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ORIGINAL RESEARCH

Altered asymmetries of diffusion and volumetry in basal ganglia of schizophrenia

Hui He[1] · Cheng Luo[1,2] · Ning Li[1,2] · Zhiliang Li[1,2] · Mingjun Duan[1] · Gang Yao[1] · Hongming Wang[1] · Manxi He[1] · Dezhong Yao[1,3]

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Abstract

Basal ganglia, which include the striatum and thalamus, have key roles in motivation, emotion, motor function, also contribute to higher-order cognitive function. Previous researches have documented structural and functional alterations in basal ganglia in schizophrenia. While few studies have assessed asymmetries of these characters in basal ganglia of schizophrenia. The current study investigated this issue by using diffusion tensor imaging, anatomic T1-weight image and resting-state functional data from 88 chronic schizophrenic subjects and 92 healthy controls. The structural characteristic, including fractional anisotropy, mean diffusivity (MD) and volume, were extracted and quantified from the subregions of basal ganglia, including caudate, putamen, pallidum and thalamus, through automated atlas-based method. The resting-state functional maps of these regions were also calculated through seed-based functional connectivity. Then, the laterality indexes of structural and functional features were calculated. Compared with healthy controls, schizophrenic subjects showed increased left laterality of volume in striatum and reduced left laterality of volume in thalamus. Furthermore, the difference of laterality of subregions in thalamus is compensatory in schizophrenic subjects. Importantly, the severity of patients' positive symptom was negative corelated with reduced left laterality of volume in thalamus. Our findings provide preliminary evidence demonstrating that the possibility of aberrant laterality in neural pathways and connectivity patterns related to the basal ganglia in schizophrenia.

Keywords Schizophrenia · Basal ganglia · Diffusion tensor imaging · Magnetic resonance imaging · Asymmetry

Introduction

Schizophrenia is a complex psychiatric disorder, which is affecting about one percentage of the population in the world (Bhugra 2005). Schizophrenic subject is always characterized by both positive and negative symptoms, as well as cognitive impairment. The hyperactive dopamine of basal ganglia is the dominant hypothesis to interpret the symptoms of schizophrenia (Abi-Dargham 2004). Specifically, prior research has reported that structural and functional changes of basal ganglia, such as volumetric changes, is closely related to characteristic symptoms of patients with schizophrenia (van Erp et al. 2016). Understanding the structural and functional abnormality of basal ganglia might enhance our knowledge about pathophysiology of schizophrenia.

The primarily regions within basal ganglia include the striatum, globus pallidus, thalamus and substantia nigra (Parent 1990). The caudate and putamen regions are two subregions of striatum, which is the principal component of basal ganglia (Ballmaier et al. 2008). In human brain the basal ganglia receive information from cerebral cortex, and send projections back to cortex through thalamus. This neural circuit is supporting the various functions of basal ganglia, including motivation, emotion, motor and cognitive processing (Cropley et al. 2006). Many neuroimaging studies have been

✉ Cheng Luo
chengluo@uestc.edu.cn

✉ Mingjun Duan
fourhospital@163.com

[1] The Clinical Hospital of Chengdu Brain Science Institute, MOE Key Lab for Neuroinformation, University of Electronic Science and Technology of China, Chengdu 610054, People's Republic of China

[2] High-Field Magnetic Resonance Brain Imaging Key Laboratory of Sichuan Province, School of life Science and technology, University of Electronic Science and Technology of China, Chengdu 610054, People's Republic of China

[3] Research Unit of NeuroInformation, Chinese Academy of Medical Sciences,2019RU035, Chengdu, China

employed in exploring the pathophysiology of schizophrenia (Dong et al. 2018a; He et al. 2017; Javitt 2009). Specifically, the alteration of structural characters of basal ganglia has been repeatedly reported in schizophrenia (Glenthoj et al. 2007; Mamah et al. 2007). The abovementioned results might suggest the possibility of aberrant structure in neural pathway relate with the basal ganglia in schizophrenia.

