

Review

Hypothesis: A promising effect of 5-HT_{1A} receptor agonists in alleviating motor symptoms of Parkinson's disease

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Parkinson's disease (PD) is a disease caused by degeneration of dopaminergic neurons of substantia nigra, pars compacta. The fact that serotonergic system is also involved in PD has been raised from previous studies. Drugs that have effect on 5-HT_{1A} receptors of basal ganglia might inhibit and facilitate serotonin and dopamine release, respectively. Augmentation of 5-HT_{1A} agonists (e.g., buspirone) to anti-parkinsonian and neuroleptic drugs (D2 receptor blockers) may increase efficiency of anti-parkinsonian drugs and may also prevent motor complications induced by neuroleptic drugs.

Key words: 5-HT_{1A} receptor, motor symptom, Parkinson disease.

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disease occurring approximately 1% of population over the age of 50 years. Its most prominent symptoms are tremor, muscle stiffness and bradykinesia. Some non-motor symptoms such as cognitive impairment, anxiety and depression usually coexist - comorbid. The disease is accompanied by preferential loss of dopaminergic neurons of the substantia nigra pars compacta (SNc) (Scholtissen et al., 2006).

However, other neurotransmitters such as serotonin are also involved in the neurobiology of PD (Miyawaki et al., 1997). There are some reports stating that 5-HT exerts an inhibitory effect on striatal dopamine (DA) release (De Deurwaerdere et al., 2004). 5-HT_{1A} receptors are widely distributed throughout the basal ganglia (Vollenweider et al., 1999).

They are located in dorsal raphe neurons with efferents to the striatum, and are also localized on cortical neurons sending glutamatergic projections to the basal ganglia (Knobelmann et al., 2000). Recent studies have shown that 5-HT_{1A} receptor stimulation represented antiparkinsonian effects in 6-OHDA (6-hydroxydopamine) lesioned rats (Dupre et al., 2007; Mignon and Wolf, 2007; Nayebi et al., 2010).

The findings of a clinical study showed that 5-HT_{1A} receptor stimulation in levodopa-treated parkinsonian patients can ameliorate motor fluctuations and dyskinesias (Bara-Jimenez et al., 2005). This effect is most likely caused by the increase in 5-HT_{1A} receptor activation, resulting in an inhibition of serotonin release (Riad et al., 2000). Stimulation of 5-HT_{1A} receptor is associated with an increase in dopamine turn-over (Hamon et al., 1988) and release (Ichikawa and Meltzer, 1999) from various brain regions, suggesting that 5-HT_{1A} agonists might have potential therapeutic value in the treatment of PD.

This hypothesis is supported by the finding that 5-HT_{1A} agonists can facilitate dopamine release in the striatum (Benlucif and Galloway, 1991). Therefore, adjuvant therapy with 5-HT_{1A} receptor partial agonists such as buspirone in addition to being effective in reducing symptoms of anxiety probably will be able to decrease movement complications of PD as well as neuroleptic drugs (D2 receptor blockers).

According to the above information, 5-HT_{1A} receptor agonists may decrease release of serotonin from dorsal raphe nucleus neurons and subsequently facilitate striatal dopamine release. We suggest that 5-HT_{1A} receptor agonists may have beneficial effect on treating some motor complications of PD disease and motor disorders induced by neuroleptic drugs (e.g. haloperidol). However, further preclinical and clinical investigations should be carried out to test their usefulness in diminishing motor disorders of PD.

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