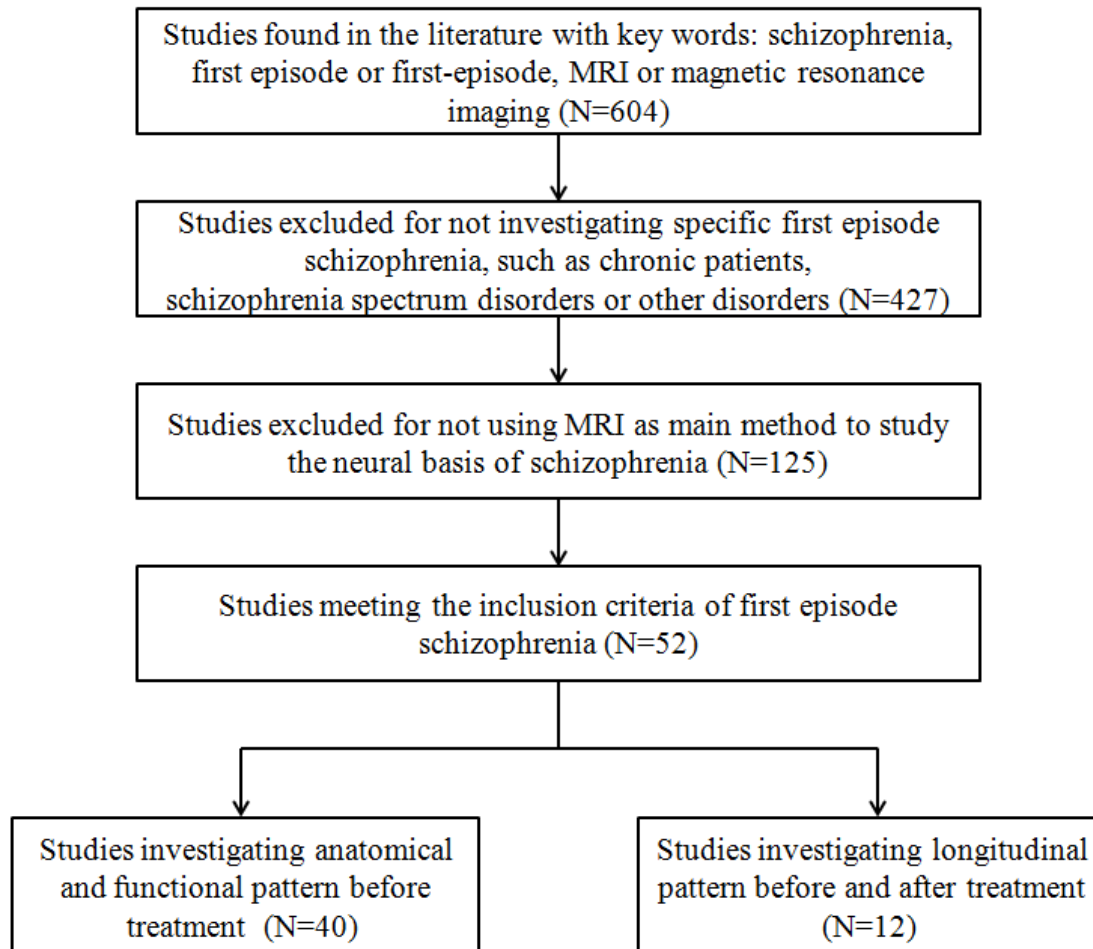


FIGURE S1. Flowchart of literature selection for anatomical and functional MRI studies in drug-naïve first episode schizophrenia before and after treatment.



**TABLE S1. Main findings of structural and functional studies in FES before treatment**

Author/Publication year	Number of subjects (male)	Diagnostic criteria	Age (mean± S.D.)	Illness duration	Education (years)	Neuropsychological assessment	Imaging parameter (Tesla/thickness )	Image methods	Analysis methods	Main findings	Methodological issues
Chua et al. /2007(1)	29 (12) FES 40 (18) HC	DSM-IV schizophrenia, schizophreniform or brief psychotic disorder	32 ± 10 33 ± 8.1	120 days	10 ± 3.1 13 ± 3.2	PANSS	1.6/3	Structural MRI	VBM/ROI	↓ Global brain volume ratios in FES: ↓ GMV in FES: bilateral caudate nuclei bilateral cingulate gyri bilateral parahippocampal gyri bilateral superior temporal gyri bilateral cerebellum right thalamus right prefrontal cortex. ↓ WMV in FES: right anterior limb of the internal capsule fronto-occipital	Older sample Short illness duration of patients Only cross-sectional

