

# Does Smoking Benefit Parkinson's Disease and Schizophrenia through Wallerian Degeneration of the Habenula?



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## Abstract

Smoking appears to reduce the risk of Parkinson's and reduce symptoms of schizophrenia. The habenula is a brain region which is implicated in both these conditions. Smoking or nicotine treatment appears to cause Wallerian degeneration of the habenula, which may be one way in which a benefit occurs in the above disorders

**Keywords:** Symptoms; Schizophrenia; Nicotine treatment; Cigarettes; Neuromodulator systems; Dopaminergic neurons; Parkinson's disease; Nicotine; Discussion

## Mini Review

### Smoking benefits Parkinson's and schizophrenia

Although smoking is well known to cause a range of life-threatening diseases there are two notable anomalies Parkinson's disease and schizophrenia. Smoking has long been known to reduce the risk of Parkinson's disease. Compelling evidence from over 60 epidemiological studies has demonstrated this [1,2]. Smoking reduces olfactory dysfunction in Parkinson's and there seems to be a greater decrease in risk when combined with a moderate intake of alcohol or caffeine [3]. Conversely ease of quitting cigarettes seems to be an early indicator of the onset of Parkinson's [4]. At present, the mechanism by which smoking protects against Parkinson's is unclear. Smoking also appears to benefit sufferers of schizophrenia. Most people (70-80%) with schizophrenia smoke. While it has been suggested that schizophrenia and smoking may be co-morbidities [5] cigarettes appear to improve psychiatric symptoms, including negative and cognitive symptoms suggesting self-medication [6]. Again, here, the mechanism of the benefit is unclear.

### The habenula is implicated in Parkinson's and schizophrenia

The habenula is a small cell mass at the posterior-dorsal-medial end of the thalamus and is conserved in all vertebrates [7].

It inhibits dopamine-releasing neurons through neuromodulator systems and thus suppresses motor behavior when an animal fails to obtain a reward or anticipates an aversive outcome [8]. Thus, here is a possible link with Parkinson's which is due to dysfunction of dopaminergic neurons and associated with dysfunctional motor behavior [9]. Indeed, inhibition of the lateral habenula improves L-DOPA-induced dyskinesia [10] and lesion of the lateral habenula reduces apomorphine-induced rotational behavior in a rat model of Parkinson's disease [11]. The habenula is involved in social interaction. It is activated after 24 hours of social isolation in adolescent rats and subsequent social play reduces neural activity in the medial part of the lateral habenula [12]. In patients with schizophrenia there was found to be an almost 6-fold increase in calcification of the habenula as determined through Computed Tomography (CT) [13]. Thus, there is evidence for a link between both Parkinson's disease and schizophrenia, and the habenula.

### The habenula and nicotine-induced wallerian degeneration

So why should smoking improve quality of life in for sufferers of Parkinson's disease and schizophrenia? Wallerian degeneration is a process whereby axonal injury at a defined site and time simultaneously affects all axons. During this process the distal portions of injured axons fragment after a predictable latent

phase which lasts for 36-44 hours. It is possible that Wallerian degeneration evolved to prevent the spread of viruses through the nervous system. Nicotine produces selective Wallerian degeneration in the medial habenula and fasciculus retroflexus [14]. Thus, smoking may have a similar effect to lesions of the habenula, which show promise for the treatment of Parkinson's disease. Since activity of and structural changes to the habenula are linked to schizophrenia, the nicotine-induced lesion of the habenula may explain the benefits of smoking here as well.

### Future Directions

If smoking does benefit some as outlined above, it has major ramifications for the treatment of Parkinson's disease and schizophrenia, and the approach of society to smoking. It has yet to be determined whether lesions of the habenula reduce symptoms of schizophrenia possibly because the development of reliable mice models of the disease is a work in progress [15]. There is certainly evidence that this could be useful in treating Parkinson's disease. Nicotine patches may be an effective treatment for both disorders and maybe the medical profession should start recommending this therapy. It is yet to be shown that nicotine alone produces the positive effects of smoking for Parkinson's disease and schizophrenia, however. In addition, nicotine patches supply considerably less nicotine than that from the cigarettes of schizophrenia sufferers.

While smoking is clearly detrimental to many aspects of health, indeed deadly, many with schizophrenia still choose to smoke. These people often struggle to find and hold down a job and are often dependent upon government pensions and the support of relatives, financially. Thus, heavily taxing tobacco products is hurting those least able to afford it. Perhaps there could be a discussion about whether those with a confirmed high risk of developing Parkinson's disease (through genetic screening), and those with schizophrenia and related disorders, could be enabled to access low-taxed tobacco products, or nicotine patches for a period, enabling them to live with dignity while they sort out the rest of their lives [16]. Tobacco and nicotine use could be overseen by healthcare professionals to reduce harmful side-effects aiming at long term cessation. Even more useful would be research programs designed to pinpoint just how it is cigarettes benefit Parkinson's and schizophrenia.

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