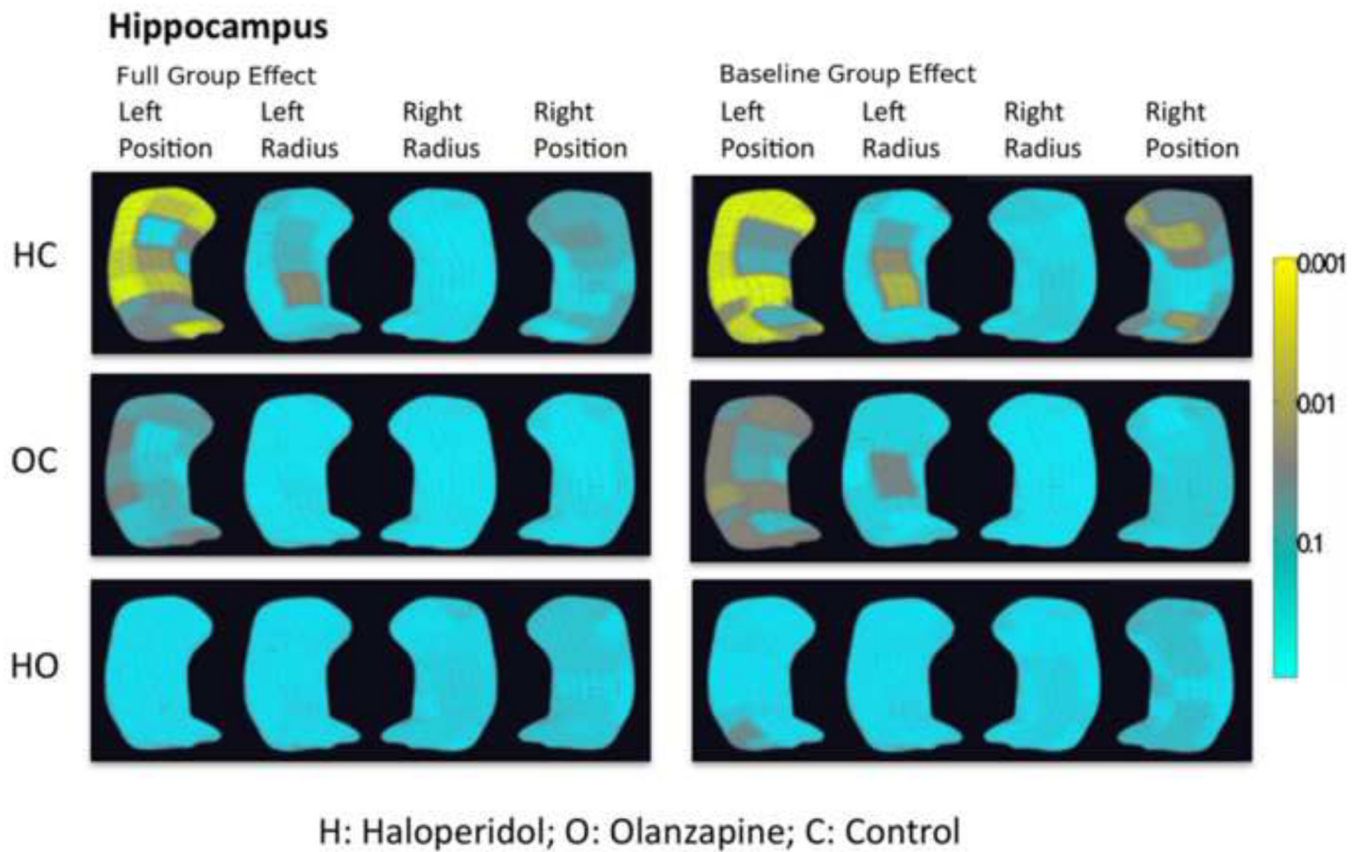
Figure 2.
Visualization of local significance in medial position and width in the hippocampus. Left:
Baseline group effect only (without repeated measures), Right: Full group effect. P-values
are visualized from cyan (p=0.1) to yellow (p=0.001). All maps are corrected for multiple
comparisons.
