Smoking and Parkinson disease

Where there is smoke there may not be fire

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Several case-control studies have demonstrated an inverse relationship between the presence of Parkinson disease (PD) and smoking cigarettes.[1,2] The risk of PD in someone who has ever smoked is about half of that of a nonsmoker.[3,4] These observations prompted some to hypothesize that smoking could protect against the development of PD. The lay press popularized this notion, and the idea inspired studies to test whether nicotine can slow disease progression.

Alternatively, the pharmacologic action of nicotine suggests a different mechanism of action. Nicotine, a rewarding drug, increases extracellular dopamine concentrations in the nucleus accumbens and produces stimulation of behavior in animals.[5] Patients with PD have fewer available nicotinic acetylcholine receptors in the brain[6] with reductions of up to 50% in the frontal and temporal areas involved in learning, memory, and execution of stimulus-seeking behaviors. Thus, patients with PD may feel less nicotine-mediated "reward" from stimulus-seeking behaviors or from cigarettes, which may make it easier for those with PD to quit smoking. This may explain an apparent neuroprotective effect of cigarettes in PD, whereas the actual underlying physiologic response may permit those with PD to quit smoking more easily than those without PD. In support of this reduced reward response, patients with PD compared to age-matched controls show fewer stimulus-seeking behaviors, such as less coffee drinking and less alcohol consumption.[1,4,7] Clarification of the precise role of exposure to cigarette smoke for either progression of PD or nicotinic response in those with PD has important implications for development of therapeutic strategies.

The report by Ritz et al.[8] in this issue examines the possibility that quitting cigarettes might be a marker for PD onset, rather than smoking itself having a neuroprotective effect. The strengths of this study include (1) data acquisition from a large Danish registry (1,808 patients with PD and 1,876 controls); (2) a case-control study design, and (3) examination of nicotine substitute use, along with the use of cigarettes, caffeinated drinks, and alcohol. As previously reported, the authors found an inverse relationship between the diagnosis of PD and cigarette smoking.[1,2] They also discovered that among former smokers who had quit, those who had extreme difficulty quitting had the lowest risk of PD. Reduced responsiveness to nicotine in patients with PD could account for this observation, as has been suggested by others.[6] Therefore, ease of smoking cessation could be a nonmotor aspect of early PD that is similar to olfactory dysfunction, REM sleep disorder, or constipation, as described in the review by Chaudhuri et al.[9] Alternatively, a lower lifelong risk of smoking in those with PD compared with controls (see table 1) could be an underlying mechanism accounting for differences in smoking behavior between patients with PD and controls. This latter hypothesis could not be tested in the study by Ritz et al.[8]

Nevertheless, this study suggests several important conclusions. One is that practicing neurologists should not recommend cigarette use or nicotine substitutes to delay onset of PD. No clinical study data support this, and the rationale may be faulty. Further development of nicotine agonist therapy for PD may not be justified. Finally, physicians, including neurologists, should encourage their patients to stop smoking, because cigarette smoking is a significant risk factor for stroke.[10] All of the past smoke about PD may have been a misinterpretation of the data. Where there is smoke, there may not be fire. That is the key message from Ritz et al.[8]

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