2011 FENS/IBRO Summer School:

Metabolic Aspects of Chronic Brain Diseases

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ay 1 (Wednesday July 20)

1:00 pm –	**Arrival and Check In**
5:00 pm	**Welcome and Introduction to the School** (Organizing committee)
5:30 pm	**"The molecular mechanisms underlying obesity"** (Giles Yeo, Cambridge)
6:30 pm	**Dinner**
8:00 pm	**"The logic of scientific discovery"** (Cyril Höschl, Prague)
9:00 pm	**Welcome reception**

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Logic of scientific discovery

Scientific discovery employs tools which are in fact our extended senses. Our senses, however, are designed primarily to help us to survive (adapt), not to „see the truth". So we can easily become victims of tricks and illusions. So does our mind, susceptible to magic thinking. That is why science has maximally to reduce the complexity of the world in order to eliminate as many of endless confounders and biases as possible. This is, however, neither sufficient nor completed process outcome of which would be "to get the truth". In clinical research, for example, the methodology of double-blind, placebo controlled trials reached almost perfection. Despite this, the *placebo-verum signal* diminishes in time. On the other hand, there were published several well done studies showing clearly a significant and clinically relevant effect of a remote healing prayer, even retrospectively! The problem lies among other things in posing wrong questions, in erroneous methods, in multiple comparisons and type one or type two errors, in premature jumping into conclusions, in publication bias, and in the misunderstanding causality. Some of these aspects will be summarized in the lecture.

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Neurobiology of schizophrenia with regard to metabolic aspects

One of the crucial questions in the study of schizophrenia is, whether the diagnosis of the disease represents one entity or a group of disorders ("Gruppe der Schizophrenien"). Nancy Andreasen suggests the term "lathomenology" for a bottleneck on the pathogenetic way from various possible etiological factors to diverse phenomenological expressions (symptoms). In the background of this common denominator, there is an anatomical and functional disruption in neuronal connectivity and communication, which can be a consequence of the incomplete or erroneous neuron formation, migration, synaptogenesis or pruning during the ontogenesis. Also apoptosis and activity dependent changes might play a role in this development. This all can happen since the conception to early adulthood and can lead to the impairment in fundamental cognitive functions. This leads to the development of clinical symptoms, either positive or negative. Schizophrenia can be regarded as a "disconnection" or "information processing disorder". There are many neural circuits, where the clinical impact of the disconnection or misconnection is worth to be studied. One of them is fronto-thalamo-cerebellar circuit with the special role of cerebellum not only in the synchronization of motor processes, but also in coordination of motor-cognitive sequences (*Arch Gen Psych 1999;56:781-787*). The disconnection of this circuits leads to "cognitive dysmetria". Mezo-cortical pathways also represent the crucial pathogenetic point. Dopaminergic fibers from ventral tegmental area to pre-frontal cortex are under the serotonergic inhibition via 5-HT2 receptors. This configuration can help to understand the dual mode of action of novel antipsychotic agents, which are effective in both positive (hyperdopaminergic state in 24ingu-limbic areas) and negative (hypodopaminergic state in prefrontal cortex) symptoms. Disconnection can play a role also in circuits involved in executive functions (fronto-parieto-temporo-cingulate). On the neurochemical level, many of dysbalances in information processing can be explained in the frame of Carlsson's scheme of psychotogenic pathways. The crucial mechanism involves striato-thalamic GABA-ergic control of gating, which is under the glutamatergic control from cortex. The scheme can explain also amphetamine model of psychosis, dopamine hypothesis of schizophrenia, glutamatergic model of schizophrenia, psychotogenic effects of hallucinogens (LSD), atropine, phencyclidine etc. Our own study on the role of serotonin regulation of psychotogenic pathways will be reported.