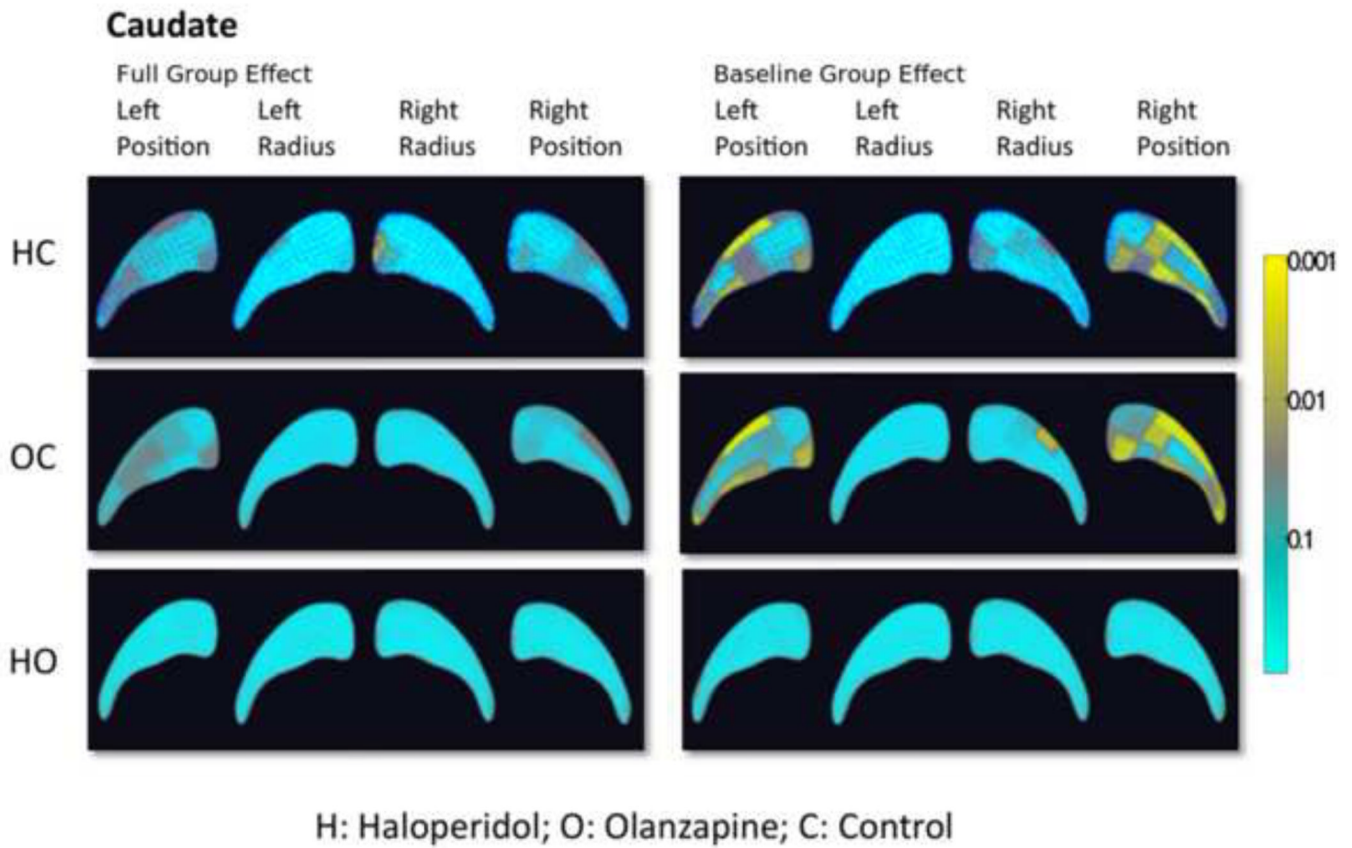
Figure 3.
Visualization of local significance in medial position and radius in the caudate. Left: Baseline group effect only (without repeated measures), Right: Full group effect. P-values are visualized from cyan (p=0.1) yellow (p=0.001). All maps are corrected for multiple comparisons.

