acute therapy studies b) Maintenance (3-month) controlled studies, with proper stratification of stabilized patients and c) Long-term (12-month) manic/depressive episode-preventive studies. Lithium, carbamazepine, sodium Valproate are examples of drugs that could serve as suitable active comparators and standard validated rating scales for the assessment of clinical states are also available. Examples of decision trees for manic or depressed index cases are possible and these are out-lined.

P04.08

Obstetric complications as risk factors for bipolar disorder

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Objective: To study whether obstetric complications increase the risk of developing bipolar disorder.

Method: The Danish Psychiatric Central Register contains data on all psychiatric hospitalizations in Denmark since 1969. The Danish Medical Birth Register covers all births in Denmark since 1973. The registers were linked using the CPR-number. In the study we have identified 161 persons born between 1973–1983 being diagnosed with bipolar disorder (after the ICD-10 classification F30 or F31 or the ICD-8 classification 296.19 or 296.39) before 1999. To each of the cases we have matched 50 controls. The controls are born the same year as the case, and are alive on the day the case has been diagnosed. All the cases and controls have an identifiable mother. The controls have no psychiatric diagnosis.

Results: The data will be present on the possible role of low birth weight and gestational age and other obstetric factors as risk factors for bipolar disorder. It will be adjusted for family history for mental disorders as well as social variables.

Conclusion: In case of a correlation between obstetric complications as risk factors for bipolar disorder it can be used as prevention.

P05. Brain imaging – structural

P05.01

A diffusion tensor and metabolite spectroscopic imaging study of white matter connectivity in schizophrenia

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Background: Structural and functional imaging of the brain has demonstrated abnormalities of both grey and white matter. Functional studies (fMRI and PET) suggest aberrant fronto-temporal connectivity, but further evidence is required. Diffusion Tensor Imaging (DTI) measures diffusion anisotropy, an indicator of the structural integrity of neuronal tracts. MR Spectroscopy studies (MRS) have found reduced N-acetyl aspartate (NAA) concentrations in frontal and temporal regions, indicating reduced neuronal density or viability. We used both techniques in an attempt to identify the structural correlates of impaired functional connectivity in schizophrenia.

Methods: Thirty patients with DSM-IV schizophrenia were compared with thirty healthy controls. DTI, MRS and sMRI were performed on all subjects. A symptom scale (PANSS) and IQ score (NART) was recorded. Data analysis included both whole brain voxel by voxel analysis using Statistical Parametric Mapping (SPM), and a region of interest approach.

Results: Data from previous smaller studies show reduced diffusion anisotropy and reduced NAA concentrations in schizophrenia. We expect to replicate these findings in our larger study and specifically localise abnormalities to fronto-temporal white matter tracts.

Conclusions: DTI and MRS have the capacity to identify the structural correlates of impaired functional connectivity in schizophrenia.

P05.02

Magnetic resonance tomography (MRT) of brain of serial sexual sadists

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Objectives: a study of the state of the terminal brain and its deep parts, as well as the skull in serial sexual sadists (SSS) with a revelation of a possible dysgenetic origin.

Methods: clinical and pathopsychological, magnetic resonance tomography.

Summary of the results obtained: The principal group included 22 SSS, the control group consisted of 28 males between 18 and 66. All were heterosexual, did not show any signs of paraphilia or sexual aggression and were in general law-abiding. In each case (100%) the following pathological MRT symptoms were revealed: dilation of subarachnoid fissures of frontal, frontal-temporal and frontal-temporal-parietal parts; dilation and flatting of contours of grooves and disordered differentiation between the grey and white substances of the frontal and frontal-temporal parts; dilation of the lateral ventricles and a significant asymmetry due to large right against left; dilation or narrowed fissure-like third ventrile; transparent partition pathology (left displacement up to 7 mm and cysts diameter up to 9 mm; dysgenetic of the callous body; congenital skull dysraphy.

Conclusions: the revealed and described cerebral deviations, changing a number of neurodynamic and psychological characteristics, create a cerebral predisposition to SSS, significantly raising the risk of serial sexual crime appearance.

P05.03

Progression of hippocampal atrophy is associated with clinical deterioration in Alzheimer's disease

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Introduction: Using quantitative magnetic resonance imaging (MRI), recent studies found atrophic changes of the medial temporal lobe structures already in early stages of Alzheimer's disease (AD). These changes were cross-sectionally correlated with the severity of dementia which led to the hypothesis that progressive medial temporal lobe atrophy might be used as a marker of disease progression.

Method: We investigated the progression rate of hippocampal atrophy with respect to rate of clinical deterioration in 13 AD patients and 8 healthy controls using volumetric MRI.

Results: Already at baseline, the AD patients showed significantly smaller hippocampal volumes than controls. While AD – in comparison to healthy ageing – was characterized by a rapid decline of hippocampal volumes (-8.1%/year) only a moderate decrease of

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whole brain volumes occurred indicating that hippocampal atrophy is not merely a function of generalized brain atrophy. Progression of hippocampal atrophy but not of whole brain atrophy was significantly correlated with clinical deterioration (r=0.6, p<0.05).