										fasciculus bilateral fornices ↑ CSF volume in FES: right lateral ventricle	
Jayakumar et al. /2005 (2)	18 (9) FES 18 (9) HC	DSM-IV schizophrenia	24.9 ± 6.3 25.7 ± 7.5	10.3 ± 5.1 months	10.9 ± 4.3 12.5 ± 2.5	PANSS	1.5/1	Structural MRI	VBM	↓ Global GM in FES ↑ Global CSF volumes in FES ↓ GMV in FES: right superior frontal gyrus left inferior frontal gyrus left cingulate left postcentral gyrus left superior temporal gyrus left inferior parietal lobule left insula bilateral caudate nuclei bilateral parahippocampal gyrus	Not stated

										left thalamus left cerebellum	
Chen et al. / 2014 (3)	86 (46) FES 86 (47) HC	DSM-IV schizophrenia	24.52 ± 0.91 25.03 ± 1.00	11.07 ± 2.26 months	11.90 ± 0.33 13.01 ± 0.33	PANSS	3.0/1	Structural MRI	VBM/ROI	↓ GMV in FES: bilateral hippocampus left inferior frontal gyrus right thalamus	only connections between ROIs were examined
Kim et al. / 2003 (4)	25 (25) FES 25 (25) HC	DSM-III-R schizophrenia	25.4 ± 6.5 25.3 ± 6.2	Not stated	13.1 ± 2.8 14.5 ± 2.0	SANS	1.5/1.5	Structural MRI	ROI	↓ GMV in FES: right posterior superior temporal gyrus	Not stated
Lacerda et al. / 2007 (5)	43 (29) FES 53 (24) HC	DSM-IV schizophrenia	24.52 ± 5.98 25.29 ± 7.34	Not stated	Not stated	BPRS SANS SAPS	1.5/1.5	Structural MRI	ROI	↑ GMV in FES: left total orbitofrontal cortex and left lateral orbitofrontal cortex	Possibility of inaccurate anatomical subdivision Lack of replication of findings
Guo et al. /2014 (6)	51 (33) FES 41 (24) HC	DSM-IV schizophrenia	22.5 ± 4.1 22.8 ± 3.9	8.4 ± 6.8 months	11.4 ± 3.3 11.9 ± 2.7	PANSS	3.0/1.1	Structural MRI	VBM	↓ GMV in FES: bilateral hippocampal gyri right middle temporal gyrus left fusiform gyrus left orbital inferior frontal	Small sample size Cross-sectional study

										gyrus	
Hu et al. /2013 (7)	51 (34) FES 59 (38) HC	DSM-IV schizophrenia	22.29 ± 3.95 23.20 ± 2.58	11.14 ± 6.40 months	11.16 ± 2.34 12.14 ± 2.42	PANSS	3.0/1.1	Structural MRI	VBM	↓ GMV in FES: bilateral hippocampal bilateral parahippocampal gyri bilateral middle temporal gyri, bilateral superior temporal gyri	Small sample size Cross-sectional study VBM-related methodological limitations
Lui et al. / 2009 (8)	68 (30) FES 68 (31) HC	DSM-IV schizophrenia	24.2 ± 8.6 24.7 ± 8.8	8.6 ± 14.3 months	11.8 ± 3.2 13.0 ± 2.9	PANSS GAF	3.0/1.0	Structural MRI	VBM	↓ GMV in FES: right superior temporal gyrus right middle temporal gyrus right anterior cingulate gyrus	VBM-related methodological limitations
Salgado-Pineda et al. / 2003 (9)	13 (13) FES 13 (13) HC	DSM-IV schizophrenia (paranoid subtype)	23.76 ± 5.65 23.36 ± 4.58	Not stated	Not stated	BPRS	1.5/1	Structural MRI	VBM/ROI	↓ GM density in FES: bilateral anterior cingulate gyrus left inferior frontal right claustrum	Not stated

