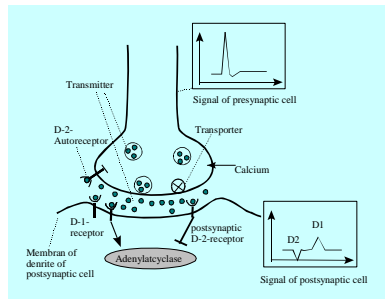


Systems Biology of the Synapse in Mental Disorders

5th International Workshop on
Computational Neuropsychiatry

May 8th /9th 2009
Department of Psychiatry
Alzheimer Saal
Nussbaumstrasse 7
Munich



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Prolog

Psychiatric disorders are based on a dysfunction of synapses in neural networks. For schizophrenia and addiction among others the dopamine and glutamatergic synapses are of relevance, for depression the norepinephrine and the serotonin synapse are more important. In dementia e.g. the deficiency of the cholinergic system is treated by anticholinergic substances. All diseases can be treated by changing the synaptic transmission by molecular switches such as receptor blockade or reuptake blockers by blockade of enzymatic degradation of transmitter etc. indicating that not only the synaptic molecular mechanisms but also the electrophysiological properties might be modulated. In many cases the significant treatment effects have a latency of about 10 days. Although important progress is made in treatment of mental disorders, still the psychopharmacological treatment is not satisfying especially regarding side effects.

This is showing that we do not understand the dynamics of pathology and reorganization of synapses.

For this reason the dynamics of various components of synaptic transmission should be studied: The kinetics of control of synthesis, storage, release, reuptake, degradation, receptor occupation, up-regulation, and down-regulation.

Additionally, the synapses have to be related to the neuron as the basic functional unit of the brain. This perspective corresponds to the molecular biological research approach that now is integrating more and more the view of systems biology. Systems biology aims to reconstruct the cell on the basis of molecular biological data. This "bottom-up" reconstruction is based on quantitative kinetic data that are integrated into mathematical models that are transformed into computerized models. By these models "in-silico"-experiments can be performed that help to understand complex networks of chemical pathways.

It seems to be helpful for understanding the dynamics and the pathology of synapses by computational models.

With this aim we started a series of workshops on "Computational Neuropsychiatry" in order to relate psychiatry to *computational modeling* in theoretical neuroscience in 2005. These workshops are designed as

communicational meetings between theoreticians such as *systems scientists*, *computational scientists* and empirical researchers such as *neuropsychiatrists* and *neurobiologists*. We started with a workshop with Arvid Carlsson and discussed his models of networks of schizophrenia. In 2006 we organized a second workshop in order to discuss clinical and experimental data and theoretical concepts of disturbances of the working memory as they are observed in patients with schizophrenia. In 2007 we discussed the perspective of Molecular Systems Biology on schizophrenia. In 2008, we applied these experiences on addiction.

We want to discuss if theoretical neuropsychiatry has essential benefits by using the tools of systems science like systemic modeling and computer simulations.

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Essex,
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----- Friday May 8 -----

13:30 Opening

Margot ALBUS, Felix TRETTER, Dan RUJESCU, Peter GEBICKE
HAERTER, Hans BRAUN, Walter MÜLLER

13:45 Introduction - Psychiatry, the Synapse and Systems Biology

Felix TRETTER, Eduardo MENDOZA
(Psychology, Physics, Univ. of Munich)

Moderation: Hans BRAUN (Univ. of Marburg)

14:15 Ingo VERNALEKEN (Psychiatry, Univ. of Aachen, FRG)

The synaptic action of antipsychotic drugs – up-regulation after receptor blockade by antipsychotics?

14:45 Discussion

15:00 Coffee Break

Moderation: Dan RUJESCU (Univ. of Munich)

15:20 Anthony GRACE (Psychiatry, Univ. of Pittsburgh, USA)

The signalling properties of dopamine networks and schizophrenia

16:05 Discussion

Moderation: Peter GEBICKE-HAERTER
(Centre for Mental Health, Mannheim, FRG)

16:20 Bita MOGHADDAM (Psychiatry, Univ. of Pittsburgh, USA)

The circuitry of glutamate synapses and schizophrenia

17:05 Coffee Break

Moderation: Michael KOCH (Univ. of Bremen, FRG)

17:20 Peter ERDI (Complex Systems, Kalamzoo College, USA)

Multi-scale modelling approach to schizophrenia as a dysconnection syndrome

18:05 Discussion

Moderation: Walter E. MÜLLER (Pharmacology, Univ. of Frankfurt, FRG)

18:20 Andreas DRAGUHN (Physiology, Univ. of Heidelberg, FRG)

No simple switch - the complex functions of chemical synapses.

18:55 Discussion

Moderation: Oliver POGARELL (Univ. of Munich)

19:15 Evening lecture

Henry MARKRAM (Brain-Mind Institute Lausanne, CH)
The Blue Brain Project: Modelling synapses in a cortical column

20:00 Discussion

20:15 End of the Session

----- Saturday May 9 -----

9:00 Dan RUJESCU, Felix TRETTER,

Introduction – more details

Moderation: Hans-Werner MEWES
(Bioinformatics, Helmholtz, Munich, FRG)

9:15 Eberhard VOIT (Georgia Institute of Technology, Georgia, USA)

A systemic model of dopamine synthesis. Intracellular dopamine signalling network

10:00 Discussion

Moderation: Uwe AN DER HEIDEN
(Mathematics, Univ. of Witten, FRG)

10:15 Wolfgang HAUBER (Physiology, Stuttgart)

Intrasynaptic Dynamics of transmitters

10:45 Discussion

11:00 Coffee Break

Moderation: n.n.

11:15 Svetlana POSTNOVA (Neurodynamics, Univ. Marburg, FRG)

A neuronal model of homeostatic processes: Activity dependent modulation of synaptic transmission

11:45 Discussion

Moderation: Georg WINTERER (Psychiatry, Univ. of Düsseldorf)

12:00 Hans LILJENSTRÖM (Biophysics, Univ. of Uppsala, Sweden)

Modelling the synapse in networks

12:30 Discussion

12:45 General Discussion & Conclusions

Dan RUJESCU, Felix TRETTER

13:30 End of the Session