Table 1

Demographic Characteristics of Patients and Controls at Baseline

	Age (years)		Baseline Whole Brain Volume (liters)	
	Mean	SS.D.	Mean	SS.D.
Haloperidol	24.14	4.89	1.335	0.129
Olanzapine	23.56	4.63	1.330	0.143
Controls	25.28	3.97	1.368	0.127

Table 2

Demographic Characteristics of Patients and Controls at Baseline

| | Gender | | Race | | | |
	Male	Female	Caucasian	African American	Other	Total
Haloperidol	102	21	65	48	10	123
Olanzapine	89	26	57	45	13	115
Controls	37	19	34	15	7	56

Table 3

Hippocampal Width, longitudinal

	left					right			
	group*time	H time	O time	C time		group*time	H time	O time	C time
M1	0.6624	0.8285	0.4288	0.8681	M1	0.5959	0.7149	0.268	0.3993
M2	0.2684	0.496	0.5267	0.5443	M2	0.1286	0.5843	0.6252	0.3771
M3	0.5937	0.848	0.4463	0.9243	M3	0.1035	0.3072	0.7212	0.3106
M4	0.4316	0.7987	0.4198	0.9024	M4	0.6955	0.4687	0.7986	0.4193
M5	0.8541	0.9529	0.8242	0.8233	M5	0.6912	0.5588	0.5296	0.864
M6	0.8278	0.9225	0.9506	0.6766	M6	0.3618	0.391	0.5278	0.8987
M7	0.4551	0.9096	0.3007	0.6498	M7	0.4054	0.7022	0.3046	0.7701
M8	**0.0257**	0.3551	0.4598	0.2977	M8	0.9882	0.6015	0.4582	0.5044
C1	0.4004	0.6636	0.3878	0.7083	C1	0.2015		0.3694	0.6508
C2	**0.0466**	0.5744	0.2765	0.2882	C2	0.3499	0.3752	0.8143	0.4528
C3	**0.0435**	0.605	0.2062	0.6757	C3	0.5941	0.5819	0.3382	0.6679
C4	0.1051	0.7993	0.2043	0.4159	C4	0.3237	0.645	0.7088	0.6142
C5	0.0724	0.9994	0.6881	0.3372	C5	0.5744	0.7552	0.4489	0.6957
C6	0.4827	0.7385	0.7506	0.5152	C6	0.0784	0.3017	0.8724	0.252
C7	0.4642	0.8178	0.38	0.3099	C7	0.1982	0.4319	0.6508	0.6335
C8	0.4102	0.5975	0.2344	0.2369	C8	0.6735	0.9479	0.4208	0.7241
L1	0.5060	0.7148	0.9592	0.4169	L1	0.7856	0.7608	0.7663	0.7836
L2	0.2458	0.3641	0.6154	0.8323	L2	0.3776	0.888	0.9058	0.4855
L3	0.4904	0.8154	0.4549	0.4732	L3	0.0718	0.2442	0.6262	0.812
L4	0.5559	0.6717	0.8233	0.5124	L4	0.8677	0.6307	0.7243	0.4845
L5	0.1429	0.756	0.4538	0.312	L5	0.5803	0.5813	0.2786	0.5243
L6	**0.0307**	0.7912	0.7098	0.2566	L6	0.9751	0.8192	0.7346	0.869
L7	0.1788	0.8045	0.2904	0.2291	L7	0.0882	0.934	0.4112	0.4792
L8	0.5361	0.8394	0.3892	0.5541	L8	0.6895	0.522	0.3051	0.5235

Time effect, P-value

Nodes: M = medial, C = Central, L = Lateral

Node number: 1 = Posterior, 8 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 4

Hippocampal Deformation, longitudinal

	left					right			
	group*time	H time	O time	C time		group*time	H time	O time	C time
M1	0.9611	0.7181	0.3917	0.2954	M1	0.8820	0.4043	0.7353	0.3789
M2	0.3344	0.7779	0.2206	0.1487	M2	0.6712	0.7558	0.1903	0.3469
M3	0.2527	0.9388	0.1902	0.2739	M3	0.8556	0.9630	0.6183	0.8667
M4	0.9031	0.9907	0.4296	0.3921	M4	0.8142	0.8220	0.6764	0.9016
M5	0.8953	0.7213	0.8323	0.4110	M5	0.2397	0.8633	0.4457	0.3838
M6	0.7936	0.7033	0.4409	0.4911	M6	0.5205	0.5850	0.7657	0.2116
M7	0.8448	0.8258	0.4403	0.3140	M7	0.7891	0.6915	0.6524	0.5085
M8	0.4775	0.9040	0.4379	0.2571	M8	0.8512	0.8042	0.8757	0.5350
C1	0.7788	0.9402	0.4375	0.3597	C1	0.9727	0.9500	0.8748	0.6064
C2	0.3819	0.8497	0.2845	0.1683	C2	0.8971	0.9609	0.4066	0.5154
C3	0.5740	0.7334	0.2720	0.3148	C3	0.9896	0.9664	0.5598	0.8666
C4	0.8610	0.8586	0.2641	0.3628	C4	0.8749	0.6688	0.8196	0.9969
C5	0.4137	0.9641	0.2729	0.1901	C5	0.5134	0.7396	0.6428	0.5320
C6	0.9071	0.7381	0.3376	0.6445	C6	0.3541	0.6080	0.3382	0.7786
C7	0.8972	0.9592	0.3328	0.3487	C7	0.5989	0.6991	0.2768	0.4375
C8	0.5955	0.9232	0.3139	0.2707	C8	0.9998	0.8317	0.5949	0.5823
L1	0.6266	0.9867	0.2847	0.2676	L1	0.9300	0.4090	0.5643	0.2999
L2	0.6306	0.9978	0.3566	0.3505	L2	0.9942	0.5367	0.5631	0.3624
L3	0.7160	0.7951	0.5331	0.8824	L3	1.0000	0.7182	0.7015	0.5703
L4	0.7369	0.9315	0.3388	0.5595	L4	0.9986	0.8504	0.8499	0.7315
L5	0.5627	0.9309	0.2972	0.2324	L5	0.7617	0.8904	0.5871	0.8680
L6	0.8191	0.7986	0.4541	0.5012	L6	0.6222	0.4962	0.5933	0.3638
L7	0.2285	0.5915	0.2726	0.1466	L7	0.9691	0.7909	0.4710	0.5614
L8	0.3612	0.9487	0.1859	0.1626	L8	0.9529	0.8134	0.6068	0.6812

Time effect, P-value

Nodes: M = medial, C = Central, L = Lateral

Node number: 1 = Posterior, 8 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 5

