Neurochemical Oscillations in the Basal Ganglia

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Abstract This work represents an attempt to elucidate the neurochemical processes in the basal ganglia by mathematical modelling. The correlation between neurochemistry and electrophysiology has been used to construct a dynamical system based on the basal ganglia’s network structure. Mathematical models were constructed for different physical scales to reformulate the neurochemical and electrophysiological behaviour from synapses up to multi-compartment systems. Transformation functions have been developed to transit between the different scales. We show through numerical simulations that this network produces oscillations in the electrical potentials as well as in neurotransmitter concentrations. In agreement with pharmacological experiments, a parameter sensitivity analysis reveals temporary changes in the neurochemical and electrophysiological systems after single exposure to antipsychotic drugs. This behaviour states the structural stability of the system. The correlation between the neurochemical dynamics and drug-induced behaviour provides the perspective for novel neurobiological hypotheses.

Keywords Neurotransmitter dynamics · Delay differential equations · Dopamine hypothesis

1. Introduction

Pharmacological studies on the treatment of psychoses suggest that the emergence of psychotic states is directly related to the abnormal dynamical behaviour of neurotransmitter systems in basal ganglia. The basal ganglia are a parallel organised and richly interconnected, set of subcortical nuclei which pattern a functional network with other brain regions such as thalamus and cortex to modulate the signal processing in brain (Alexander et al., 1986; Carlsson, 1988). Hyperactive dopaminergic transmission and hypo-functionality of glutamate systems in the basal ganglia’s network are both substantial assertions on the role of anomalies of neurotransmitter systems in producing schizophrenic

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Fig. 1 The schematic network of the human brain (LBG-network): It includes the nuclei of basal ganglia and the limbic system as well as the operating neurotransmitter systems. Each compartment is a complex of different classes of interneurons. The internal structure of any compartment is considered in the modelling. (Color figure online.)

symptoms (Carlsson, 1988; Carlsson and Carlsson, 1990; Moghaddam and Adams, 1998; Moghaddam, 2003; Moghaddam and Krystal, 2003; Coyle, 2006). There is considerable evidence that the structure of basal ganglia in the drug-naive schizophrenic patients does not significantly differ from the controls (Shenton et al., 2001). Thus, our investigations are focused only on the coupled dynamics of the neurochemical and electrophysiological processes in the basal ganglia as a part of the extended brain network in healthy patients (Fig. 1). This novel schematic network is based only on the common anatomical knowledge on the innervations and projections of morphologically separable brain regions. We call it the limbobasaloganglionic-network or LBG-network. This network is constructed as general as possible, including the basal ganglia, the limbic system, but also important nuclei such as the raphe.¹

We restrict our considerations to the main neurotransmitter systems in the LBG-brain: glutamate, GABA, acetylcholine, dopamine, histamine, and serotonin. The concentration values of these system are estimated from micro-dialysis and in vivo dialysis studies.

The quantitative analysis of the dynamics of the basal ganglia has been done in several studies, but only restricted to electrophysiological aspects (Bevan et al., 2002; Frank, 2003; Rubin and Terman, 2002, 2004; Humphries et al., 2006; Leblois et al., 2006). In this work, we would like to point out the importance of the consideration of the neurochemical dynamics, in terms of coupling the changes of the neurotransmitter concentrations with electric activities, in the analysis of neural processes.

¹Nucleus Raphe contains high concentrations of 5-HT, which is of great importance in several neurobiological investigations.