Brain lateralization is considered having highly relationship with human psychological and behavioral characteristics (Toga and Thompson 2003). Previous researches revealed that the function of left hemisphere supported language and logical thinking processing, and right hemisphere provided the functional basis for the ability of creativity and intuition (Corballis 2014). Moreover, various structural and functional studies have found the lateralization of subcortical regions in human brain (Kallai et al. 2005; Pedraza et al. 2004). Specifically, in schizophrenia, increased evidence suggests that the disruption of lateralization is related with the disconnection syndrome, which found in behavioral and psychophysiological researches (Barnett et al. 2007; Mohr et al. 2000). These findings suggest that the abnormality of lateralization is related to specific pathophysiological of schizophrenia. While, there are few studies focus on the abnormal structural and functional lateralization of basal ganglia in schizophrenia (Okada et al. 2016; van Erp et al. 2016).

Based on the findings from functional neuroimaging studies, we hypothesized that the altered structural and functional lateralization of basal ganglia would be related to the symptom of schizophrenia, and would extend our understanding of schizophrenia's pathophysiology. Therefore, in this study, we sought to determine this relationship through the asymmetry analysis of structural and functional characters in basal ganglia regions of schizophrenic subjects. We posit that these reflect local structural lateralization changes in basal ganglia are an important driving factor in pathological functional changes in schizophrenia.

Materials and methods

Subjects selection

A total of eighty-eight chronic inpatients with schizophrenia were recruited from the Clinical Hospital of Chengdu Brain Science Institute. The inpatients were confirmed using the Structured Clinical Interview for the DSM-IV Axis I disorders – clinical version (SCID-I-CV), and all were being treated with medication (e.g., antipsychotics). The psychiatric symptom of schizophrenia was assessed using Positive and Negative Symptom Scale (PANSS). Matched ninety-two healthy controls were also recruited from a volunteer panel to participate in the study. Moreover, healthy controls were screened for a history of medical or neuropsychiatric illness, as well as major neurological or psychiatric illness in their first-degree relatives. Details of demographic characteristics of both groups are showed in Table 1.

Data acquisition and image preprocessing

The experiments were performed on a 3 T MRI scanner. The high-resolution T1-weighted images were acquired using a 3-dimensional fast spoiled gradient echo sequence (repetition time (TR) = 6.008 ms, flip angle = 9-degree, matrix = 256 × 256, field of view (FOV) = 256 × 256 mm, slice thickness = 1 mm, no gap, 158 slices). Subsequently, resting state functional MRI data were acquired using gradient-echo echo planar imaging sequences (TR = 2000 ms, echo time [TE] = 30 ms, FA = 90°, matrix = 64 × 64, FOV = 240 × 240 mm^2, slice thickness/gap = 4 mm/0.4 mm, number of slices = 35), with an eight channel-phased array head coil. All subjects underwent a 510-s resting state scan to yield 255 volumes. During resting-state fMRI, all subjects were instructed to have their eyes-closed and to move as little as possible without falling asleep. After obtaining three unweighted images, diffusion-weighted images were acquired in 64 directions using a diffusion-weighted spin-echo EPI sequence (b = 1000s/mm^2, TR = 8500 ms, matrix = 128 × 128, FOV = 256 × 256 mm, slice thickness = 2 mm, 78 slices). Another three unweighted images were obtained in the anterior/posterior frequency direction to estimate and correct for susceptibility-induced distortions.

The structural images were processed using the SPM8 toolbox, with spatial normalization to the MNI-space using a diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL), and segmentation into grey matter (GM), white matter and cerebrospinal fluid. The segmented GM was modulated using nonlinear deformation. The resulting image was masked at a probability of 20%. For DTI images, head motion was removed by aligning 15 diffusion-weighted scans to *bo* image. Eddy current distortions were corrected by affine registration to the reference *bo* image. Then, the fractional anisotropy (FA) and mean diffusivity (MD) maps were obtained from the eigen values through Diffusion Toolkit 0.6 (http://trackvis.org/dtk/).

