

### 253. D2 Receptor Binding in Drug-Naive Patients Examined with FLB457 and Raclopride

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**Background:** The dopamine hypothesis states that schizophrenia is related to an abnormal central dopaminergic neurotransmission. Most positron emission tomography (PET) studies of D2 receptors in the striatum have not supported this theory. The present aim was to examine extrastriatal regions with a relatively low D2 receptor density but of a high potential interest for the pathophysiology of schizophrenia. One of these regions is the thalamus where recent studies have reported structural as well as functional abnormalities in schizophrenic patients.

**Methods:** A total of twenty neuroleptic naïve schizophrenic patients were examined with PET (Siemens ECAT EXACT 47). Nineteen patients and seventeen controls were examined with [<sup>11</sup>C]raclopride. Nine patients and eight controls were examined with [<sup>11</sup>C]FLB457. Regional binding potential values were calculated using the simplified reference tissue model.

**Results:** In agreement with previous studies, there was no significant difference between patients and controls with regard to the D2 binding in the striatum. However, in the study with [<sup>11</sup>C]raclopride as well as in the study with [<sup>11</sup>C]FLB457 a significant lower D2 binding potential was demonstrated in the right medial thalamus.

**Conclusions:** The finding of a low D2 receptor binding in the right medial thalamus of schizophrenic patients strengthen the hypothesis that thalamus is a key region in the pathophysiology of schizophrenia. Taken together with previous results the finding may correspond to an aberrant function in the thalamo-cortical circuitry.

### 254. Young First-Degree Relatives of Schizophrenia Patients Show Alterations in Programmed Neurodevelopment

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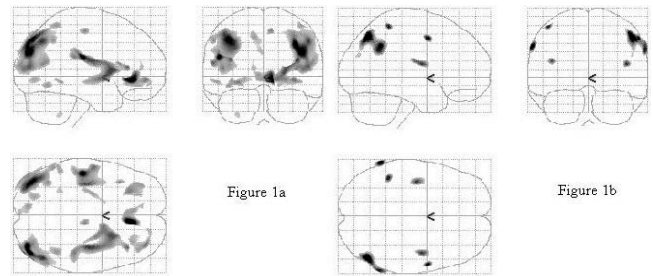
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**Background:** Schizophrenia is a neurodevelopmental disorder possibly mediated by genetic factors (Lewis & Levitt, 2002). Genetic risk in first-degree relatives (HR-S) of patients (Gottesman & Gould, 1982) may interact with altered patterns of synaptic pruning associated with the illness (Keshavan et al., 1994). This hypothesis was examined by assessing the relationship between age and cortical gray matter concentration in a sample of non-psychotic HR-S. Separate analyses were conducted in a control group (HC) with no family history of psychosis.

**Methods:** T<sub>1</sub>-weighted MRI images (1.5T) from 34 HR-S subjects (Mean age = 15.3 yrs, Range 8-22 yrs, 16 males) and 33 HC subjects (Mean age = 16.6 yrs, Range 7-25 yrs, 18 males) were included. Voxel-wise analyses (using SPM '99) were conducted on smoothed gray matter maps (12 fwhm). Preset thresholds ( $p < 10^{-5}$ , uncorrected) were used.

**Results:** Consistent with normal pruning during adolescence (Durston et al., 2001), significant negative correlations ( $t_{30} > 5.05$ ) were observed in HC across uni- and heteromodal cortices (Fig 1a). This relationship was absent in HR-S ( $t_{31} > 5.02$ ; Fig 1b).

**Conclusions:** The absence of negative correlations in HR-S suggests altered neurodevelopment in individuals at risk for the illness. This may result from early pruning (and plateauing) of gray matter, or lack of neuronal/synaptic proliferation in the first decade of life. Future studies of at-risk children can elucidate the timing of neurodevelopmental alterations in risk for schizophrenia.



### 255. A Voxelwise Analysis of the Relationship between White Matter Integrity and Impulsivity in Men with Schizophrenia

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**Background:** Using diffusion tensor imaging (DTI), we have previously found that impulsivity was inversely associated with white matter integrity (WM) in right inferior frontal regions in men with schizophrenia. However, it is unclear whether these correlations are strictly localized to such regions or are more widespread.

**Methods:** DTI were acquired from 25 men with schizophrenia. Fractional anisotropy (FA) from these images was transformed into Talairach space. Correlations between FA and motoric aspects of impulsivity, as measured by the Barratt Impulsiveness Scale, were examined on a voxelwise basis, with a minimum extent threshold of 50 contiguous voxels and a minimum alpha of .05.

**Results:** We replicated our previous finding of an inverse association between impulsivity and right inferior frontal WM, and also found negative correlations between FA and impulsivity in the anterior cingulate and insula bilaterally, as well as in the left angular gyrus WM. Positive correlations were obtained in the left inferior parietal lobule, right superior temporal gyrus, and left fusiform gyrus.

**Conclusions:** WM integrity in a set of fronto-temporo-limbic areas was inversely associated with impulsiveness. These areas have been implicated in a neural circuit that modulates impulsive aggressiveness. Increased WM integrity in more isolated regions also was associated with impulsiveness. A number of hypotheses to account for these latter correlations will be discussed. The voxelwise method used in the current study can serve as an important hypothesis-generation mechanism.

### 256. Fornix Integrity and Hippocampal Volume in Schizophrenia

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**Background:** The hippocampus is a well-studied brain region in schizophrenia. The fornix is the main white matter fiber tract connecting the hippocampus with other brain regions. However, very few studies have evaluated the fornix in schizophrenia. In this study, we investigated the fornix using Diffusion tensor imaging (DTI), which is sensitive to the detection of white matter abnormalities. We also measured hippocampal volume and its association with fornix integrity.

