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NEUROPHYSIOLOGY 2021: Therapeutic effect of novel antidepressant drugs interfering with receptors of neurotransmitters and neuropeptides- Euro Akademie Pößneck, Germany

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Introduction:
Major depression is a frequent psychiatric disease, which is mainly treated by different antidepressant drugs. However, one third of the depressive patients remain treatment-resistant. In major depression, in the brainstem, hippocampus and prefrontal cortex, alterations of neurotransmitters and neuropeptides and the belonging neural networks are updated. Starting from these findings, novel antidepressant drugs and combination of different antidepressant drugs are suggested. In the prefrontal cortex, glutamatergic neurons, which receive a postsynaptic excitatory potential from D2 dopaminergic neurons, exert a presynaptic inhibition upon M1 muscarinic cholinergic neurons via NMDA receptors. Medium spiny GABAergic/somatostatin neurons, which receive projections from M1 muscarinic cholinergic neurons, presynaptically inhibit D2 dopaminergic neurons via GABAA/somatostatin1 receptors. The combination of an NMDA receptor antagonist , for example ketamine with an M1 muscarinic cholinergic receptor antagonist, for example scopolamine, exert a rapid, long-lasting antidepressant effect. In preclinical studies, the antidepressant effect of orvepitant, an NK1 receptor antagonist, has been demonstrated: this antagonist reaches a complete antagonism of NK1 receptors. In clinical studies, the combination of an NMDA receptor antagonist with an M1 muscarinic cholinergic receptor antagonist should be investigated indepth as well as the therapeutic effect of orvepitant. In clinical studies, the antidepressant effect of a triple reuptake inhibitor should be examined and compared to current antidepressant drugs. The superior therapeutic effect of antidepressant drugs like venlafaxine, a selective noradrenaline and serotonin reuptake inhibitor and bupropion, a selective dopamine and nordrenaline reuptake inhibitor and their adverse effects will be pointed out. Non-pharmacological measures to enhance the antidepressant effect will also be discussed.

Objectives: Major depression is a frequent psychiatric disease. One- third of the depressive patients remain treatment-resistant; thus, it is urgent to find novel antidepressant drugs.
In major depression, in several brain areas the neural networks involved and the alterations of neurotransmitters and neuropeptides are updated. According to these networks, new pharmacological agents and effective combinations of antidepressant drugs achieving a more efficacious antidepressant treatment are suggested.

Results: In the neural networks, the prefrontal cortex has been included. In this brain area, glutamatergic neurons, which receive an activating potential from D2 dopaminergic neurons, presynaptically inhibit M1 muscarinic cholinergic neurons via NMDA receptors. Medium spiny GABAergic/somatostatin neurons, which receive projections from M1 muscarinic cholinergic neurons, presynaptically inhibit D2 dopaminergic neurons via GABAA/somatostatin1 receptors. The combination of an NMDA receptor antagonist with an M1 muscarinic cholinergic receptor antagonist can achive a rapid, long-lasting antidepressant effect. In preclinical studies, the antidepressant effect of orvepitant, an NK1 receptor antagonist, has been demonstrated: this antagonist reaches a complete blockade of NK1 receptors. In clinical studies, the combination of an NMDA receptor antagonist with an M1 muscarinic cholinergic receptor antagonist should be investigated indepth as well as the therapeutic effect of orvepitant. In clinical studies, the antidepressant effect of a triple reuptake inhibitor should be examined and compared to current antidepressant drugs.

Conclusions: IGD presents some characteristics that are not extensive to online GD. These specificities have potentialclinical implications and they need to be further studied

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