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Update on neural networks involved in generalized epilepsy

Introduction: Based on interaction between classical neurotransmitters and neuropeptides between each other, a neural network in the hippocampus, the thalamus and the cortex is developed.

Methods/Materials: In generalized epilepsy alterations of ion channels and neurotransmitter and neuropeptide concentrations can be induced genetically or exogenously. An enlarged neuronal network is described in order to point out the epileptogenesis as a consequence of the interaction between the corresponding neurotransmitters and neuropeptides and of stimulus enhancing the neurotransmitter imbalance.

Results: The neural network reads as follows: Dopaminergic neurons in the hippocampus transmit a strong postsynaptic excitatory impulse via D2 receptors to glutaminergic neurons which strongly inhibit serotonergic neurons via NMDA receptors. The glutamtergic neurons can enhance epileptogenesis via an excitotoxic, postsynaptic excitatory effect via NMDA, AMPA and kainate receptors. The serotonergic neurons with a low activity transmit a weak activating impulse via 5-HT2C receptors to GABAergic neurons which weakly inhibit dopaminergic neurons via GABAA receptors. A withdrawal of GABAergic presynaptic inhibition of dopaminergic neurons can cause an epileptic seizure. GABAergic neurons weakly inhibit glutamatergic neurons in the thalamus, which transmit a strong activating impulse via NMDA receptors to glutamatergic neurons in the cortex. The cortical glutamateragic neurons can enhance the activity of the dopaminergic neurons in the hippocampus via D2 receptors. Other serotonergic neurons transmit a weak activating impulse to serotonergic neurons via 5-HT7 receptors. Neuropeptide Y containing neurons in the dentate gyrus weakly inhibit glutamtergic neurons via NPY2 receptors and transmit a weak activating impulse to GABAergic neurons via NPY1 receptors. The serotonergic neurons transmit a weak postsynaptic excitatory impulse via 5-HT2C receptors to GABAergic neurons which weakly inhibit adenosine neurons via GABAA receptors. The adenosine neurons with a high activity transmit a strong activiting impulse via A2A receptors to glutamtergic neurons which strongly inhibit serotonergic neurons via the subtype 5 of the glutaminergic metabotropic receptors. The mechanism

of action of conventional antiepileptic drugs such as valproic acid, carbamazepine, phenytoin and ethosuximide and newer antiepileptic drugs, such as lamotrigine, levetiracetam and topiramate is pointed out according to the neural network.

According to the neural networks described the following possible pharmacological options could exert an antiepileptic effect:

- Combined GABAA agonists and NMDA antagonists.
- KA or AMPA receptor antagonists, which would inhibit epileptic glutamate emptying.
- NPY2 receptor agonists, which would inhibit glutamate emptying.
- A2A receptor antagonists, which would enhance serotonin levels.
- m5GluR receptor antagonists, which would enhance serotonin levels.

Conclusion: It is important to examine neuronal networks in generalized epilepsy in order to optimize a multimodal pharmacotherapy of the disease.

References

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Biography

Felix-Martin Werner studied human medicine at the university of Bonn. He has been working as a medical teacher in the formation of geriatric nurses, occupational therapists and assistents of the medical doctor at the Euro Academy in Pößneck since 1999. He has been doing scientific work at the Institute of Neurosciences of Castilla and León (INCYL) in Salamanca (Spain) since 2002. With Prof. Rafael Coveñas, he assisted at over 30 national and 12 international congresses of neurology and published over 60 reviews about neural networks in neurological and psychiatric diseases. Since 2014, Dr. Werner has belonged to the editorial board of the Journal of Cytology & Histology.

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