Functional image preprocessing was performed using NIT (Neuroscience Information Toolbox) (L. Dong et al. 2018a, 2018b) according to a standard pipeline and briefly described here. Slice time and head motion correction, normalization (3 mm * 3 mm * 3 mm) into EPI template were performed. Further the images were spatial smoothed (FWHM 6 mm). Detrending analysis was performed. Temporal filtering was performed at bandpass 0.01–0.08 Hz. Then the sources of nuisance signals were removed from these images, including six motion parameters and their first temporal derivative, white matter signal and cerebrospinal fluid signal. The global signal was not regressed out (Yang et al. 2014). Moreover,

Table 1. Demographic and clinical characteristics of the participants

	Patients with Schizophrenia	Healthy controls	*p*
Gender (Male/Female)	59/29	56/36	0.389[a]
Age (years)	38.84 ± 11.74	37.91 ± 14.52	0.638[b]
Education level (years)	9.69 ± 4.99	10.65 ± 3.25	0.123[b]
PANSS-positive score	13.55 ± 5.75	–	–
PANSS-negative score	20.90 ± 6.07	–	–
PANSS-global score	62.77 ± 12.49	–	–

Indicated values are shown mean ± standard deviation. PANSS: Positive and Negative Symptom Scale

[a] indicates the *p* values from the comparison analysis (Chi-square test)

[b] indicates the *p* values from the comparison analysis (two sample t-test)

subjects who had a maximum translation in any of orthogonal direction larger than 3 mm or rotation larger than 3 degree were excluded. Then, the functional map was obtained through Pearson correlation between seed and whole brain voxel within grey matter mask.

Structural and functional laterality analyses

Fourteen paired subregions (left and right hemisphere) within basal ganglia system were defined based on the Human Brainnetome Atlas (Fan et al. 2016), including ventral and dorsal caudate, dorsolateral and ventromedial putamen, globus pallidus, nucleus accumbens, and eight subregions of thalamus (Fig. 1). First, for the structural map, the mean structural characters value (volume, FA and MD) of these regions was extracted. Furthermore, the laterality index (LI) was defined as a metric of asymmetry for a given left and right basal ganglia regions. The LI was measured as the ratio [(left - right)]/[left + right]. This is commonly used to assess the brain structural asymmetry (Wang et al. 2001; Wyciszkiewicz and Pawlak 2014). Second, for the functional maps, the LI was assessed for a given left and right basal ganglia regions. Within each subject, the number of significant correlated voxels ($p < 0.001$) were calculated in left and right functional networks. Then, the LI of functional maps was measured as the ratio [(left - right)]/[left + right]. Finally, we compared the structural and functional LI values between schizophrenic and healthy subjects through two-sample t-test respectively. The gender, education years and age of the subjects were used as covariates. False discovery rate (FDR) correction was used for multiple comparisons ($p < 0.05$).

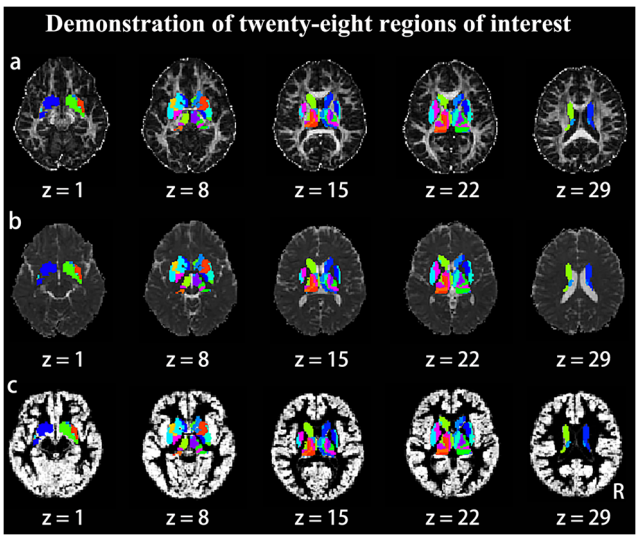

Fig. 1 Demonstration of twenty-eight regions of interest for a healthy subject. All regions were overlaid in FA (**a**), MD (**b**) and volume (**c**) maps. The different color represents the variable region