Hippocampal Width Full Group Effects

	left				right		
	HC	OC	HO		HC	OC	HO
M1	0.4396	0.9694	0.6242	M1	0.7874	0.7883	0.5023
M2	0.7946	0.9391	0.6242	M2	0.9893	0.7269	0.5023
M3	0.3858	0.7747	0.9212	M3	0.8162	0.7269	0.5023
M4	0.3858	0.7426	0.9951	M4	0.9893	0.9091	0.9064
M5	0.4820	0.9868	0.6242	M5	0.8138	0.8626	0.5561
M6	0.7946	0.7426	0.8928	M6	0.5340	0.7279	0.5023
M7	0.7946	0.9694	0.9212	M7	0.5340	0.7269	0.9064
M8	0.2057	0.9391	0.1944	M8	0.8162	0.8964	0.9064
C1	0.2057	0.7426	0.9212	C1	0.7744	0.8964	0.5023
C2	0.5291	0.7747	0.8928	C2	0.5340	0.8426	0.5023
C3	**0.0214**	0.7426	0.3256	C3	0.8162	0.8626	0.5023
C4	**0.0214**	0.5760	0.6242	C4	0.9893	0.7269	0.5023
C5	0.1689	0.7426	0.9368	C5	0.7744	0.8626	0.5023
C6	0.2057	0.7438	0.6242	C6	0.8138	0.9091	0.5023
C7	0.5291	0.7426	0.8928	C7	0.9893	0.7269	0.5561
C8	0.3858	0.5760	0.6242	C8	0.7744	0.7269	0.9064
L1	0.3858	0.7438	0.9368	L1	0.7874	0.7269	0.9064
L2	0.6177	0.7747	0.9368	L2	0.7744	0.8250	0.9064
L3	0.7946	0.7426	0.9368	L3	0.5340	0.8426	0.9064
L4	0.7946	0.9391	0.9368	L4	0.7744	0.7269	0.5561
L5	0.6177	0.7438	0.6242	L5	0.8162	0.8426	0.5023
L6	0.5291	0.7426	0.9368	L6	0.8162	0.8626	0.5561
L7	0.2057	0.7747	0.3256	L7	0.8138	0.7269	0.5561
L8	0.6284	0.7747	0.8398	L8	0.7874	0.8627	0.5023

FDR-corrected significance values

Cross-sectional with repeated measures component

Nodes: M = medial, C = Central, L = Lateral

Node number: 1 = Posterior, 8 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 6

Hippocampal Width Baseline Group Effects

	left				right		
	HC	**OC**	**HO**		**HC**	**OC**	**HO**
M1	0.7451	0.6138	0.6006	M1	0.6323	0.8251	0.6629
M2	0.6875	0.5964	0.6681	M2	0.7573	0.8251	0.8227
M3	0.3579	0.4833	0.8010	M3	0.5906	0.9691	0.8227
M4	0.2657	0.4833	0.8010	M4	0.8135	0.9691	0.8227
M5	0.6490	0.7403	0.6681	M5	0.6200	0.8251	0.6629
M6	0.7694	0.4194	0.6681	M6	0.3984	0.9691	0.5048
M7	0.7451	0.7103	0.6006	M7	0.5906	0.8251	0.8227
M8	**0.0296**	0.4833	0.6006	M8	0.3984	0.9819	0.5048
C1	0.6490	0.4833	0.9947	C1	0.3984	0.8251	0.8227
C2	0.7694	0.9773	0.6681	C2	0.3984	0.8251	0.5382
C3	**0.0068**	0.4194	0.6006	C3	0.3984	0.9819	0.5048
C4	**0.0068**	**0.0406**	0.6681	C4	0.3984	0.9819	0.5048
C5	**0.0189**	**0.0406**	0.8995	C5	0.3984	0.9691	0.5382
C6	0.1118	0.4833	0.6681	C6	0.5725	0.9819	0.5048
C7	0.7694	0.4833	0.9681	C7	0.6153	0.8251	0.9506
C8	0.7694	0.4833	0.6681	C8	0.3984	0.8251	0.8227
L1	0.7178	0.9660	0.6681	L1	0.5725	0.8251	0.8881
L2	0.7694	0.4833	0.6681	L2	0.8135	0.9691	0.8227
L3	0.7178	0.4833	0.8010	L3	0.3984	0.8251	0.8227
L4	0.7178	0.4833	0.8010	L4	0.5659	0.9691	0.5048
L5	0.5496	0.9773	0.6681	L5	0.5906	0.9691	0.8227
L6	0.7694	0.4833	0.6681	L6	0.5725	0.9691	0.8227
L7	0.2657	0.4833	0.8010	L7	0.8135	0.9691	0.8227
L8	0.2805	0.4833	0.6681	L8	0.6323	0.9691	0.7785

FDR-corrected significance values

Cross-sectional without repeated measures component

Nodes: M = medial, C = Central, L = Lateral

Node number: 1 = Posterior, 8 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 7

