Mini Review Open Access

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Introduction

Parkinson's disease (PD), a progressive neurodegenerative disorder, pathogenesis of which is characterized by a prominent degeneration of dopaminergic (DA-ergic) neurons in basal ganglia (striatum and substantia nigra (SN)) and a profound loss of dopamine resulting in patient motor dysfunctions [1]. The data available indicate multilateral pathogenesis of PD. Thus, the degeneration of nigrostriatal DA-ergic neurons is accompanied by alterations in the expression and functional activity of different subtypes of nicotinic acetylcholine receptors (nAChR) [2-4]. nAChRs belong to the superfamily of ligand-gated ion channels [5]. These are transmembrane proteins, composed of five homologous subunits, 18 different subunits being so far identified. Pharmacological profile of nAChR is determined by an array of subunits forming one or another receptor subtype. The cholinergic neurons represent a small percentage of the neuronal cell bodies in basal ganglia; however nAChRs are abundantly expressed in striatum and SN, occupying pre-, and extra-synaptic locations. Most of neuronal nAChRs are localized pre-synaptically on nerve terminals, have a regulatory function and are involved in the brain plasticity by modulating calcium-dependent release of different neurotransmitters including dopamine [6,7]. Acetylcholine modulates dopamine release via an interaction with multiple subtypes of nAChRs present on the

no consistent Lewy body-like formation is found [48]. On the other hand, there are great species di erences between humans and animals used to produce the models. Still the role of nAChRs in human brain is not completely understood and future studies are needed to further uncover the impact of the nicotinic cholinergic system on the human brain functioning. Recent studies of brain nAChR distribution in cognitively intact patients with early stage of PD showed an up-regulated cholinergic activity at the striatal and possibly cortical level [49]. Higher nAChR density may occur as a compensatory mechanism to maintain dopaminergic tone [50], however more detailed studies are necessary to address this hypothesis. It can be assumed that the upregulation of distinct nAChR subtypes may result in improvement of patient conditions, but the possible ways to achieve this task are still to be discovered.

Conclusion

In summary, the present review indicates involvement of di erent nAChR subtypes in the molecular pathogenesis PD. us, degeneration of nigrostriatal DA-ergic neurons in the animal PD models is accompanied by alterations in the expression level and functional activity of particular nAChR subtypes. However, some questions concerning the role of nAChRs in PD remain to be answered. In this relation animal models may shed light on the participation of speci c nAChR subtypes in mechanisms of brain plasticity and the trigger mechanism responsible for the transition from pre-symptomatic stage to symptomatic one. Furthermore, the involvement of the central and peripheral nAChRs in the manifestation of such PD symptoms as autonomic dysfunction, pain, sleep de cits and the development of

tegmental area a6ß2* receptors in mediating systemic nicotine effects on dopamine release, locomotion, and reinforcement. J Neurosci 30: 5311–5325.