										left pulvinar, dorsomedial bilateral thalamic nuclei caudate nuclei left hippocampus left parahippocampal gyrus ↑ GM density in FES: left insula left superior temporal gyrus left putamen nucleus right supramarginal gyrus ↓ GMV in FES: bilateral thalamus	
Okugawa et al./ 2007 (10)	14 (7) FES 16 (8) HC	DSM-IV schizophrenia	29.8 ± 6.3 29.8 ± 4.3	Not stated	Not stated	PANSS	1.5/ (1.5/3)	Structural MRI	ROI	↓ Volumes in FES: anterior vermis posterior superior vermis	High onset age for schizophrenia Small sample size

Joya et al. / 2002 (11)	18 (11) FES 22 (14) HC	DSM-III-R schizophrenia or schizoaffective disorder	28 ± 7 30 ± 8	10 ± 9 months	Not stated	PANSS	1.5/1.5	Structural MRI	ROI	↓ Bilateral entorhinal volumes in FES:	Not stated
Szeszko et al. / 2003 (12)	24 (16) FES 34 (21) HC	Research Diagnostic Criteria for schizophrenia or schizoaffective disorder or DSM-IV schizophrenia, schizophreniform disorder, or schizoaffective disorder	25.4 ± 5.5 26.5 ± 6.8	Not stated	3.6 ± 0.8 2.8 ± 1.3 ( Hollingshead-Redlich system )	SANS	1.5/1.5	Structural MRI	ROI	↓ Anterior hippocampal volume in FES	Methodology –related omission of abnormalities Possibility of inaccurate anatomical subdivision
Joyal et al. / 2003 (13)	18 (11) FES 22 (14) HC	DSM-III-R schizophrenia or schizoaffective disorder	28 ± 7 30 ± 8	10 ± 9 months	Not stated	PANSS	1.5/1.5	Structural MRI	ROI	↓ Bilateral amygdala volumes in FES	Not stated
Rizos et al. / 2011 (14)	20 (8) FES 20 (11) HC	Not stated	30.75 ± 10.52 34 ± 4.70	Not stated	11.15 ± 2.92 12.61 ± 3.32	PANSS	1.5/3	Structural MRI	ROI	↓ Hippocampus volume in FES	Small sample size
Shad et al. / 2006 (15)	14 (12) FES 21 (15) HC	DSM-IV schizophrenia	26.23 ± 7.50 24.29 ± 5.73	104 ± 126 days	Not stated	BPRS SANS SAPS SUMD	1.5/1.5	Structural MRI	ROI	↓ Dorsolateral prefrontal cortex volumes in FES	Small sample size
Cahn et al. / 2002	20 (16)	DSM-IV	27.6 ±	Not	11.6 ± 3.0	PANSS	1.5/1.2	Structural MRI	Volume	↑ Third ventricle	Small sample size

(16)	FES 20 (16) HC	schizophrenia	6.43 27.2 ± 6.30	stated	12.7 ± 3.0					volume in FES	No IQ testing Different height between groups
Chua et al. / 2003 (17)	19 (17) FES 31 (24) HC	DSM-IV schizophrenia	31.6 ± 8.2 33.6 ± 7.6	27.9 ± 27.7 months	Not stated	Not stated	1.5/1.5	Structural MRI	Volume	↑ Lateral ventricles volume in FES	Use of neuroleptics before scan
Laakso et al. / 2001 (18)	18 (11) FES 22 (14) HC	DSM-III-R schizophrenia or schizoaffective disorder	28 ± 7 30 ± 8	10 ± 9 months	Not stated	PANSS	1.5/1.5	Structural MRI	ROI	N.S.	Not stated
Molina et al. / 2004 (19)	22 (14) FES 44 (24) HC	DSM-IV schizophrenia	23.0 ± 3.5 29.4 ± 8.9	0.6 ± 0.2 years	12.2 ± 0.7 12.1 ± 0.5	PANSS	1.5/1.5	Structural MRI	ROI	N.S.	Cross sectional data collection Different proportion of males and females between groups
Prasad et al. / 2004 (20)	33 (23) FES 43 (21) HC	DSM IV psychotic disorders	M:24.84 ± 6.42 F:25.34 ± 7.73 M:24.28 ± 6.15 F:23.74 ± 8.75	Not stated	13.14 ± 2.8 15.65 ± 2.3	BPRS	1.5/1.5	Structural MRI	ROI	N.S. in parahippocampus volumes	Possibility of inaccurate anatomical boundaries



