Background and aims: Deficits in response inhibition are considered as candidate endophenotypes of altered prefrontal brain function in Attention Deficit Hyperactivity Disorder (ADHD). Electrophysiological methods like Event-Related Potentials (ERPs) are adequate to measure abnormalities in brain functions underlying those deficits and to assess functionally relevant polymorphisms directly affecting neurotransmission systems and brain function. This principle of imaging genomics with ERPs has been demonstrated as early as 1999 for the serotonin transporter promoter polymorphism affecting prefrontal brain function (Fallgatter et al., International Journal of Neuropsychopharmacology, 1999).

Methods: We employed a multi-channel EEG during performance of a Go-NoGo task to assess the electrophysiological basis of response inhibition. The ERP-measure derived from this protocol was termed NoGo-Anteriorisation (NGA) and is characterized by a high interindividual stability, high short- and long-term test-retest reliability and, moreover, is independent from age- and gender.

Results: In patients with ADHD during childhood and adulthood the NGA was diminished as compared to age- and sexmatched healthy controls. Furthermore, a three-dimensional source location analysis with LORETA indicated an electrical dysfunction of the ACC in the patient groups. Moreover, the 158 val/val variants of the COMT gene were associated with an even worse prefrontal brain function.

Conclusions: These results exemplify the measurement of disease related disturbances in brain function in ADHD with ERPs. Future studies will show whether such electrophysiological endophenotypes may contribute to the diagnosis of subgroups of ADHD and whether they may serve as endophenotypes to further clarify genetic contributions to the disease.

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Paired associate learning in subjects at risk for psychosis: fMRI study

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Background: Executive and mnemonic impairments have been well documented in the high-risk states for development of psychosis and have been pinpointed as a possible core neuropsychological dysfunction. However, their neurofunctional correlates are still not clear.

Method: fMRI was used in 17 patients at risk for developing psychosis (ARMS, "at risk mental state") and 10 patients with a first episode of psychosis (FEP) and 15 age-matched healthy comparison subjects to examine neural responses to increasing difficulty of mnemonic engagement in an object−location paired associate memory task. Groups were matched in terms of age, IQ, gender, and psychopathology ratings. Accuracy and reaction time were recorded during the scan.

Results: As the mnemonic load increased, response latency increased and response accuracy decreased in an approximately linear fashion. No main effect for group was observed. However, a trend towards decreased accuracy in FEP subjects, as compared with controls, was evident. As the task difficulty increased, increased brain activity was observed in the medial frontal cortex and in the medial posterior parietal cortex. Between-groups differences in activation were observed in a cluster spanning the MFG, SFG and SMA and in the right precuneus. However, these neurofunctional abnormalities were more evident in the most demanding level of the task than in the

easy level, with the ARMS groups showing less activation than controls and higher activation than FEP.

Conclusion: Abnormal neural activity in medial frontal cortex and posterior parietal cortex during paired associate learning task may represent a neurofunctional substrates of vulnerability to psychosis.

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Age-related decline in 5-HT2A and 5-HTU sites in the rhesus monkey hypothalamus

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Serotonin 2A receptors (5-HT2A), and serotonin reuptake transporters (5-HTU) are involved in regulating some autonomic and cognitive processes. While the pre-synaptic and post-synaptic distribution of 5-HT2A receptors is unknown in the primate hypothalamus, in cortex, the majority of 5-HT2A receptors are located post-synaptically on pyramidal and glial cells. The density of 5-HT2A and 5-HTU sites declines with age in the primate and rodent hippocampus and frontal lobe but such changes have not been documented in the hypothalamus. To assess age-related changes in the density of 5-HT2A and 5-HTU binding sites in the rhesus monkey (Macaca mulatta) hypothalamus, autoradiographic ligand binding was utilized within the anterior, tuberal, and posterior hypothalamus, and the mammillary body (MMB) of 11-17 monkeys (4.4-31.8 yo). 5-HTU binding was assayed with tritiated citalopram and 5-HT2A with iodiated dimethoxyaminopropane (DOI). The density of 5-HTU binding was significantly reduced with age in the anterior (R= -0.57, N= 16, P=0.021), tuberal (R= -0.627, N= 17, P= 0.007), and posterior (R= -0.053, N= 15, P= 0.042) hypothalamus. Conversely, only the MMB displayed a significantly lower 5-HT2A density in aged animals (R=- 0.631, N= 11, P= 0.037). These results show a significant age-related decline in CIT binding throughout the hypothalamus, suggesting an age-related reduction in its serotonergic innervation. While we were unable to evaluate 5-HT U binding in the MMB, our results show a significant decline in DOI binding in this nucleus. Future studies are needed to determine the 5-HT2A receptor distribution in the monkey hypothalamus. (Supported by NIH Grant-P01-AG00001-29 and RR-00165).

P309

The WHO (Ten) well-being index as a screening instrument for major depression in a population-based sample

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Background: The present study evaluated the association between the WHO (Ten) Well-being index and major depression assessed by the Major Depression Inventory (MDI) and Schedules for Clinical Assessment in Neuropsychiatry (SCAN). The main aim was to examine how well the WHO (Ten) Well-being index worked as a screening instrument for depression in a population-based sample.

