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Ketamine and antidepressant effects

Author	Message
Bernhard Mitterauer Joined: 07 Jun 2005 Posts: 24	Posted: Mon Jan 10, 2011 10:38 am Post subject: Ketamine and antidepressant effects quote edit Ketamine may block NMDA receptors in astrocytes causing a rapid antidepressant effect Bernhard J. Mitterauer The rapid antidepressant response after ketamine administration in treatment-resistant depressed patients suggests a possible new approach for treating mood disorders as compared to the weeks or months required for standard medication. However, the mechanisms underlying this action of ketamine [a glutamate N-methyl-D-aspartate acid (NMDA) receptor antagonist] is unclear (Diazgranados et al, 2010). Li et al (2010) observed that ketamine rapidly activated the mammalian target of rapamycin (mTOR) pathway, leading to increased synaptic signaling proteins and increased number and function of new spine synapses in the prefrontal cortex of rats. Importantly, these researchers admit that the mechanims underlying rapid antidepressant actions have not been identified so far and that they are likely more complicated than simple NMDA receptor blockade. From a pure neurobiological view this may be true, but not if we also refer to glial-neuronal synaptic units. Given the fact that glial-neuronal synaptic units are experimentally well established, we are faced with the question of the role of astrocytes in the pathophysiology of depression. I have hypothesized (Mitterauer 2010 a, b) that in depression an astrocytic syncytiopathy – caused by a downregulation of connexins – may lead to an upregulation of astrocytic receptors. Such an excess of astrocytic receptors exerts a relative lack of neurotransmitters such that the synaptic information processing is imbalanced. It has been experimentally verified that astrocytes express all receptors for the occupancy with the cognate neurotransmitter types (Verkhratsky and Butt, 2007). Hence, a basic mechanism of the rapid antidepressant effects of NMDA-blockers can be deduced from this testable model. Supposing that in therapy-resistant depression a significant excess of NMDA receptors in astrocytes causes a severe relative lack of glutamate which cannot be balanced by reuptake inhibitory drugs, the blockade of the excess of NMDA receptors in astrocytes may rapidly balance synaptic information processing. Note that all of the various neurotransmitters and their receptors in the neuronal and glial cell systems may play a role in depression. Therefore, my model of depression might open a new dimension in the development of

antidepressants, especially what the treatment of patients with a chronic depression concerns.

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