Yao et al. /2014 (12)	68 (30) FES 68 (31) HC	DSM-IV schizophrenia	24.2 ± 8.6 24.7 ± 8.8	8.6 ± 14.3 months	11.8 ± 3.2 13.0 ± 2.9	PANSS GAF	3.0/1.0	Structural MRI	VBM	↓ WMV in FES: bilateral posterior limb of the internal capsule right subgyral frontal white matter	Short illness duration of patients No direct evidence of neuropathogenesis
Ren et al. / 2013 (22)	100 (41) FES 100 (41) HC	DSM-IV schizophrenia	24.30 ± 7.45 24.39 ± 7.58	6.25 ± 11.04 months	12.32 ± 3.02 3.15 ± 2.45	PANSS GAF	3.0/1.0	Structural MRI/ Resting-state fMRI	VBA	↓ GMV in FES: left paracentral left inferior parietal lobules ↑ GMV in FES: the left and right thalamus anterior cingulate cortex insula, orbital frontal gyrus ↓ ALFF in FES: right inferior left superior frontal gyrus bilateral medial frontal gyrus bilateral	Not stated

										inferior parietal lobule bilateral precuneus ↑ ALFF in FES: bilateral putamen bilateral occipital regions	
Guo et al. / 2014 (23)	49 (30) FES 50 (23) HC	DSM-IV schizophrenia	22.69 ± 4.62 23.48 ± 2.49	22.45 ± 6.71 months	10.94 ± 2.40 11.46 ± 1.78	PANSS	3.0/4	Structural MRI/ Resting-state fMRI	VBM/ network analysis	↓ GMV in FES: left medial prefrontal cortex right anterior cingulate cortex left superior temporal cortex left inferior temporal gyrus left fusiform gyrus, right lingual gyrus ↑ Driving effect in FES: from the left medial	Cross-sectional study No neuropsychological assessment Only rest data

										<p>prefrontal cortex to the sensorimotor regions.</p> <p>↑ Driving effect in FES:</p> <p>from the right anterior cingulate cortex to the sensorimotor regions</p> <p>↓ Feedback in FES:</p> <p>from the sensorimotor regions to the right anterior cingulate cortex</p> <p>↑ and ↓ causal connectivity in FES:</p> <p>bilateral sensorimotor regions</p>	
Prasad et al. / 2007 (24)	30 (23) FES 44 (23)	DSM-IV schizophrenia or schizoaffective	24.66 ± 7.71 24.90 ±	2.32 ± 1.89 months	Not stated	PANSS	1.5/1.5	Structural MRI	VBM	↓ GMV in HSV 1+ FES (compared to	Not stated

	HC	disorder	6.8							herpes simplex virus 1- FES ): Brodmann area 9 Brodmann area 32 ↓ GMV in HSV 1+ FES (compared to herpes simplex virus 1- HC ): Brodmann area 9 Brodmann area 32	
Xiang et al. /2013 (25)	74 (30) FES 55 (25) HC	DSM-IV schizophrenia	25 ± 8.3 25 ± 8.8	Not stated	12.7 ± 2.9 12.4 ± 3.0	BPRS SANS SAPS	3.0/1	Structural MRI	Surface based analysis	↑ Right inferior temporal surface area in pro-allele carriers of Ser307Pro polymorphism FES (compared to Ser/Ser carriers FES)	Not stated
Shad et al. / 2004 (26)	total: 35 (24) poor sight: 17 (90)	DSM IV schizophrenia or schizoaffective disorder	total: 26.3 ± 7.0 poor sight: 26.13 ±6.7 good	Poor sight: 147 ± 159 days	Not stated	BPRS SANS SAPS GAF	1.5/1.5	Structural MRI	Volume	↓ Right dorsolateral prefrontal cortex volume in poor insight FES	Small sample size Insight was assessed by single categorical item