Validation analysis

To ensure a high reproducibility of our statistical results, the half of schizophrenic and healthy subjects were randomly selected from each group respectively. Then, the statistical analysis was performed. Gender, education years and age were used as the potential confounding covariates in the statistical analysis. The significance threshold of the group difference for the ANOVA was set to FDR corrected.

Correlations with pathological factors

The partial correlation analysis was performed between the altered LI and symptom scores of schizophrenic subjects with age, gender, and education years as covariates in this study. FDR correction ($p < 0.05$) was used for multiple comparisons.

Results

Demographic characteristics and clinical symptoms

There were no significant differences between two groups in distribution of age, gender and education years. Only 62 schizophrenic subjects participated in the evaluation of PNASS. Detailed information is shown in Table 1.

Table 2 Significant altered the left laterality index of structural characters in schizophrenia

Structural characters	Regions	T score
Volume	GP	3.83
	dCa	3.39
	mPFtha	−4.23
	lPFtha	−3.91
	cTtha	−3.72
	Otha	−3.46
MD	Stha	3.64
	cTtha	−3.81

GP: globus pallidus; dCa: dorsal caudate; mPFtha: medial prefrontal thalamus; lPFtha: lateral prefrontal thalamus; cTtha: caudal temporal thalamus; Otha: occipital thalamus; Stha: sensory thalamus; MD: mean diffusivity

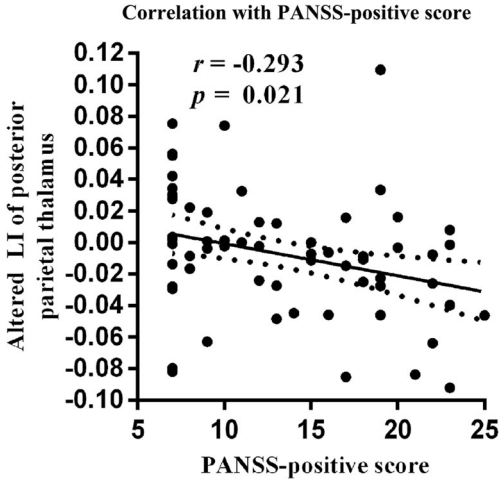

Fig. 2 The negative correlation between negative score in PANSS and the decreased laterality index of posterior parietal-thalamus in schizophrenic subjects

Group comparisons of laterality index of structural characters

First, for the volume of each region of basal ganglia, the increased left lateralities were observed in pallidus and dorsal caudate of schizophrenia. The decreased left lateralities were found in four subregions of thalamus, including occipital-thalamus, caudal-thalamus, lateral-thalamus and posterior parietal-thalamus of schizophrenia (Table 2). Second, for MD value, the decreased left laterality was observed in caudal-thalamus. The increased left laterality was found in sensory-thalamus (Table 2). Third, for FA value, there was no significant difference in regions of basal ganglia. Additionally, there are no significant LI difference of functional connectivity number between two groups. Furthermore, the similar results were observed through validation analysis.

Relationship between clinical symptom and laterality index

We observed an inverse correlation ($r = -0.293$, $p = 0.021$, uncorrected result) between PANSS-positive value and the LI of posterior parietal thalamus of schizophrenic subjects(Fig. 2). No other significant correlations were found between altered LI of structural characters and PANSS scores. There is also no significant relationship between altered LI and medication dosage, and education years of schizophrenic subjects respectively.

