Felix-Martin Werner, Epilepsy J 2021, Volume 07

Treatment of generalized epilepsy according to a neural network

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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, while results from the audiogenic animal model are taken into consideration.

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 D_2 receptors to glutaminergic neurons which strongly inhibit serotonergic neurons via NMDA receptors. The glutaminergic 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 $5\text{-}HT_{2C}$ receptors to GABAergic neurons which weakly inhibit dopaminergic neurons via $GABA_A$ receptors. A withdrawal of GABAergic presynaptic inhibition of dopaminergic neurons can cause an epileptic seizure. GABAergic neurons weakly inhibit glutaminergic neurons in the thalamus, which transmit a strong activating impulse via NMDA receptors to dopamineragic neurons in the cortex. The cortical glutaminergic can enhance the activity of the dopaminergic neurons in the hippocampus via D_2 receptors. Other serotonergic neurons transmit a weak activating impulse to serotonergic neurons via $5\text{-}HT_7$ receptors. Neuropeptide Y containing neurons in the dentate gyrus weakly inhibit glutaminergic neurons via NPY_2 receptors and transmit a weak activating impulse to GABAergic neurons via NPY_1 receptors. The serotonergic neurons transmit a weak postsynaptic excitatory impulse via $5\text{-}HT_{2C}$ receptors to GABAergic neurons which weakly inhibit adenosine neurons via $GABA_A$ receptors. The adenosine neurons with a high activity transmit a strong activiting impulse via A_{2A} receptors to glutaminergic neurons which strongly inhibit serotonergic neurons via the subtype 5 of the glutaminergic metabotropic receptors.

The mechanism of action of conventional 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 $GABA_A$ agonists and NMDA antagonists.
- KA or AMPA receptor antagonists, which would inhibit epileptic glutamate emptying.

- NPY_2 receptor agonists, which would inhibit glutamate emptying.
- A_{2A} receptor antagonists, which would enhance serotonin levels.
- m5GluR receptor antagonists, which would enhance serotonin levels
- $5\text{-}HT_7$ receptor agonists, which would increase serotonin levels.
- nAch alpha7 agonists.

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

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.