	good sight: 18 (15) 0 HC		sight:25.36 ± 7.83	good sight: 143 ± 287 days							
Cheung et al. / 2008 (27)	25 (13) FES 26 (11) HC	DSM-IV schizophrenia	28.5 ± 9.4 28.2 ± 9.2	180 days	Not stated	PANSS	1.5/5	DTI	VBA/ROI	↓ FA in FES: left fronto-occipital fasciculus left inferior longitudinal fasciculus white matter adjacent to right precuneus, splenium of corpus callosum right posterior limb of internal capsule white matter adjacent to right substantia nigra left cerebral peduncle corpus callosum splenium	Between-group sex difference Thick and non-contiguous slices sequence DTI voxel-based methodological limitations
Cheung et al. /2011	34 (17)	DSM-IV	25.4 ± 7.5	Not	6-18	PANSS	1.5/5	DTI	VBA	↓ FA in FES:	No illness duration

(28)	FES 32 (17) HC	schizophrenia	27.6 ± 8.5	stated	6-18						right frontal lobe left anterior cingulate gyrus left superior temporal gyrus right middle temporal gyrus right middle cingulate gyrus left cuneus	Thick slice sequence
Guo et al. / 2012 (29)	20 (9) FES 26 (14) HC	DSM-IV paranoid schizophrenia	24 ± 4.86 23.62 ± 4.16	6.60 ± 3.10 months	13.25 ± 2.41 3.38 ± 2.53	PANSS	1.5/4	DTI	Tract-based spatial statistics	↓ FA in FES: right superior longitudinal fasciculus right fornix right internal capsule right external capsule	Small sample size Only paranoid subtype No neuropsychological testing	
Huang et al. / 2010 (30)	66 (30) FES 66 (30) HC	DSM-IV schizophrenia	24.2 ± 8.4 24.5 ± 8.6	8.8 ± 14.1 months	11.5 ± 3.1 12.7 ± 2.5	PANSS	3.0/1	Resting-state fMRI	VBA	↓ ALFF in FES: medial prefrontal lobe ↑ ALFF in FES: left and right putamen	The effects of physiological noise	
He et al. / 2012 (31)	104 (49) FES	DSM-IV schizophrenia or schizophreniform	25.36 ± 8.26 26.61 ±	39.54 ± 31.88 weeks	12.14 ± 3.061 12.74 ± 3.532	PANSS	3.0/5	Resting-state fMRI	VBA/ Network analysis	↓ fALFF in FES : bilateral medial	Case-control design Limited seeds and	

	104 (50) HC	psychosis	8.904							prefrontal cortex orbitofrontal cortex ↑ fALFF in FES: bilateral putamen ↑ Functional connectivity with the default mode network in patients: left insula bilateral dorsolateral prefrontal cortex	methods in network analysis Possible false anticorrelated results
Guo et al. / 2014 (32)	49 (30) FES 50 (23) HC	DSM-IV paranoid schizophrenia	22.69 ± 4.62 23.48 ± 2.49	22.45 ± 6.71 months	10.94 ± 2.40 11.46 ± 1.78	PANSS	3.0/4	Resting-state fMRI	Functional homotopy	↓ VMHC in FES: precuneus precentral gyrus superior temporal gyrus middle occipital gyrus fusiform gyrus/cerebellum lobule VI.	The non-correlation between white matter/ gray matter abnormalities and findings Lack of structural data Cross-section design
Li et al. / 2015 (33)	26 (13)	DSM-IV	14.51 ±	Not	Not stated	PANSS	3.0/4	Resting-state	Functional	↓ VMHC values	Small sample size