Hippocampal Deformation Full Group Effects

	left				right		
	HC	OC	HO		HC	OC	HO
M1	**0.0079**	0.0752	0.7655	M1	0.1833	0.6100	0.3733
M2	0.1197	0.5293	0.7655	M2	0.5543	0.6707	0.3680
M3	**0.0271**	0.2168	0.7655	M3	0.3076	0.6100	0.4154
M4	**0.0079**	0.3169	0.7655	M4	0.6575	0.6100	0.3680
M5	0.4365	0.6990	0.7655	M5	0.6150	0.6100	0.5107
M6	**0.0271**	0.2174	0.7655	M6	0.6150	0.6100	0.3680
M7	**0.0018**	0.0997	0.7655	M7	0.1267	0.7488	0.3680
M8	**0.0012**	**0.0354**	0.7655	M8	0.0896	0.6100	0.3680
C1	**0.0012**	**0.0354**	0.7655	C1	0.1984	0.7863	0.6735
C2	0.0620	0.2174	0.7655	C2	0.9746	0.7488	0.3680
C3	**0.0271**	0.2168	0.7655	C3	0.1833	0.7588	0.5107
C4	**0.0044**	0.1582	0.7655	C4	0.6150	0.6100	0.4542
C5	**0.0151**	0.3274	0.7655	C5	0.3076	0.8371	0.5399
C6	0.5531	0.5293	0.7655	C6	0.1521	0.9357	0.3680
C7	**0.0043**	0.0831	0.7655	C7	0.0696	0.8371	0.3680
C8	**0.0014**	0.1582	0.7655	C8	0.1502	0.8371	0.3680
L1	**0.0271**	0.1434	0.7655	L1	0.1709	0.8371	0.3680
L2	**0.0392**	0.3274	0.7655	L2	0.0696	0.6100	0.3680
L3	0.0867	0.3274	0.7655	L3	0.1344	0.6100	0.4154
L4	**0.0000**	**0.0354**	0.7655	L4	0.1267	0.6100	0.7010
L5	**0.0029**	0.0831	0.7655	L5	0.4503	0.6100	0.6872
L6	**0.0012**	**0.0354**	0.7655	L6	0.1833	0.6100	0.4154
L7	**0.0000**	0.1157	0.7655	L7	0.1836	0.6707	0.6735
L8	**0.0000**	0.0662	0.7655	L8	0.1833	0.6100	0.3680

FDR-corrected significance values

Cross-sectional with repeated measures component

Nodes: M = medial, C = Central, L = Lateral

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Node number: 1 = Posterior, 8 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 8

Hippocampal Deformation Baseline Group Effects

	left				right		
	HC	OC	HO		HC	OC	HO
M1	**0.0048**	**0.0393**	0.9244	M1	**0.0321**	0.4092	0.3072
M2	0.2094	0.1619	0.6284	M2	0.0562	0.4092	0.3072
M3	**0.0348**	**0.0232**	0.6284	M3	0.3127	0.3936	0.5867
M4	**0.0018**	**0.0250**	0.6284	M4	0.4924	0.4092	0.8997
M5	0.1774	0.3576	0.7572	M5	0.5309	0.4092	0.3072
M6	0.0608	0.1150	0.7837	M6	0.5960	0.6479	0.5867
M7	**0.0010**	**0.0330**	0.7572	M7	**0.0321**	0.4092	0.6235
M8	**0.0048**	**0.0250**	0.6284	M8	**0.0084**	0.4092	0.2232
C1	**0.0131**	**0.0255**	0.9472	C1	**0.0202**	0.4092	0.5361
C2	0.1774	0.2787	0.7572	C2	0.3399	0.5710	0.3072
C3	**0.0004**	**0.0250**	0.6284	C3	**0.0120**	0.4092	0.3072
C4	**0.0004**	**0.0250**	0.7801	C4	0.9634	0.4092	0.3072
C5	0.1312	0.1397	0.9403	C5	0.6639	0.4092	0.7668
C6	0.0608	0.1021	0.6284	C6	**0.0321**	0.4092	0.3104
C7	**0.0014**	**0.0232**	0.9244	C7	**0.0084**	0.5453	0.3072
C8	**0.0013**	**0.0285**	0.6284	C8	0.0538	0.8802	0.3072
L1	**0.0004**	**0.0250**	0.3304	L1	0.0562	0.5134	0.6864
L2	**0.0019**	**0.0250**	0.0576	L2	**0.0120**	0.4092	0.3072
L3	**0.0199**	0.0569	0.3304	L3	0.0550	0.4092	0.5867
L4	**0.0004**	**0.0144**	0.9244	L4	0.1265	0.4092	0.7902
L5	**0.0018**	**0.0250**	0.8571	L5	0.4924	0.4315	0.7547
L6	**0.0012**	**0.0250**	0.6284	L6	0.0795	0.4092	0.5867
L7	**0.0000**	0.0708	0.6284	L7	**0.0405**	0.4335	0.6235
L8	**0.0000**	**0.0250**	0.6284	L8	0.0550	0.4315	0.3104