Discussion

The current study combined structural imaging and asymmetry approaches to characterize the structural features of basal ganglia in schizophrenic subjects and its relationship with clinical symptoms of schizophrenia. Consist with our hypothesis, the principal results of this study are schizophrenia-specific leftward asymmetry of volume for striatum, while rightward asymmetry of volume for thalamus. We also found a schizophrenic-specific balance altered laterality of MD in left and right subregions of thalamus. Additionally, the altered left laterality of thalamus was related with positive symptom of schizophrenic subjects. These findings suggest that the altered basal ganglia structures might play a key role in pathophysiology of schizophrenia.

The striatum, which is a main part of basal ganglia, have crucial role in motor and reward functions of human brain (Wichmann and Delong 2011). Within striatum, the function of caudate nucleus contributes to the planning and execution of behavior required for goals (Grahn et al. 2008), Caudate also joins in goal-directed behavior in social contexts (King-Casas et al. 2005). Together, caudate could guide individual's behavior based on response-dependent feedback to the desired outcome. Moreover, among the loop circuits of basal ganglia, the globus pallidus is located in the central position, which regulate the function of cerebral cortical via the projection to thalamus (Jaeger and Kita 2011). Previous study found schizophrenic subjects have higher blood flow in left pallidus, and functional hyperactive of left caudate compared to healthy controls (Duan et al. 2015; Early et al. 1987). Specifically, recent animal study found the functional interaction between pallidus and frontal cortex is ipsilateral and sensitive to antipsychotic drugs (Saunders et al. 2015). Thus, it is suggested that there may be abnormal asymmetry in functional pathways related to striatum in schizophrenia. In this study, we found increased leftward asymmetry of volume for caudate and pallidus in schizophrenic subjects. Our findings provided preliminary evidence demonstrating that the aberrant laterality in neural pathways might be related to striatum.

Within basal ganglia system, thalamus is one key role in integrating and coordinating of cortical activity by a cortico-

thalamic circuit (Horn and Blankenburg 2016). Altered cortico-thalamic functional connectivity was observed in schizophrenia, which have provided a potential specific-alteration pattern of subregions of thalamus (Gong et al. 2019). Converging evidence revealed that the abnormality of thalamus is central to schizophrenic pathophysiology, which contribute to clinical symptoms of schizophrenia (Steullet 2019). Moreover, recent study found the changes of cortico-thalamic networks could be embedded into disrupted cortico-striatum-thalamic loops of schizophrenia (Avram et al. 2018; Martino et al. 2017). The effect of changes of striatum will most likely lead to an altered function on thalamus or striatum-thalamus functional connectivity in schizophrenia. Consistent with these researches, in this study, we found reduced leftward asymmetry of volume and diffusion for subregions of thalamus in schizophrenic subjects. The reduced asymmetry of thalamus was negatively related with positive symptom of schizophrenic subjects. Moreover, increased leftward asymmetry of diffusion was observed in patients for posterior parietal-thalamus region. The difference of laterality of subregions in thalamus might be compensatory in schizophrenic subjects. Our findings provided evidence indicating that the aberrant laterality in thalamus might play a crucial role in disrupted cortico-striatum-thalamic loops of schizophrenia.

While our study provides evidence demonstrating the role of structural asymmetry of basal ganglia in understanding the pathophysiology of schizophrenia, several limitation points need to be further addressed. First, the inpatients of this study are chronic schizophrenic subjects with antipsychotic medication. The asymmetry of basal ganglia might be associated with antipsychotic treatment. Moreover, the education years of healthy group is higher than schizophrenia group. Although there is no significant relationship between laterality of structural feature and medication dosage, and education years in schizophrenia group. We should validate our finding in first-episode schizophrenic subjects. Second, we only assessed the structural character of basal ganglia, we should further measure the structural connectivity within basal ganglia and with cortical cortex in schizophrenic subjects.

