10mm and 20 mm above the AC. Females had significantly higher FA in the left hemisphere compared to the right hemisphere whereas no significant differences in FA asymmetry were evident among the males on any of the slices examined. Females also had significantly higher left hemisphere FA compared to males on the slice 20mm above the AC. FA asymmetry indices [((Right - Left) / (Right + Left)) * 100] were also computed for the frontal regions on each slice. Independent groups t-tests revealed significant sex differences in FA asymmetry indices on the slices 10mm and 20mm above the AC. These findings may have relevance for understanding the neurobiological basis of sex differences in some cognitive functions (e.g., language) in healthy humans and highlight the importance of considering these differences in interpreting the results of DTI studies in psychiatric and neurologic populations.

NO EVIDENCE FOR ALTERED CAUDATE NUCLEUS VOLUME IN NEUROLEPTIC-NAIVE FIRST EPISODE PATIENTS

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Magnetic resonance imaging (MRI) studies suggested elevated caudate nucleus volume (CNV) in schizophrenic patients treated with typical neuroleptics. There are also conflicting reports that untreated first-episode patients may exhibit even smaller CNV than controls. We compared the CNV of newly diagnosed neuroleptic-naive psychotic patients to an age- and sex-matched healthy control group, to investigate whether a putative CNV change is present in first episode patients not confounded by treatment effects. The mean age of the control group was 25.8 years (SD=6.2), and 25.5 years for the patient group (SD=5.8). The 37 patients met DSM-IV criteria for schizophrenia (N=26), schizophreniform disorder (N=6), delusional disorder (N=3), or schizoaffective disorder (N= 2). The mean duration of untreated psychosis was 24.4 months (SD=31.6). We used a GE Signa 1.5 T MRI scanner to obtain a coronal three-dimensional radio-frequency spoiled-gradient recalled-echo (SPGR) sequence for quantifying cerebrospinal fluid, gray matter, and white matter volumes in 37 unmedicated psychotic patients and 37 healthy controls. Regions of interest (ROI) delineating the caudate nuclei bilaterally were drawn manually using BrainImage software. The neuroleptic-naive patients showed a mean CNV of 8.40 cc (SD=1.01) and the controls of 8.55 cc (SD=1.16). There was no significant difference between groups (T= .606; p= .547). This cross-sectional MRI study found no evidence for a significant volumetric alteration in neuroleptic-naive first-episode patients.

HIPPOCAMPAL VOLUMES ANALYSIS ON MAGNETIC RESONANCE IMAGES IN SCHIZOPHRENIC AND NON AFFECTED FAMILY MEMBERS - GENETIC LOADING AND IMPACT OF OBSTETRIC COMPLICATIONS

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Genetical predisposition and environmental impacts could cause brain morphological changes. The hippocampus is one of the key regions for schizophrenia. In a large family sample we studied magnetic resonance images (MRI) of schizophrenic patients as well as their relatives and a healthy control group. In addition we collected data on obstetric complications or additional environmental factors which possibly harm brain structures. MRI's were acquired on 1.5 Tesla scanners at the medical centers of the University of Dusseldorf (Siemens) and the University of Bonn (Philips). We included 50 schizophrenics, 88 relatives and 53 controls. Status of genetic loading of the families was determined as monoaffected (only a single schizophrenic patient over three generations), multiple affected (two or more patients affected with schizophrenia) or not clearly to identify. We got 14 schizophrenic patients and 33 relatives from monoaffected families and 32 patients and 49 relatives from multiple affected families. Compared to controls we found a bilateral volume reductions in schizophrenics (right: 15%, left: 14%) but also slight changes (right: 10%, left: 6%) in the non affected relatives. Seemingly hippocampal volumes of relatives range in between patients and controls. Since most subjects of the multiple affected group were scanned in Dusseldorf and most of the monoaffected families in Bonn the analysis for the status of genetic loading was performed separately for the two medical centers. In multiple affected families the hippocampal volumes were larger than in monoaffected families (right: between 3% and 5%, left: between 2% and 11%). These differences were only significant for the Dusseldorf sample, left side. A lot of patients or relatives from both kinds of families had obstetric complications (n=39). We calculated correlations between hippocampal volumes and number of labor delivery complication (LDC) of degree 3 or higher. There was bilaterally a significant negative correlation in relatives (right: r=-041, p=0.016, left: r=-0.49, p=0.003). For patients correlation was significant only in the left hemisphere (left: r=-0.37, p=0.044). Supported by the Deutsche Forschungsgemeinschaft (Fa 241/2-3)

