Proposed Neuromorphological Mechanism of Dopamine-2 Receptor Blocker Model of Parkinsonism

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Received: ……………. February 2020
Accepted: ……………. May 2020

ABSTRACT

Haloperidol is known to induce Parkinsonism by blocking dopamine-2 receptors (D₂R). However, the mechanism in which Parkinsonism is induced is not well known. In this study, the mechanism of D₂R inhibition model of Parkinsonism was proposed via neuromorphological findings observed in primary motor cortex and dorsal striatum. Sixteen female Wistar rats with average weight of 150 g were distributed into 4 groups (NS and -D₂I, -D₂II, -D₂III). Parkinsonism was induced using 5 mg/kg, 10 mg/kg and 15 mg/kg of haloperidol for 21 days. Parkinsonism was accessed with the rotarod and parallel bar. Primary motor cortex (M1) and dorsal striatum (CPu) were processed and stained using haematoxylin and eosin (H&E) and Nissl stains. The density of Nissl bodies was examined with ImageJ software version 1.46. Data was analysed by one way analysis of variance and significant level was set at p ≤ 0.05. The results showed that prolong inhibition of D₂R induces Parkinsonism by progressive deterioration of nuclear components, displacement and extrusion of nucleus leading to intracytoplasmic vacuoles in Betz cells of M1. This was projected to be associated with membrane damage. Neurofibrils were proposed to be lost following the numerous shrunken perikaryons observed in M1 and CPu. 70.6% of Nissl bodies were lost to high dose of haloperidol, this was purported to cause decline in protein synthesis and mitochondrial functions leading to decrease in synaptic plasticity and resulting in Parkinsonism.

Key words: Haloperidol; Parkinsonism; Dopamine-2 receptor; Histology; Nissl bodies

INTRODUCTION

Neuroleptics are known to have strong affinity for different subtypes of dopamine receptors (Mauri et al. 2014). Studies have shown that dopamine receptors have higher affinity for neuroleptics than dopamine (Howes et al. 2009; Berke 2018). For this reason, anti-psychotics binds to dopamine receptors even better than dopamine and without triggering G-protein. Binding of anti-psychotics to dopamine receptor disables dopamine from binding to its receptive site (Howes et al. 2009; Peng et al. 2016). The therapeutic action of anti-psychotics is their ability to bind to dopamine receptors without generating action potentials by opening ion channels (Lee et al. 2004; Lieberman et al. 2016). Anti-psychotic drugs alter dopaminergic neurotransmission system at both presynaptic and postsynaptic neuron level because dopamine-2 receptors are present on postsynaptic membrane, soma, dendrites and nerve terminals of presynaptic neurons (Vallone

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