Conclusion: These findings indicate that progressive hippocampal volume reduction underlies clinical deterioration in AD and might serve as a morphometric index of disease progression.

P05.04

MR volumetry during acute alcohol withdrawal and abstinence

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Although recovery of brain volume with abstinence from alcohol in chronic drinkers is known to occur, the mechanism behind is not clear.

Measurements of segmented brain tissue class volumes (grey matter (GM), white matter (WM) and CSF) were obtained in 6 chronic alcoholics in acute withdrawal and abstinence using MRI. Subjects were studied within 48 hours after last drink, one and two months later. 11 healthy subjects were scanned twice within one month. Drinking data and cognitive test measures were obtained.

Intracranial and GM volumes did not change between scans. For patients, increase in relative WM volume between scan 1 and 2 ranged between 2.1 and 22.4%. Between scan 2 and 3, increase in total relative WM volume ranged between 5.3 and 14.0%. One individual resumed drinking and was again investigated during acute withdrawal. The measured decrease of 8.5% (relative WM volume) corresponded to the WM increase between scan 1 and 2. GM and WM volumes in healthy subjects were constant over time.

Changes in brain volume in chronic alcoholics during withdrawal and abstinence appears confined to the white matter.

P05.05

Reliability and reproducibility of MR brain tissue segmentation

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Reliability and reproducibility of segmented tissue class volumes: grey matter (GM), white matter (WM) and CSF were investigated using BRAINS and a 1.5 T MRI. Right and left side volume measurements were obtained using a continuous and a discrete classifier.

Two different sets of MR-scans were used: 10 subjects (inter- and intrareliability) and 11 subjects (scan-rescan reproducibility). Intraclass correlation (ICC) coefficient (r) was used as reproducibility index.

For the first scan set, values were 87.0% total brain volume (TBV) of intracranial volume (54.5% GM, 32.5% WM) and 13.0% CSF (continuous) and 93.5% TBV (57.1% GM, 36.5% WM) and 6.4 % CSF (discrete). For the second set, values were 86.3% TBV (54.5% GM, 31.8% WM) and 13.7% CSF (continuous) and 93.0% TBV (57.5% GM, 35.5% WM) and 7.0% CSF (discrete). For both sets, TBV was 7% larger and CSF volume 7% smaller by the discrete classification than the continuous.

Inter- and intrareliability: ICCs were above 0.99 for continuous and discrete measures except GM (discrete) (r2 >0.96). Scan-rescan reproducibility: ICCs for continuous and discrete classifications were excellent (r2 >0.99 and r2 >0.97).

P05.06

Cerebellar vermis volume reduction in patients with chronic schizophrenia

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Cognitive deficits have been reported in patients with schizophrenia. A reduction of the size of the posterior vermis has been associated with cognitive dysfunction in the fragile X syndrome. Since the posterior vermis may be involved in cognitive dysfunction, we hypothesised that the volume of the posterior vermis may be reduced in schizophrenia. To test this hypothesis, we compared the volumes of cerebellar subregions between sixty schizophrenic subjects, fulfilling DSM-IV criteria, and fifty-seven healthy subjects, of both genders, using high resolution MRI. The subjects were examined in a 1.5 Tesla GE Signa system (Milwaukee, Wis, USA) at the Karolinska Hospital. The cerebellar anterior vermis, posterior superior vermis, posterior inferior vermis and hemispheres were manually parcellated and measured using the software BRAINS. The statistical evaluation revealed a significant diagnostic effect for all vermian subregions with smaller absolute ($p < 0.005$) and relative volumes ($p < 0.001$) in the schizophrenic subjects. There was no difference for the cerebellar hemispheres or the intracranial volume. These preliminary findings suggest that the subdivisions of the vermis have reduced volumes in neuroleptic-treated schizophrenic patients.

P06. Brain imaging – functional

P06.01

Vagus nerve stimulation and fMRI in treatment-resistant depression

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Objective: Vagus Nerve Stimulation (VNS) has shown promising antidepressant effects in treatment-resistant depression, however, the mechanisms of action of VNS are not known. We report on brain activity during the first exposure to VNS (VNS initiation) in patients with treatment-resistant depression utilizing functional MRI (fMRI).

Method: Scans were acquired on 8 subjects (46.2 years±6.8) at VNS initiation. Serial interleaved VNS and fMRI techniques were used. Immediately before scanning, stimulation was reprogrammed to provide a 7 sec on–108 sec off stimulation cycle. A 440 Hz tone was interleaved in 7 second trains on alternate 57.5 sec epochs of a VNS epoch. The VNS-TONE cycle was repeated 10 times.

Results: Data was collected from 8 active VNS fMRI sessions and 8 placebo. During VNS, increased rCBF in hypothalamus, orbitofrontal, medial temporal, and medial prefrontal cortex occurred. Tone activation (auditory cortex) is consistent with previous studies. Placebo scans are being analyzed.

Conclusion: Interleaved VNS and fMRI may help understand the regional neurobiological effects of VNS in patients with treatment-resistant depression.

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