Conclusion

The current study demonstrated the differences of laterality of diffusion and volumetry in schizophrenic subjects by asymmetry analysis. Critically, the positive symptom score of schizophrenic subjects was positively correlated with their reduced leftward asymmetry of volume for thalamus. Our findings provide preliminary findings for aberrant laterality changes of basal ganglia, further highlighting the evidence that these changes might have potential related to the disrupted cortico-striatum-thalamic loops of schizophrenia.

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Author contributions HH, CL, MD and DY had made a substantial contribution to the conception and drafting and revising the article; NL, ZL, GY, HW and MH had made a substantial contribution to the analysis and interpretation of the data, and then they gave final approval of the version to be published.

Compliance with ethical standards

Conflict of interest No conflicts of interest to declare.

Ethical approval All procedures performed in study involving participants were in accordance with the Ethics Committee of the Chengdu Mental Health Center in accordance with the Helsinki Declaration.

Informed consent Informed consent was obtained from all subjects included in the study.

References

Abi-Dargham, A. (2004). Do we still believe in the dopamine hypothesis? New data bring new evidence. *International Journal of Neuropsychopharmacology, 7*, S1–S5. https://doi.org/10.1017/S1461145704004110.

Avram, M., Brandl, F., Bauml, J., & Sorg, C. (2018). Cortico-thalamic hypo- and hyperconnectivity extend consistently to basal ganglia in schizophrenia. *Neuropsychopharmacology, 43*(11), 2239–2248. https://doi.org/10.1038/s41386-018-0059-z.

Ballmaier, M., Schlagenhauf, F., Toga, A. W., Gallinat, J., Koslowski, M., Zoli, M., Hojatkashani, C., Narr, K. L., & Heinz, A. (2008). Regional patterns and clinical correlates of basal ganglia morphology in non-medicated schizophrenia. *Schizophrenia Research, 106*(2–3), 140–147. https://doi.org/10.1016/j.schres.2008.08.025.

Barnett, K. J., Kirk, I. J., & Corballis, M. C. (2007). Bilateral disadvantage: Lack of interhemispheric cooperation in schizophrenia. *Consciousness and Cognition, 16*(2), 436–444. https://doi.org/10.1016/j.concog.2006.06.007.

Bhugra, D. (2005). The global prevalence of schizophrenia. *PLoS Medicine, 2*(5), e151; quiz e175. https://doi.org/10.1371/journal.pmed.0020151.

Corballis, M. C. (2014). Left brain, right brain: Facts and fantasies. *PLoS Biology, 12*(1), e1001767. https://doi.org/10.1371/journal.pbio.1001767.

Cropley, V. L., Fujita, M., Innis, R. B., & Nathan, P. J. (2006). Molecular imaging of the dopaminergic system and its association with human cognitive function. *Biological Psychiatry, 59*(10), 898–907. https://doi.org/10.1016/j.biopsych.2006.03.004.

Dong, D., Wang, Y., Chang, X., Luo, C., & Yao, D. (2018a). Dysfunction of large-scale brain networks in schizophrenia: A meta-analysis of resting-state functional connectivity. *Schizophrenia Bulletin, 44*(1), 168–181. https://doi.org/10.1093/schbul/sbx034.

Dong, L., Luo, C., Liu, X., Jiang, S., Li, F., Feng, H., Li, J., Gong, D., & Yao, D. (2018b). Neuroscience information toolbox: An open source toolbox for EEG-fMRI multimodal fusion analysis.

Frontiers in Neuroinformatics, 12, 56. https://doi.org/10.3389/fninf.2018.00056.

Duan, M., Chen, X., He, H., Jiang, Y., Jiang, S., Xie, Q., Lai, Y., Luo, C., & Yao, D. (2015). Altered basal ganglia network integration in schizophrenia. *Frontiers in Human Neuroscience, 9*, 561. https://doi.org/10.3389/fnhum.2015.00561.