Methods: A questionnaire including the WHO (Ten) Well-being index and the MDI was sent out to a randomly selected adult Swedish population and 10 441 persons participated. Psychiatrists using SCAN interviewed a selected sample. Sensitivity, specificity, Receiver Operating Characteristics (ROC) and Area Under the Curve (AUC) were calculated.

Results: When a cut-off score ≤ 8 for the Well-being scale was used and depression according to SCAN was the index of validity the sensitivity was 0.81 and the specificity 0.81. When depression according to the algorithm of the MDI was used the sensitivity was 0.89 and the specificity was 0.86 at a cut-off score of ≤ 12. There were no age or gender differences between true positive persons versus false negative persons. The AUC was good (0.86) when using SCAN and when using the DSM-IV algorithm of the MDI excellent (0.93).

Conclusion: The WHO (Ten) Well-being scale can be used as s simple screening instrument for depression in population-based studies. However, the scale needs to be further evaluated in order to examine if the recommended cut-off score in the present study could be replicated in other surveys.

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The effect of low-frequency rTMS on regional brain metabolism (PET) in auditory hallucinations as the background for neuronavigated rTMS

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Background: Auditory hallucinations are characteristic symptoms of schizophrenia with high clinical importance. It was repeatedly reported that low frequency ($\leq$1Hz) repetitive transcranial magnetic stimulation (rTMS) diminishes auditory hallucinations. A neuroimaging study elucidating the effect of rTMS in auditory hallucinations has not yet been published.

Objective: To evaluate the changes of brain metabolism after low-frequency rTMS in patients with auditory hallucinations.

Methods: Low-frequency rTMS (0.9Hz, 100% of motor threshold, 20 min.) applied to the left temporo-parietal cortex was used for ten days in the treatment of medication-resistant auditory hallucinations in schizophrenia (N=12). The effect of rTMS on the brain metabolism (18FDG PET) was measured before and after the treatment.

Results: We found a significant improvement in the total and positive symptoms, and on the hallucination scales (HCS, AHRS). The rTMS decreased the brain metabolism in the left superior temporal gyrus and in interconnected regions and effected increases in the contralateral cortex and in the frontal lobes (SPM).

Conclusion: The findings implicate that the effect is connected with decreased metabolism in the cortex underlying the rTMS site while facilitation of metabolism is propagated by transcallosal and intrahemispheric connections. Stereotactic neuronavigation of rTMS (SN rTMS) is a unique technology to target the rTMS coil with a high degree of anatomic accuracy based on the evaluation of the neuroimaging. Our finding enable the use of stereotactic neuronavigation of rTMS in auditory hallucination and pilot data are presented.

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Inhibin b as a possible marker of antipsychotic induced sexual dysfunction in schizophrenic men

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Background and aims: AISD (Antipsychotic induced sexual dysfunction) is one of the most important reasons for therapeutic noncompliance. AISD is often described as adverse events of hyperprolactinemia, induced due to immoderate D2 occupancy (more than 72%) in the tuberoinfundibular system. Consequently the sex steroids decrease. Regulation of Follitropin secretion involves a complex balance between stimulation by GnRH from the hypothalamus, inhibitory feedback by sex steroids, Inhibins A (in both sexes) and B (in male) from the gonads and autocrine/paracrine modulation by Activin and Follistatin within the pituitary.

Method: We have tried to verify the hypothesis that inhibins could be a better marker of sexual dysfunction than prolactinemia in patients (16 men and 11 women) with stable therapy and psychopathology with a diagnosis of schizophrenia, age 18-40 years. Follitropin, Lutropin, Prolactin, TSH, Estradiol, Progesterone, Testosterone, Inhibin A (in women) and B, Activin and Follistatin were used to measure the endocrinological condition. Structured Adverse Effects Rating Scale, UKU (hyperprolactinemia), Arizona Sexual Experience Scale and International Index of Erectile dysfunction in men were used to detect sexual dysfunction.

Results: Inhibin B in men, not in women, correlated with sexual dysfunction ($p < 0.05$). Prolactinemia did not correlate with this side effect, it correlated with the absence of the menstrual cycle in women.

Conclusions: Inhibin B may be used as a marker of the functional condition in antipsychotic induced sexual dysfunction in men. Results are limited by the sample size. Further study is needed to evaluate the importance and specificity of Inhibin B.

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Novel evidence for the involvement of the mirror neuron system in emotional processing

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Background and aims: Mirror Neurons (MNs) constitute a system for matching action observation and execution and for recognising socially meaningful gesticulation. Here we explored the possibility that this system also contributes to emotional processing. To test this hypothesis, a novel affective startle paradigm was developed to investigate MNs and emotional processing.

Methods: Fifty healthy participants completed a startle experiment where they were presented with 36 emotionally valenced pictures equally split into positive, negative and neutral categories. All pictures were preceded by emotionally congruent primes, half of which consisted of a videoclip showing a biologically meaningful hand-object interaction and half that consisted of a control stimulus showing static images of the interaction. Acoustic startle probes were presented during picture viewing at 2.5, 3, 3.5, 4 and 4.5 second intervals and startle eyeblink responses were recorded.

Results: Startle amplitude was magnified only for emotionally negative pictures. This effect was present when the images were preceded by a prime containing biological motion but not a static prime.