FDR-corrected significance values

Cross-sectional without repeated measures component

Nodes: M = medial, C = Central, L = Lateral

Node number: 1 = Posterior, 8 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 9

Caudate Width, longitudinal

	left					right				
	group*time	H time	O time	C time		group*time	H time	O time	C time	
S1	0.4142	0.5760	0.6267	0.7861	S1	**0.0485**	0.3394	0.2699	0.5159	S1
S2	0.3372	0.6921	0.4018	0.8490	S2	0.3413	0.3453	0.8512	0.6438	S2
S3	0.2076	0.2615	0.9604	0.4140	S3	0.0614	0.2802	0.5813	0.9255	S3
S4	0.0870	0.3686	0.2562	0.8396	S4	**0.0290**	0.0952	0.1125	0.1445	S4
S5	**0.0493**	0.2855	0.4266	0.5134	S5	0.0510	0.1412	0.1864	0.3177	S5
S6	0.8957	0.8337	0.8484	0.8202	S6	0.1930	0.6024	0.1608	0.2389	S6
S7	0.9501	0.4663	0.4903	0.5104	S7	0.3063	0.3672	0.5012	0.8832	S7
C1	0.1553	0.4470	0.3540	0.9169	C1	0.7192	0.3272	0.3458	0.4155	C1
C2	0.2774	0.4195	0.5831	0.8989	C2	0.0537	0.4207	0.4060	0.4069	C2
C3	0.5504	0.9066	0.3352	0.3704	C3	0.1676	0.5459	0.9531	0.2944	C3
C4	0.1975	0.8472	0.6632	0.2907	C4	0.4134	0.5381	0.5346	0.9188	C4
C5	0.4423	0.4209	0.8739	0.4506	C5	0.4630	0.5220	0.9278	0.8196	C5
C6	0.1829	0.4146	0.4135	0.9842	C6	0.7247	0.9491	0.4365	0.4752	C6
C7	0.1673	0.4489	0.3788	0.8205	C7	0.3614	0.4642	0.7740	0.7944	C7
I1	**0.0192**	0.3365	0.8223	0.4632	I1	0.3340	0.5548	0.5658	0.5467	I1
I2	0.2834	0.4246	0.5146	0.8606	I2	**0.0404**	0.1684	0.3122	0.4200	I2
I3	0.8863	0.4450	0.3442	0.4475	I3	0.1951	0.9252	0.2216	0.4258	I3
I4	0.1104	0.8690	0.6667	0.3568	I4	0.7113	0.9724	0.7240	0.5354	I4
I5	0.0575	0.5192	0.4982	0.3361	I5	0.3246	0.5219	0.4911	0.6820	I5
I6	0.2550	0.4593	0.8483	0.3436	I6	0.4099	0.2916	0.6604	0.4786	I6
I7	0.8933	0.8006	0.4638	0.5107	I7	0.4341	0.9785	0.3300	0.8027	I7

Time effect, P-value,

Nodes: S = Superior, C = Central, I = Inferior

Node number: 1 = Posterior, 7 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 10

Caudate Deformation, longitudinal

	left					right			
	group*time	H time	O time	C time		group*time	H time	O time	C time
S1	0.9861	0.4929	0.8584	0.5787	S1	0.8925	0.8553	0.3313	0.7306
S2	0.6928	0.4639	0.9544	0.5855	S2	0.9519	0.6819	0.8879	0.9753
S3	0.5208	0.3056	0.9789	0.9699	S3	0.8032	0.2438	0.6067	0.3910
S4	0.6751	0.3526	0.9776	0.5423	S4	0.3285	0.1281	0.0842	0.1062
S5	0.8437	0.4741	0.7944	0.3633	S5	0.8655	0.5915	0.3086	0.5155
S6	0.8784	0.4074	0.9386	0.5248	S6	0.9162	0.7661	0.2761	0.4080
S7	0.8708	0.4453	0.8262	0.3956	S7	0.9947	0.7959	0.3954	0.4315
C1	0.9379	0.4545	0.8982	0.4129	C1	0.6343	0.6203	0.3441	0.6105
C2	0.7516	0.4367	0.6694	0.7032	C2	0.8422	0.9828	0.4074	0.4268
C3	0.8865	0.3926	0.8006	0.5203	C3	0.6645	0.4640	0.5141	0.7548
C4	0.9998	0.8795	0.8355	0.7476	C4	0.3577	0.1494	0.4356	0.2541
C5	0.6249	0.1833	0.9050	0.2799	C5	0.6658	0.5035	0.2570	0.3665
C6	0.8911	0.4805	0.9973	0.6810	C6	0.8733	0.7533	0.7235	0.8158
C7	0.6802	0.4463	0.9634	0.7740	C7	0.7422	0.7542	0.7627	0.9831
I1	0.9190	0.4179	0.9388	0.4874	I1	0.7464	0.5265	0.3664	0.4866
I2	0.6176	0.2985	0.9603	0.4445	I2	0.9680	0.8486	0.6127	0.5951
I3	0.5878	0.4155	0.9058	0.3210	I3	0.9558	0.9135	0.8015	0.7926
I4	0.9378	0.7851	0.8517	0.7458	I4	0.9161	0.6180	0.8890	0.7973
I5	0.4842	0.3357	0.8080	0.5894	I5	0.9077	0.9845	0.7752	0.8804
I6	0.6150	0.5205	0.6709	0.7599	I6	0.8146	0.9435	0.7015	0.8898
I7	0.8343	0.5257	0.6726	0.5882	I7	0.7904	0.7642	0.7922	0.9626