	FES 25 (13) HC	schizophrenia	1.94 14.37 ± 2.97	stated				fMRI	homotopy	in early-onset FES: superior temporal cortex postcentral gyrus ↓ intrinsic functional connectivity in early-onset FES : bilateral postcentral gyrus precentral gyrus supplemental motor area superior temporal cortex insula ↑ intrinsic functional connectivity in early-onset FES : bilateral caudate medial prefrontal gyrus thalamus posterior	Cross-sectional design Unmatched age range between groups No neuropsychological and socioeconomic status and IQ data Voxel-wise method related limitation
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										cingulate cortex precuneus	
Yang et al. / 2014 (34)	26 (13) FES 25 (13) HC	DSM-IV schizophrenia	14.51 ± 1.94 14.37 ± 2.97	Not stated	Not stated	PANSS	3.0/4	Resting-state fMRI	Network analysis	An intrinsic connectivity network associated with diagnosis: precuneus bilateral angular gyri. An intrinsic connectivity network associated with multivariate symptom patterns: left superior temporal gyrus, right superior temporal gyrus left inferior frontal gyrus right inferior frontal gyrus.	Small sample size Interpretation of relative severity of positive and negative symptoms is not well established The diagnoses on the EOS patients were not reached employing a standardized interview
Scheuerecker et al. / 2008 (35)	23 (19) FES (3)	DSM-IV schizophrenia	31.6 ± 11.1	Not stated	10.3 ± 1.8 12.4 ± 1.3	PANSS CGI	1.5/1.5	Task-fMRI (working	VBA	↓ Activation in FES:	Uncorrected statistical threshold

	washed out) 23 (19) HC		32.6 ± 9.9			BPRS CGI		memory)		right ventrolateral prefrontal cortex ↑ Activation in FES: temporal regions	
van Veelen et al. / 2010 (36)	30 (30) FES 36 (36) HC	DSM-IV schizophrenia, schizoaffective or schizophreniform disorder	24.7 ± 4.2 24.3 ± 4.6	5.08 ± 0.84 months	13.2 ± 2.4 11.7 ± 2.8	PANSS CGI	1.5/4	Task-fMRI (working memory)	ROI	↓ Activation in FES: left dorsolateral prefrontal cortex	Only male patients Relative low severity of patients Potential confounder on task performance
Esslin et al. / 2012 (37)	27 (20) FES 27 (20) HC	DSM-IV schizophrenia, schizoaffective or delusional disorder	27.8 ± 7.4 27.1 ± 5.9	Not stated	11.4 ± 1.8 11.8 ± 1.5	PANSS CGI	1.5/4	Task-fMRI (comprehensive)	ROI	↓ Activation in FES: right ventral striatal	Limited regarding patients' cooperation and the necessity treatment
Braus et al. / 2002 (38)	12 (6) FES 11 (6) HC	DSM-IV as well as ICD-10 schizophrenia	25.1 ± 4.8 29.4 ± 6.2	Not stated	10.6 ± 1.8 12.0 ± 1.4	BPRS	1.5/3	Task-fMRI (sensory)	VBA	↓ Activation in FES: right thalamus right prefrontal cortex bilateral parietal lobe ↓ Activation in FES:	Small sample size Patients were not examined for oculomotor and motion perception deficit or spatial and nonspatial working memory

										left acoustic cortex.	
Ji et al. /2013 (39)	15 (9) FES 15 (8) HC	DSM-IV paranoid schizophrenia	26.27 ± 7.24 24.73 ± 5.34	7.10 ± 6.4 months	9.00 ± 3.93 9.97 ± 2.31	PANSS	1.5/6	Task-fMRI (sensory gating)	ROI	↓ Activation in FES: bilateral hippocampus bilateral thalamus	Small sample size Low field MRI scanner Liberal statistical threshold
van Veelen et al. / 2011 (40)	35 (32) FES 43 (39) HC	DSM-IV schizophrenia, schizoaffective or schizophreniform disorder	24.18 ± 4.24 24.08 ± 4.65	5.20 ± 4.32 months	11.91 ± 2.86 13.05 ± 2.26	PANSS CGI	1.5/4	Task-fMRI (language)	ROI	↓ Lateralization index in FES: inferior frontal gyrus superior temporal gyrus	Small number of female patients Performance data were obtained for limited tasks
<b>Most frequently reported brain regions in structural studies: cingulate gyrus; parahippocampal gyrus/ hippocampus; superior temporal gyrus; thalamus.</b>											
<b>Most frequently reported brain regions in functional studies: medial prefrontal area; dorsolateral prefrontal area; thalamus; superior temporal gyrus.</b>											

Abbreviations: FES: first episode schizophrenia. HC: healthy control. N.S.: no significant. GMV: grey matter volume. WMV: white matter volume. GM: grey matter. FA: fractional anisotropy. CSF: cerebrospinal fluid. ALFF: amplitude of low-frequency fluctuations. VMHC: voxel-mirrored homotopic connectivity. HSV: herpes simplex virus subtype. ↓ decreased. ↑ increased.