VOLUMETRIC BRAIN REGIONS AND THEIR RELATION TO COGNITIVE FUNCTION: A FAMILY STUDY ON SCHIZOPHRENIA

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We explored, in a sample of 188 individuals, the putative neural substrates of intelligence, memory and executive processing, while examining whether the pattern of function/structure relationship is different in schizophrenic patients (n=56) and their relatives (n=85) from that of controls (n=47). MRI data were acquired using a single 1.5 Tesla General Electric Signa System. Volumetric measurements were made on spoiled-gradient images employing a software package that uses stereological principles, and were obtained for Whole Brain Volume (WBV), Prefrontal region (PFR), Leteral Ventricles (LV), Third Ventricle (3rdV), R/L Temporal Lobe (rTL/lTL), R/L Hippocampus (RHp/LHp) and Cerebellum (CER). Full IQ (FIQ) and verbal IQ (VIQ) correlated with WBV (FIQ r.28, p.005; VIQ r.28, p.004), and RHp (FIQ r.31, p.001; VIQ r.26, p.008). The latter was also associated with Performance IQ (PIQ) (r.28, p.005). Left Hippocampal size was predictive, in the expected direction, of VIQ, and in controls and relatives only, of FIQ (Con r.35, p<.001; Rel r.36, p<.001) and PIQ (Con r.21, p.004; Rel r.37, p<.001). Verbal memory was linked to CER (r.25, p.01), and inversely to LHp (-.27, p.006). Visual memory was also associated, in relatives only, with the CER (r.32, p.001)and the LHp (r.35, p<.001). These data suggest (1) a dissociation between LHp and FIQ/PIQ in schizophrenia, indicating a loss of normal structure/function relationship, which may reflect a functional compensation, occuring as a result of an early brain insult. Since the dissociation does not extent to relatives, it is presumed that

the pattern is related to the pathophysiology of schizophrenia per se; and (2) the relatives use different pathways to process visual information, perhaps, reflecting a variation in encoding strategy which may be the result of a compensatory process with a beneficiary effect.

VOXEL-BASED MORPHOMETRIC ANALYSIS OF STRUCTURAL BRAIN ABNORMALITIES IN EARLY-ONSET SCHIZOPHRENIA

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Early-Onset Schizophrenia (EOS) is a rare condition. EOS has been suggested to have a higher rate of premorbid abnormalities in social function, and motor and language ability. Thus, EOS patients may have more pronounced brain structural abnormalities relative to those with adult-onset schizophrenia (AOS). Using a region-of-interest (ROI) approach, a few structural magnetic resonance imaging (MRI) studies reported brain abnormalities in EOS, but the regions examined are limited. Recently, voxel-based morphometric techniques have become available and provide a means of investigating volumetric abnormalities automatically over the entire cerebral structure. The aim of this study was to explore brain abnormalities of gray matter and white matter in those with EOS. We recruited those individuals with onset equal to 16 years or less and defined them as EOS. Eighteen right-handed DSM-IV Schizophrenia patients (mean=15.8 years, SD=1.8) and 18 right-handed age- and gender-matched healthy comparison subjects (mean=15.8 years, SD=1.3) were included. All of the subjects and their parents received a complete description of the study, and written informed consent was obtained from both participants and their parents. All subjects were scanned with a GE Signa 1.5-T system. Three-mm thick, contiguous, interleaved, near axial dual-echo fast spin-echo data were obtained to provide whole brain coverage. The imaging data were analyzed using automated computational methods which produce separate gray and white matter tissue maps. The analytical procedures were performed using the software 'SMaRT' which allows for voxel-based morphometry. We found significant reductions in gray matter volumes in the bilateral caudate nucleus, putamen and globus pallidus in patients with EOS compared to controls (p=0.005). The patient group also showed significant volume reductions in white matter tracts in the bilateral frontal and parietal areas (p=0.024). These findings differ from those of previous of patients with AOS. Patients with AOS tend to have rather larger basal ganglia structures which are attributable to long-term exposure to antipsychotic agents. Therefore, the decrement in the basal ganglia in EOS we found may represent the pathophysiology underlying the disease process. Our finding of volume reductions in white matter tracts suggests a disruption in the widely distributed neural circuits in EOS patients. We wish to thank the Stanley Foundation for financial support.

