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Excess of astrocyte receptors in depression

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Excess of astrocyte receptors in tripartite synapses may cause a severe disorder of information processing and behavior in depression

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Depression is an extremely common disorder, ranking second in the global burden of disease. Here I present an outline of a novel biocybernetic model that may be explanatory for depressive behavior (Mitterauer, 2008a). My hypothesis is that if the information processing in tripartite synapses is severely delayed, the behavior generating systems in the brain stem reticular formation cannot decide in real time which mode of behavior is appropriate to a specific sensory information of the environment.

This pathophysiological mechanism leads to a persistence of some modes of behavior (e.g. sleeping, eating, working, etc.) and, in parallel, the system is incapable of producing an appropriate behavior to rapidly changing situations in the environment. Such a severe disorder of behavior may essentially be caused by an excess of astrocyte receptors which cannot be sufficiently occupied by the cognate neurotransmitters, and thus, the information processing in tripartite synapses is protracted. Since our self-understanding is basically dependent on an effective behavior in the inner and outer environment, self-understanding is also affected in depression (Mitterauer, 1994).

The normal signalling pathway at a tripartite synapse can be described as follows (Araque et al, 1999): during synaptic neurotransmission, neurons release neurotransmitters from synaptic nerve terminals into the synaptic cleft to communicate with other neurons. The transmitter released from the synapse (or other co-released neurotransmitter) can spill over from the synaptic cleft and reach neurotransmitter receptors in adjacent glial cells (astrocytes or perisynaptic Schwann cells), eliciting intracellular increases in Ca2+ concentration in the glial cells (astrocytes). The increase in the astrocyte Ca2+ concentration causes it to release a chemical transmitter from the astrocyte ("gliotransmitter") that negatively feeds back to the presynaptic and postsynaptic nerve terminals, temporarily turning off and thus modulating synaptic neurotransmission (see also Newman, 2005).

If the set of astrocyte receptors and the amount of neurotransmitter is balanced, then an undisturbed synaptic information processing is possible.

In contrast, unbalanced synaptic systems may cause severe behavioral disorders like depression. In the case of depression, the excess of astrocyte receptors leads to a relative lack of neurotransmitter so that not enough substances are available for the occupancy of all astrocyte receptors. As a consequence, the production of gliotransmitters is prolonged and, therefore, the negative feedback mechanism interrupting neurotransmission is protracted. Formally speaking, such tripartite synapses are underbalanced (this formalism is described in Mitterauer, 2007; 2008b).

In a computer simulation (Mitterauer, 2008a) it can be demonstrated how a delay in synaptic information processing affects the various modes of behavior in the sense of a severe displacement. This means that some modes of behavior (e.g. sleeping) persist ("must do") and, in parallel, an incapability to produce other modes of behavior (e.g. eat, communicate) occurs ("cannot do"). Most importantly, the clinical results of an investigation of patients with a major depression support this novel model of depression essentially based on a disorder of synaptic glial-neuronal interactions (Rothuber et al, 2007).

My model of the pathophysiology of depression is experimentally testable. First of all, the already identified receptors on astrocytes (Kettenmann, Steinhäuser, 2005) must be further investigated in post mortem brains of patients with depression. Both qualitative and quantitative investigations are necessary. In addition, methods for in vivo investigations of astrocytic receptors in human brains must be developed.
The overexpression of glial receptors in depression may be essentially caused by mutations in astrocytes. These may occur spontaneously and/or be activated by stress. What the biological treatment of depression concerns, new approaches are necessary, for example substances that block the excess of astrocyte receptors. Such a therapeutic approach could be especially effective in patients with chronic depressions, where the various antidepressants presently applied are unsuccessful.

References cited:
Kettenmann H., Steinhäuser C. (2005) Receptors for neurotransmitters and hormones. In: Neuroglia, Kettenmann H., Ransom BR (eds). Oxford University Press, Oxford, pp 131-145.
Mitterauer B. (1994) Biokybernetik der Depression. Der informierte Arzt 1: 50-57.
Mitterauer B. (2007) Synaptic imbalance in mental disorder. Artificial Ingenuity. Apr.11.
Mitterauer B. (2008a) Excess of astrocyte receptors in tripartite synapses may cause a severe disorder of information processing and behavior in depression. The Journal of global issues and solution. Vol VIII (3). http://www.bwwsociety.org/journal/html/
Mitterauer B (2008b) Synaptic imbalances in endogenous psychoses (in review process)
Newman EA (2005) Glia and synaptic transmission. In: Neuroglia, Kettenmann H., Ransom BR (eds). Oxford University Press, Oxford, pp 355-366.
Rothuber H. et al (2007) Loss of self-understanding: a behavior-oriented model of depression. Med Sci Monit 13: CR1-CR7.