Time effect, P-value,

Nodes: S = Superior, C = Central, I = Inferior

Node number: 1 = Posterior, 7 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 11

Caudate Width Full Group Effects

	left				right		
	HC	**OC**	**HO**		**HC**	**OC**	**HO**
S1	0.9961	0.9999	0.9995	S1	1.0000	0.9999	1.0000
S2	0.9961	0.9999	0.9995	S2	1.0000	0.9999	1.0000
S3	0.9961	0.9999	0.9995	S3	1.0000	0.9999	1.0000
S4	0.1134	0.2961	0.9995	S4	1.0000	0.9999	1.0000
S5	0.9961	0.9999	0.9995	S5	1.0000	0.9999	1.0000
S6	0.9961	0.9999	0.9995	S6	1.0000	0.9999	1.0000
S7	0.9961	0.9999	0.9995	S7	0.9366	0.9999	1.0000
C1	0.9961	0.9999	0.9995	C1	0.9382	0.9999	1.0000
C2	0.9961	0.9999	0.9995	C2	1.0000	0.9999	1.0000
C3	0.9961	0.9999	0.9995	C3	1.0000	0.9999	1.0000
C4	0.9961	0.9999	0.9995	C4	1.0000	0.9999	1.0000
C5	0.9961	0.9999	0.9995	C5	1.0000	0.9999	1.0000
C6	0.9961	0.9999	0.9995	C6	1.0000	0.9999	1.0000
C7	0.9961	0.9999	0.9995	C7	1.0000	0.9999	1.0000
I1	0.9961	0.9999	0.9995	I1	1.0000	0.9999	1.0000
I2	0.9961	0.9999	0.9995	I2	1.0000	0.9999	1.0000
I3	0.9961	0.9999	0.9995	I3	1.0000	0.9999	1.0000
I4	0.9961	0.9999	0.9995	I4	1.0000	0.9999	1.0000
I5	0.9961	0.9999	0.9995	I5	1.0000	0.9999	1.0000
I6	0.4820	0.9999	0.9995	I6	0.1796	0.9999	1.0000
I7	0.4865	0.9999	0.9995	I7	**0.0042**	0.9999	1.0000

FDR-corrected significance values

Cross-sectional with repeated measures component

Nodes: S = Superior, C = Central, I = Inferior

Node number: 1 = Posterior, 7 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 12

Caudate Width Baseline Group Effects

	left				right		
	HC	**OC**	**HO**		**HC**	**OC**	**HO**
S1	1.0000	1.0000	0.9999	S1	0.9977	0.9995	0.9998
S2	1.0000	1.0000	0.9999	S2	0.9977	0.9995	0.9998
S3	1.0000	1.0000	0.9999	S3	0.9977	0.9995	0.9998
S4	1.0000	1.0000	0.9999	S4	**0.0252**	**0.0042**	0.9998
S5	1.0000	1.0000	0.9999	S5	0.4704	0.2972	0.9998
S6	1.0000	1.0000	0.9999	S6	0.9977	0.9995	0.9998
S7	1.0000	1.0000	0.9999	S7	0.7069	0.9995	0.9998
C1	1.0000	1.0000	0.9999	C1	0.4919	0.9995	0.9998
C2	1.0000	1.0000	0.9999	C2	0.4930	0.9995	0.9998
C3	1.0000	1.0000	0.9999	C3	0.4704	0.9995	0.9998
C4	1.0000	1.0000	0.9999	C4	0.4704	0.8266	0.9998
C5	1.0000	1.0000	0.9999	C5	0.2153	0.4802	0.9998
C6	1.0000	1.0000	0.9999	C6	0.9977	0.9995	0.9998
C7	1.0000	1.0000	0.9999	C7	0.9977	0.9995	0.9998
I1	1.0000	1.0000	0.9999	I1	0.9977	0.9995	0.9998
I2	1.0000	1.0000	0.9999	I2	0.9977	0.9995	0.9998
I3	1.0000	1.0000	0.9999	I3	0.7069	0.9995	0.9998
I4	1.0000	1.0000	0.9999	I4	0.9977	0.9995	0.9998
I5	1.0000	1.0000	0.9999	I5	0.9977	0.9995	0.9998
I6	1.0000	1.0000	0.9999	I6	0.0938	0.8266	0.9998
I7	1.0000	1.0000	0.9999	I7	**0.0415**	0.9995	0.9998