HIPPOCAMPAL VOLUMES IN SCHIZOPHRENIC TWINS

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Hippocampal volume reduction is a robust correlate of schizophrenia, but its etiology remains unclear. Studies of children and siblings of schizophrenic patients have suggested that both genetic predisposition and environmental risk factors may contribute to hippocampal volume reduction in schizophrenia, but only twin and adoption studies can separate genetic from shared environmental influences. To examine the contributions of genetic and environmental factors to hippocampal volume reduction in schizophrenia measurements were taken from high resolution MRI scans obtained on 7 MZ twin pairs concordant for schizophrenia, 16 MZ and 32 DZ pairs discordant for schizophrenia, ascertained so as to be representative of all such probands in a Finnish birth cohort, along with 28 MZ and 26 DZ healthy comparison twin pairs without a family history of psychosis. Mean hippocampal volume differences between groups were examined using mixed model regression analysis, and intraclass correlation differences between monozygotic and dizygotic pairs were compared using t-tests. Probands hippocampal volumes were smaller than those of their non-schizophrenic MZ and DZ co-twins and healthy subjects, probands non-ill co-twins hippocampal volumes were smaller than those of healthy subjects, but non-ill MZ and DZ co-twins of schizophrenic patients did not differ from each other. The intraclass correlations (ICCs) for hippocampal volumes among healthy MZ pairs were larger than those among healthy DZ pairs, but the ICCs for hippocampal volumes among discordant MZ and DZ pairs were equivalent. Healthy subjects hippocampal volumes decreased significantly with age, while those of the probands and their co-twins did not. These findings indicate that while hippocampal volume in healthy subjects is under substantial genetic control, hippocampal volume in schizophrenic patients and their relatives is likely to be influenced to a greater extent by unique and shared environmental factors.

SCHIZOPHRENIA, BRAIN VOLUMES AND GENETICS: AN MZ TWIN MODEL

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Brain imaging studies have consistently demonstrated gray matter volume deficits in patients with schizophrenia. Furthermore, a growing body of evidence suggests that genetic factors play a role in the risk of developing schizophrenia and that structural brain abnormalities may represent an intermediate phenotype. The present study was designed to examine the neuroanatomical correlates of a (possible) genetic predisposition to develop schizophrenia and the relative contributions of genetic and non-genetic factors to these brain abnormalities. MRI scans of the brains were obtained from 14 pairs of monozygotic (MZ) concordant twins, 10 pairs of MZ discordant twins, and 17 pairs of MZ healthy control twins. Volumes of whole brain, hippocampus, third and lateral ventricles were measured. A genetic role for brain volumes in schizophrenia is suggested when MZ concordant and discordant twins differ from MZ healthy control pairs. A difference in brain volumes between the schizophrenic patients and the non-schizophrenic (co-)twins is considered as evidence for non-genetic influences. Volume measurements (controlled for sex and age) were analyzed using repeated measure-MANCOVA with Concordant (concordant, healthy control) and Discordant (discordant, healthy control) as between-subjects factors and Pair (twin 1, twin 2) as within-subjects factors. Significant main Concordant and Discordant effects were found for whole brain and hippocampus reflecting decreased volumes in both the concordant and discordant twins compared to the healthy control twins. Furthermore, significant