Early, T. S., Reiman, E. M., Raichle, M. E., & Spitznagel, E. L. (1987). Left globus pallidus abnormality in never-medicated patients with schizophrenia. *Proceedings of the National Academy of Sciences of the United States of America, 84*(2), 561–563. https://doi.org/10.1073/pnas.84.2.561.

Fan, L., Li, H., Zhuo, J., Zhang, Y., Wang, J., Chen, L., Yang, Z., Chu, C., Xie, S., Laird, A. R., Fox, P. T., Eickhoff, S. B., Yu, C., & Jiang, T. (2016). The human Brainnetome atlas: A new brain atlas based on connectional architecture. *Cerebral Cortex, 26*(8), 3508–3526. https://doi.org/10.1093/cercor/bhw157.

Glenthoj, A., Glenthoj, B. Y., Mackeprang, T., Pagsberg, A. K., Hemmingsen, R. P., Jernigan, T. L., & Baaré, W. F. J. P. R. N. (2007). Basal ganglia volumes in drug-naive first-episode schizophrenia patients before and after short-term treatment with either a typical or an atypical antipsychotic drug. *154*(3), 199–208.

Gong, J., Luo, C., Li, X., Jiang, S., Khundrakpam, B. S., Duan, M., Chen, X., & Yao, D. (2019). Evaluation of functional connectivity in subdivisions of the thalamus in schizophrenia. *The British Journal of Psychiatry, 214*(5), 288–296. https://doi.org/10.1192/bjp.2018.299.

Grahn, J. A., Parkinson, J. A., & Owen, A. M. (2008). The cognitive functions of the caudate nucleus. *Progress in Neurobiology, 86*(3), 141–155. https://doi.org/10.1016/j.pneurobio.2008.09.004.

He, H., Yang, M., Duan, M., Chen, X., Lai, Y., Xia, Y., Shao, J., Biswal, B. B., Luo, C., & Yao, D. (2017). Music intervention leads to increased insular connectivity and improved clinical symptoms in schizophrenia. *Frontiers in Neuroscience, 11*, 744. https://doi.org/10.3389/fnins.2017.00744.

Horn, A., & Blankenburg, F. J. N. (2016). Toward a standardized structural–functional group connectome in MNI space. *124*, 310-322.

Jaeger, D., & Kita, H. (2011). Functional connectivity and integrative properties of globus pallidus neurons. *Neuroscience, 198*, 44–53. https://doi.org/10.1016/j.neuroscience.2011.07.050.

Javitt, D. C. (2009). Sensory processing in schizophrenia: Neither simple nor intact. *Schizophrenia Bulletin, 35*(6), 1059–1064. https://doi.org/10.1093/schbul/sbp110.

Kallai, J., Csatho, A., Kover, F., Makany, T., Nemes, J., Horvath, K., et al. (2005). MRI-assessed volume of left and right hippocampi in females correlates with the relative length of the second and fourth fingers (the 2D:4D ratio). *Psychiatry Research, 140*(2), 199–210. https://doi.org/10.1016/j.pscychresns.2004.05.010.

King-Casas, B., Tomlin, D., Anen, C., Camerer, C. F., Quartz, S. R., & Montague, P. R. (2005). Getting to know you: Reputation and trust in a two-person economic exchange. *Science, 308*(5718), 78–83. https://doi.org/10.1126/science.1108062.

Mamah, D., Wang, L., Barch, D., de Erausquin, G. A., Gado, M., & Csernansky, J. G. (2007). Structural analysis of the basal ganglia in schizophrenia. *Schizophrenia Research, 89*(1–3), 59–71. https://doi.org/10.1016/j.schres.2006.08.031.