**Methods:** Line-scan DTI was used to evaluate diffusion in the fornix in 21 male chronic patients with schizophrenia and 34 age-matched male control subjects. Maps of fractional anisotropy (FA) and apparent diffusion coefficient (ADC) were generated to quantify diffusion within the fornix. We also used high spatial resolution MRI to measure hippocampal volume.

**Results:** Mean FA ( $p=0.041$ ) and cross-sectional area of fornix ( $p=0.002$ ) were significantly reduced in male patients compared with normal controls. Mean ADC was also significantly increased in the patients with schizophrenia ( $p=0.003$ ), whereas hippocampal volume was bilaterally reduced in patients compared with controls ( $p=0.008$ ). Cross-sectional area of the fornix was positively correlated with bilateral hippocampal volume for the schizophrenic group only (left:  $r=0.457$ ,  $p=0.025$ , right:  $p=0.477$ ,  $p=0.018$ ).

**Conclusions:** These findings demonstrate integrity disruption of the fornix in patients with schizophrenia. They also suggest that hippocampal abnormalities contribute to disruption of neural circuit such as prefrontal-subcortical network.

### 257. Progression of STG Gray Matter Volume Decrease in First-Episode Schizophrenia but not in First Episode Mania

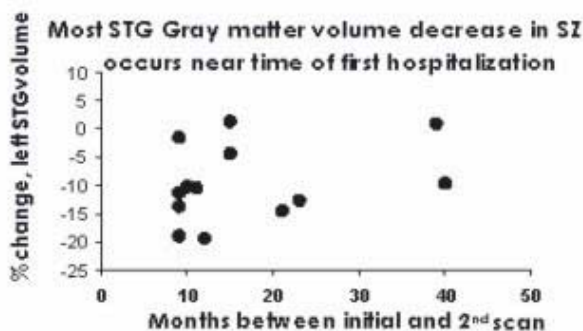
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**Background:** In first-episode schizophrenia (FE SZ) compared with controls and first-episode affective (manic) psychosis (FE AFF) there were reductions in gray matter volume in the left superior temporal gyrus (STG) and its components of Heschl's Gyrus (HG) and Planum Temporale (PT) at the time of first hospitalization. However, it was not known whether there would be additional volume reduction over time.

**Methods:** Right-handed subjects were initially scanned with high-resolution MRI and rescanned a mean 1.5 years later with the same GE 1.5 T scanner. Regions of interest (ROI) were manually defined.

**Results:** FE SZ ( $N=13$ ) showed significant decreases in gray matter volume over time in the left posterior STG (9.6%), left anterior STG (8.4%), left HG (6.9%), and left PT (7.2%) compared with FE AFF ( $N=15$ ) or controls ( $N=22$ ). No group differences in the rate of change over time were present in medial temporal lobe and right-sided STG ROI.



The figure shows most of these FE SZ changes occurred within the first few months of hospitalization. The greater the degree of FE SZ volume loss the

greater was the conceptual disorganization on the BPRS ( $\rho=0.67$ ,  $p<0.01$ ). Furthermore, the greater the HG volume decrease the greater the mismatch negativity decrease.

**Conclusions:** In FE SZ, but not FE AFF, post-onset progression of left STG gray matter volume reduction is present and is associated with clinical symptoms and functional abnormalities.

### 258. PrefrontalCortical and White Matter Abnormalities in First-Episode Schizophrenia

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**Background:** There is considerable evidence from magnetic resonance (MR) imaging studies that patients with schizophrenia have frontal lobe structural abnormalities. Few studies, however, have investigated anatomically relevant grey and white matter volumes of frontal lobe subregions in patients close to illness onset.

**Methods:** We utilized methods for cortical parcellation of the frontal lobes to compute grey and white matter volumes of the superior frontal gyrus, anterior cingulate gyrus and orbital frontal lobe. One hundred twenty four contiguous T1-weighted coronal MR images (slice thickness = 1.5mm) were acquired through the whole head using a 3D Fast SPGR IR Prep sequence on a 1.5T GE imaging system in 76 (52M/24F) patients with first-episode (FE) schizophrenia and 82 (37M/45F) healthy comparison subjects. Brain volumes were measured in each hemisphere by an operator blind to group membership and hemisphere.

**Results:** After controlling for the effects of age and total intracranial contents mixed models analyses revealed that patients had significantly ( $p < .05$ ) smaller anterior cingulate white matter volumes and smaller total (grey + white) superior frontal gyrus volumes compared to healthy volunteers.

**Conclusions:** These findings suggest that prefrontal anatomic pathology is present early in the course of illness in schizophrenia and may involve volumetric alterations in both the grey and white matter.

### 259. Does Depression Predict Quality of Life in Outpatients with Schizophrenia Spectrum Disorders?

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**Background:** The prognostic significance of affective symptoms co-occurring with schizophrenia continues to be debated. Schizoaffective disorder is generally associated with better outcome than schizophrenia. However, the presence of comorbid depression in schizophrenia has been associated with poorer outcome. This study explored the impact of depression, as captured by diagnosis and dimensional rating, on quality of life.

**Methods:** Twenty-two male and 3 female outpatient veterans diagnosed with schizophrenia or schizoaffective disorder were evaluated with the Calgary Depression Scale for Schizophrenia (CDSS), the Positive and Negative Syndrome Scale (PANSS), and the Quality of Life Scale (QLS). Subjects were