VBM: voxel-based morphometry. VBA: voxel-based analysis. ROI: region of interesting, CGI: Clinical Global Impressions, BPRS: Brief Psychiatric Rating Scale, PANSS: Positive and Negative Syndrome Scale

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**TABLE S2. Main findings of longitudinal structural and functional studies in FES before and after treatment**

Author/ Publication year	Number (male)	Diagnostic criteria	Age (mean ±S.D.)	Illness duration	Educati on (years)	Imaging parameter (Tesla/ thickness)	Image methods	Analysis methods	Following time	Types of medicine	Pretreatment main findings (compare to HC):	Posttreatment main findings	Methodological issues
Prasad et al. / 2005 (1)	FES: 27 baseline 25 (17) at 1 year 19 (13) at 2 year 0 HC	DSM-IV schizophrenia or schizoaffective disorder	1 year: 25.36 ± 7.84 2 year: 26.69 ± 8.04	Not stated	Not stated	1.5/1.5	Structural MRI	ROI	1year / 2years	Not stated	Not stated	GMV of the total and left dorsolateral prefrontal cortex at baseline predicted functional outcome in FES at 1 but not at 2 years.	Small sample size Short duration of follow-up Only dorsolateral prefrontal cortex were examined
Rizos et al. / 2014 (2)	14 (8) FES 0 HC	DSM-IV schizophrenia	29.71 ± 10.21	8.00 ± 4.60 months	13.00 ± 3.65	1.5/3	Structural MRI	ROI	8 months	SGAs	Not stated	↓ Left hippocamp al volume in FES (compare to pretreatmen t)	Small sample size Indirect measurement of brain BDNF levels Both proBDNF and BDNF were recognized
Ebdrup et al. / 2011 (3)	22 (15) FES 28 (21) HC	DSM-IV schizophrenia	26.2 ± 5.4	Not stated	Not stated	3.0/Not stated	Structural MRI	ROI/Volume	FES: 7.3 ± 1.0m	SGAs	↓ Volume in caudate	Progressive bilateral	Considerable attrition during

			28.4 ± 6.0						HC: 7.7 ± 2.3m		nucleus and hippocampus	striatal and hippocampal volume loss in FES	the 6-month Potential type II error in subgroups comparison. Liberal statistical threshold
Li et al./ 2012 (4)	40 (23) FES 23 (14) HC	DSM-IV schizophrenia or schizophreniform psychosis	24.05 ± 7.75 22.49 ± 5.83	9.33 ± 12.72 months	12.50 ± 2.94 12.80 ± 3.42	3.0/1	Structural MRI	Tensor-based morphometry	6 weeks	Conventional antipsychotics / SGAs	Not stated	↑ Right putamen GMV in FES (difference maps versus HCs' difference maps)	Low ratio of follow-up Different type of antipsychotics
Theberge et al. / 2014 (5)	16 (14) FES 16 (14) HC	DSM-IV schizophrenia or schizophreniform psychosis	25 ± 8 29 ± 12	96 ± 108 weeks	11-13 (10 or less) 14-16 (10 or less)	4.0/2.75	Structural MRI	VBM	10 months / 30 months	Conventional antipsychotics / SGAs	N.S.	↓ GMV in left precuneus at 10 months (compare to pretreatment) ↓ GMV in left precuneus (expanded to frontal,	Small sample size



												temporal, parietal and limbic lobes) at 30 months (compare to pretreatment)	
Prasad et al./ 2011 (6)	26 (17) FES 38 (21) HC	DSM-IV schizophrenia or schizoaffective disorder	23.59 ± 7.82 23.05 ± 4.85	2.12 ± 2.26 months	Not stated	1.5/1.5	Structural MRI	VBM/ROI	1 year	Not stated	Not stated	↓ GMV in posterior cingulate gyrus in HSV1+ FES (compare to pretreatment) N.S. in HSV1- FES	Differences in medications between the exposed and unexposed patients Potential practice effects All subjects evaluated at baseline were not available for follow-up evaluations
Mané et al. / 2009 (7)	15 (12) FES 11 (8) HC	DSM-IV schizophreniform disorder or schizophrenia	25.56 ± 5.77 30.31 ± 4.36	5.78 ± 5.55 months	Not stated	1.5/1.5 DSM-IV schizophreniform disorder or schizophreni	Structural MRI	VBM	4 years	SGAs	Not stated	↓ GMV in FES (difference maps versus HCs'	Small sample size Cannabis use of patients

