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Chapter IV

Neurobiology of the ventral basal ganglia loop

Introduction

Although much research has been done to elucidate the functions of basal ganglia (BG), these structures are still a very timely area of research and a source of knowledge about how brain networks work under physiological and under pathophysiological conditions. From a basic point of view, the basal ganglia can be considered as an example of how phylogenetically old pathways ascending from the midbrain interact with phylogenetically young pathways descending from the cortex. The basal ganglia may also serve as an example of how the amino acid transmitter glutamate, a main mediator of information flow, interacts with dopamine which probably has modulatory functions.

This symposium is the continuation of a series of symposia that have taken place during the previous congresses on Amino Acids. By far, it does not cover all aspects of basal ganglia functions and dysfunctions. Rather, it reports on some actual and new developments in this field of research.

R. M. Kostrzewa, J. P. Kostrzewa and R. Brus indicate how an imbalance created by lesioning one of the neural circuits (dopaminergic) to BG results not only in altered sensitivity of homologous (dopaminergic) receptors but also sensitization of heterologous receptors (that is, those for other neurotransmitter systems). Additionally, they show that dopamine denervation creates a neural environ whereby the excitatory effects of amino acid neurotransmitters are potentially more neurotoxic. They summarize by proposing that L-DOPA, the major treatment in Parkinson's disease, may actually be protective to the neuropil, a conclusion that runs counter to current views on L-DOPA as a drug that might accelerate progression of Parkinson's disease.

B. D. Kretschmer reports on the ventral pallidum which so far has received less attention than the input structures, i.e. the striatum/n.accumbens or the output structures of the BG. The ventral pallidum is part of the ventral loop of the basal ganglia which is regarded to be closely related to the brain reward system. Using brain microdialysis in combination with behavioural measurements, it was found that dopamine-activity in the ventral pallidum can be correlated with behavioural changes, but no such correlations were found between the glutamatergic activity or the GABAergic activity and behaviour. It may be concluded from these data that a meso-pallidal dopaminergic projection critically controls information flow through the ventral loop.

Another major structure of the ventral loop is the prefrontal cortex. T. M. Tzschentke performed intracranial self stimulation (ICSS) experiments combined with microdialysis. ICSS in the prefrontal cortex increased dopamine and glutamate release in the ventral tegmental area (VTA) and in the nucleus accumbens. Infusions of kynurenic acid into the VTA blocked the dopamine release and also self-stimulation behaviour. He concluded that ICSS in the prefrontal cortex, may depend critically on dopamine release in the nucleus accumbens, which is, in turn, mediated by an increase in glutamate-release in the VTA. Using lesion techniques and place preference conditioning, it was found that the different subareas in the prefrontal cortex are differentially involved in the mediation of reward and that different rewarding drugs act differentially upon the various subareas.

Pathological disturbances of transmitter activities in the ventral loop of the BG are considered to play a major role in schizophrenia. T. H. Svensson, J. M. Mathe and M. V. Fagerquist report on the intriguing fact that uncompetitive NMDA receptor-antagonists (MK-801 or PCP) and AMPA receptor-antagonists have opposite effects on locomotion and other behavioural variables. While MK-801 produces behavioural stimulation that shares some similarities with psychotic symptoms, AMPA-receptor-antagonists have mainly behavioural depressant effects but do not induce catalepsy. Here it is reported that AMPA receptor-antagonists selectively suppressed conditioned avoidance response in the rat. Since this is typical for all antipsychotic drugs it is postulated that AMPA receptor-antagonists show an antipsychotic profile.

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