Martino, M., Magioncalda, P., Yu, H., Li, X., Wang, Q., Meng, Y., … Ma, X. J. S. (2017). Abnormal resting-state connectivity in a substantia nigra-related striato-thalamo-cortical network in a large sample of first-episode drug-naive patients with schizophrenia. *44*(2), 419–431.

Mohr, B., Pulvermuller, F., Cohen, R., & Rockstroh, B. (2000). Interhemispheric cooperation during word processing: Evidence for callosal transfer dysfunction in schizophrenic patients. *Schizophrenia Research, 46*(2–3), 231–239.

Okada, N., Fukunaga, M., Yamashita, F., Koshiyama, D., Yamamori, H., Ohi, K., Yasuda, Y., Fujimoto, M., Watanabe, Y., Yahata, N., Nemoto, K., Hibar, D. P., van Erp, T., Fujino, H., Isobe, M., Isomura, S., Natsubori, T., Narita, H., Hashimoto, N., Miyata, J., Koike, S., Takahashi, T., Yamasue, H., Matsuo, K., Onitsuka, T., Iidaka, T., Kawasaki, Y., Yoshimura, R., Watanabe, Y., Suzuki, M., Turner, J. A., Takeda, M., Thompson, P. M., Ozaki, N., Kasai, K., & Hashimoto, R. (2016). Abnormal asymmetries in subcortical brain volume in schizophrenia. *Molecular Psychiatry, 21*(10), 1460–1466. https://doi.org/10.1038/mp.2015.209.

Parent, A. (1990). Extrinsic connections of the basal ganglia. *Trends in Neurosciences, 13*(7), 254–258.

Pedraza, O., Bowers, D., & Gilmore, R. (2004). Asymmetry of the hippocampus and amygdala in MRI volumetric measurements of normal adults. *Journal of the International Neuropsychological Society, 10*(5), 664–678. https://doi.org/10.1017/S1355617704105080.

Saunders, A., Oldenburg, I. A., Berezovskii, V. K., Johnson, C. A., Kingery, N. D., Elliott, H. L., Xie, T., Gerfen, C. R., & Sabatini, B. L. (2015). A direct GABAergic output from the basal ganglia to frontal cortex. *Nature, 521*(7550), 85–89. https://doi.org/10.1038/nature14179.

Steullet, P. J. S. R. (2019). Thalamus-related anomalies as candidate mechanism-based biomarkers for psychosis.

Toga, A. W., & Thompson, P. M. (2003). Mapping brain asymmetry. *Nature Reviews. Neuroscience, 4*(1), 37–48. https://doi.org/10.1038/nrn1009.

van Erp, T. G., Hibar, D. P., Rasmussen, J. M., Glahn, D. C., Pearlson, G. D., Andreassen, O. A., et al. (2016). Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. *Molecular Psychiatry, 21*(4), 547–553. https://doi.org/10.1038/mp.2015.63.

Wang, L., Joshi, S. C., Miller, M. I., & Csernansky, J. G. (2001). Statistical analysis of hippocampal asymmetry in schizophrenia. *Neuroimage, 14*(3), 531–545. https://doi.org/10.1006/nimg.2001.0830.

Wichmann, T., & Delong, M. R. (2011). Deep-brain stimulation for basal ganglia disorders. *Basal Ganglia, 1*(2), 65–77. https://doi.org/10.1016/j.baga.2011.05.001.

Wyciszkiewicz, A., & Pawlak, M. A. J. T. N. J. (2014). Basal ganglia volumes: MR-derived reference ranges and lateralization indices for children and young adults. 27(5), 595–612.

Yang, G. J., Murray, J. D., Repovs, G., Cole, M. W., Savic, A., Glasser, M. F., Pittenger, C., Krystal, J. H., Wang, X. J., Pearlson, G. D., Glahn, D. C., & Anticevic, A. (2014). Altered global brain signal in schizophrenia. *Proceedings of the National Academy of Sciences of the United States of America, 111*(20), 7438–7443. https://doi.org/10.1073/pnas.1405289111.