						a						difference maps): left superior temporal gyrus right orbitofrontal gyrus bilateral lingual gyrus right cuneus	
Wang et al. / 2013 (8)	35 (16) FES 22 (14) HC	DSM-IV schizophrenia	23.84 ± 6.96 22.41 ± 5.96	7.26 ± 5.32 months	12.37 ± 3.11 12.84 ± 3.41	3.0/3	DTI	VBA	6 weeks	Conventional antipsychotics / SGAs	↓ FA in FES around the right posterior cingulate gyrus ( extend to the right anterior corona and radiata precentral gyrus)	↓ FA in FES (compare to HC): bilateral anterior cingulate gyrus right anterior corona radiata of the frontal lobe	Undetected subtle abnormalities Small sample size Possibility of incorrect statistic approach Uncertain underlying pathological mechanism

Lui et al. / 2011 (9)	34 (13) FES 34 (13) HC	DSM-IV schizophrenia	24.6 ± 8.5 25.0 ± 8.0	7.8 ± 12.4 months	12.1 ± 3.0 13.4 ± 2.8	3.0/5	Resting-state fMRI	VBA/ Network analysis	6 weeks	SGAs	Not stated	↑ ALFF in FES (compare to pretreatment): right inferior parietal lobule left superior parietal lobule bilateral medial frontal cortex right inferior frontal gyrus left superior frontal gyrus left superior temporal gyrus right caudate	The influence of physiological noise cannot be rule out completely Lack of consensus about the exact physiological nature of ALFF
Nielsen et al. / 2012 (10)	23 (16) FES 24 (20) HC	ICD-10 schizophrenia or schizoaffective psychoses	26.0 ± 6.7 25.7 ± 5.9	Not stated	11.5 ± 2.3 15.3 ± 2.6	3.0/2.4	Task-fMRI (comprehensive)	VBM/ROI	6 weeks	SGAs	↓ Activation in FES: bilateral ventral	N.S. (compare to HC)	Previous drug abuse and current occasional drug

											striatum		use in patients Smoking chronicity was not assessed
Goghari et al. / 2013 (11)	19 (11) FES 26 (17) HC	DSM-IV schizophrenia, schizoaffective disorder, schizophreniform disorder, psychosis not otherwise specified, and major depressive disorder with psychotic features	18.9 ± 3.6 20.9 ± 2.1	Not stated	11.4 ± 2.7 14.3 ± 1.8	3.0/1	Structural MRI /Task-fMRI (working memory)	ROI	4 weeks / 8 weeks	SGAs	N.S. in middle frontal thickness	N.S. (compare to HC in 4 weeks) ↑ Rostral middle frontal thickness in FES (compare to HC in 9 weeks)	Small sample size Sample was not matched for age Consisted of patients on different kind and dose of medication
Veelen et al. (12)	23 (not stated) FES 33 (not stated) HC	DSM-IV schizophreniform disorder or schizophrenia	25.3 ± 4.6 24.5 ± 4.7	4.9 ± 4.4 months	11.2 ± 2.7 13.2 ± 2.4	1.5/4	Task-fMRI (working memory)	ROI	10.1 ± 2.2 weeks	SGAs	↓ Activation in FES: dorsolateral prefrontal lobe	N.S. in dorsolateral prefrontal lobe (compare to HC)	Short follow up time Only male patients Different kind of medication

Abbreviations: FES: first episode schizophrenia. HC: healthy control. N.S.: no significant. GMV: grey matter volume. GM: grey matter. FA: fractional anisotropy. HSV: herpes simplex virus subtype. BDNF: Brain Derived Neurotrophic Factor. SGAs: second-generation antipsychotics. ALFF: amplitude of low frequency fluctuations. ↓ decreased. ↑ increased.

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