FDR-corrected significance values

Cross-sectional without repeated measures component

Nodes: S = Superior, C = Central, I = Inferior

Node number: 1 = Posterior, 7 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 13

Caudate Deformation Full Group Effects

	left				right		
	HC	OC	HO		HC	OC	HO
S1	0.1664	0.2702	0.8603	S1	0.7576	0.5684	0.9845
S2	**0.0284**	0.2624	0.7428	S2	0.1591	0.2219	0.9845
S3	0.2470	0.1533	0.8603	S3	**0.0200**	**0.0368**	0.9845
S4	0.1470	0.1527	0.9557	S4	**0.0200**	**0.0294**	0.9845
S5	**0.0284**	0.1533	0.8636	S5	0.1591	0.2212	0.9845
S6	**0.0284**	0.3195	0.7428	S6	0.2176	0.3045	0.9845
S7	0.1470	0.7325	0.7428	S7	0.8461	0.7941	0.9929
C1	0.2221	0.2624	0.7428	C1	0.4312	0.5684	0.9845
C2	0.0936	0.3480	0.8603	C2	0.5297	0.5919	0.9845
C3	**0.0466**	0.0525	0.7428	C3	0.8877	0.8217	0.9845
C4	0.2470	**0.0494**	0.7428	C4	0.1591	0.7446	0.9845
C5	0.4138	0.1825	0.8636	C5	0.8290	0.7446	0.9845
C6	0.3860	0.6511	0.7428	C6	0.7576	0.4053	0.9845
C7	0.2562	0.7552	0.7428	C7	0.9838	0.7048	0.9845
I1	**0.0284**	0.0525	0.8603	I1	0.4175	0.4053	0.9845
I2	**0.0462**	0.1621	0.7428	I2	0.1591	0.2219	0.9845
I3	0.0725	0.0525	0.8636	I3	0.1591	0.2835	0.9845
I4	0.3637	0.2624	0.8636	I4	0.1591	0.4053	0.9845
I5	0.4138	0.7048	0.8636	I5	0.5297	0.7672	0.9845
I6	**0.0495**	**0.0494**	0.8509	I6	0.1591	0.2219	0.9845
I7	0.2381	0.0676	0.7428	I7	0.7576	0.5684	0.9845

FDR-corrected significance values

Cross-sectional with repeated measures component

Nodes: S = Superior, C = Central, I = Inferior

Node number: 1 = Posterior, 7 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control

Table 14

Caudate Deformation Baseline Group Effects

	left			right			
	HC	**OC**	**HO**		**HC**	**OC**	**HO**
S1	0.0743	0.2664	0.8307	S1	0.1673	**0.0037**	0.7606
S2	**0.0050**	**0.0475**	**0.0168**	S2	**0.0298**	**0.0084**	0.9127
S3	**0.0156**	**0.0147**	0.7103	S3	**0.0000**	**0.0005**	0.9127
S4	**0.0000**	**0.0000**	0.7655	S4	**0.0000**	**0.0000**	0.7602
S5	**0.0011**	**0.0011**	0.7103	S5	**0.0007**	**0.0005**	0.9127
S6	**0.0320**	0.2426	0.7103	S6	**0.0320**	0.1998	0.9127
S7	**0.0110**	0.3421	0.7655	S7	0.4242	0.4343	0.9127
C1	**0.0298**	**0.0028**	0.7103	C1	**0.0298**	**0.0017**	0.7606
C2	0.0757	0.3548	0.8420	C2	0.0851	**0.0263**	0.9127
C3	0.5321	0.3770	0.7727	C3	0.5587	0.3206	0.9747
C4	**0.0320**	0.2342	0.7103	C4	0.2261	0.7065	0.9127
C5	0.5321	0.1274	0.7655	C5	**0.0048**	**0.0042**	0.9127
C6	0.5321	0.5157	0.7727	C6	0.5338	0.0888	0.9127
C7	0.0757	0.4582	0.4253	C7	0.5942	0.1708	0.9127
I1	**0.0102**	**0.0114**	0.8307	I1	**0.0011**	**0.0005**	0.9127
I2	**0.0042**	**0.0147**	0.7655	I2	**0.0011**	**0.0036**	0.9127
I3	**0.0042**	**0.0047**	0.8420	I3	**0.0068**	**0.0076**	0.9127
I4	**0.0298**	**0.0114**	0.8466	I4	**0.0011**	**0.0063**	0.9127
I5	0.1560	0.3069	0.8307	I5	**0.0320**	0.2195	0.7606
I6	**0.0108**	**0.0050**	0.7727	I6	**0.0070**	**0.0028**	0.7602
I7	0.1356	**0.0131**	0.7103	I7	0.3164	**0.0202**	0.9127

FDR-corrected significance values

Cross-sectional without repeated measures component

Nodes: S = Superior, C = Central, I = Inferior

Node number: 1 = Posterior, 7 = Anterior

Groups: H = Haloperidol; O = Olanzapine; C = Control