Influence of paraquat on dopaminergic transporter in the rat brain

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Abstract: Selective toxicity of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a parkinsonism inducing compound, is well known to be related to an uptake of its active metabolite MPP⁺ into dopaminergic neurons by dopamine transporter (DAT). The aim of the present study was to examine whether paraquat, a commonly used herbicide, which is an 1-methyl-4-phenyl-pyridinium ion (MPP⁺) analogue, affects DAT in vivo in rats. Paraquat administered at a dose of 10 mg/kg ip decreased the binding of [3H]GBR 12,935 to DAT measured by quantitative autoradiography in the dorsal and ventral caudate-putamen, but not in the substantia nigra pars compacta. Moreover, this compound increased the level of 3-methoxytyramine (3-MT) and 3-MT/dopamine ratio in the anterior and posterior caudate-putamen measured by HPLC with electrochemical detection. No other alterations in the levels of dopamine and its metabolites were found in the caudate-putamen and substantia nigra. The present study seems to suggest that systemic paraquat administration affects striatal DAT and dopamine metabolism in the nigrostriatal neurons in rats which may be crucial for its neurotoxic effects on dopaminergic neurons.

Key words: Paraquat, dopamine transporter, autoradiography, dopamine turnover, Parkinson’s disease, rat

Introduction

Degeneration of dopaminergic nigrostriatal neurons localized in the substantia nigra pars compacta and a dramatic loss of dopamine in the striatum (nucleus caudatus and putamen) are the main causes of symptoms of Parkinson’s disease [5]. However, a factor which triggers degenerative process is not known, so far. In the early 1980s, a few young drug-abusers were poisoned by a home-made heroin contaminated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and rapidly developed parkinsonian symptoms which were indiscernible from symptoms of Parkinson’s disease [9]. This accident has prompted researchers to hypothesize that Parkinson’s disease may be induced by some unknown environmental compounds structurally similar to MPTP.

Paraquat (1,1’-dimethyl-4,4’-bipyridinium dichloride), a potent, widely used herbicide is an analogue...