Correspondence

Reduced Risk for Parkinson's Disease in Smokers

The possibility that the incidence of Parkinson's disease may be reduced by smoking has received widespread recent publicity. This may seem a bizarre idea, but several epidemiological studies, from countries as diverse as Italy,[1] China,[2] and the USA[3] have provided supporting evidence for it. Indeed, it is possible that stopping smoking is a risk factor for Parkinsonism.[4]

In an article recently published in this journal, the current author[5] suggested that Parkinsonism is elevated in regions where glaciation has removed iodine from the soils. It was argued further that exposure to such an iodine deficiency during gestation and infancy increased the number of dopamine receptors in the brain and so raised susceptibility to dopamine oxidation. Such dopamine deficiency is known to cause elevated cytotoxic glutamate levels. The author termed this process the iodine-dopachrome-glutamate hypothesis.

If this hypothesis is correct and smoking really does protect against Parkinson's disease, there must be some substance(s) in cigarette smoke that mitigates glutamate's neurotoxic effects. The most logical candidate for this role appears to be nicotine. Maggio and colleagues,[6] for example, have shown that nicotine prevents experimental Parkinsonism in rodents. Chronic nicotine infusion also improves rat memory. These effects seem to occur because nicotine augments dopaminergic neurotransmission[8-10] apparently increasing dopamine levels and reducing dopamine utilization in the substantia nigra and forebrain.[11]

In addition, Shimohama and colleagues[12] have shown that nicotinic cholinergic receptor stimulation induces neuroprotection against glutamate cytotoxicity because it inhibits the formation of nitric oxide. If, as this author has suggested, the toxicity of glutamate is the key to the brain degeneration seen in Parkinsonism, it is hardly surprising smoking, therefore, is protective against the disease.

The purpose of this letter is not to promote smoking in an effort to reduce glutamate and hence Parkinson's disease. Nicotine, however, can be obtained in other ways. It has been shown, for example, that dermal plasters (containing nicotine) can perhaps improve short-term memory in Alzheimer's patients[13] and may, therefore, also be an option for the treatment of Parkinsonism.

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References

1. Smargiassi A, Mutti A, De Rosa A; De Palma G, Negrotti A, Calzetti S: A case control study of occupational and environmental risk factors for Parkinson's disease in the Emilia-Romagna region of Italy. *Neurotoxicology,* 1998;19(44-5): 709-12.
2. Chan DK, Woo J, Ho SC, Pang, CP, Law LK, Ng PW, Hung WT, Kwok T, Hui E, Orr Y, Leung MF, Kay R. Genetic and environmental risk factors for Parkinson's disease in a Chinese population. *J Neurol Neurosurg Psychiat,* 1998; 65(5): 781-4.
3. Sasco AJ, Paffenbarger RS Jr: Smoking and Parkinson's disease. *Epidemiology,* 1990;1(6): 460-5.
4. Gorell JK Rybicki BA, Johnson CC, Peterson EL: Smoking and Parkinson's disease: a dose-response relationship. *Neurology,* 1999; 52(l): 115-9.
5. Foster HD: Parkinson's disease, multiple sclerosis and amyotrophic lateral sclerosis: the iodine-dopachrome-glutamate hypothesis. *J Orthomol Med,*1999; 14: 128-136.
6. Maggio R, Riva M, Vaglini F, Fornai F, Molteni R, Armogida M, Racagni G, Corsin R: Nicotine prevents experiental parkinsonism in rodents and induces striatal increases of neurotrophic factors. *J Neurochem,* 1998; 71(6): 2439-46.
7. Levin ED, Kim P, Meray R. Chronic nicotine working and reference memory effects in the 16-arm radial maze: interactions with D I agonist and antagonist drugs. *Psycho-pharmacol,* (Berlin)1996; 127(l): 25-30.
8. Russ RD. 1998. Acute nicotine pretreatment augments dopaminergic pulmonary vasodilation. *Proc Soc Exp Biol Med,* 1998; 291(1): 69-76.

9. Kubo T, Amano IL Kurahashi K, Misu Y: Nicotine-induced regional changes in brain noradrenaline and dopamine turnover in rats. *J Pharmacobiodyn,* 1989; 12 (2): 107-12.
10. Sershen IL Hashim A, Harsing L, Lajtha A: Chronic nicotine-induced changes in dopaminergic system: effects on behavioural response to dopamine agonist. *Pharmacol Biochem Behav,* 1991; 39(2): 545-7.
11. Fuxe K, Janson AK Jansson A, Andersson K, Eneroth P, Agnati LF: Naunyn Schmiedebergs *Arch Pharmacol,* 1991; 341(3): 171-81.
12. Shimohama S, Akaike A, Kimura 1:Nicotine-induced protection against glutamate cytotoxicity. Nicotinic cholinergic receptor-mediated inhibition of nitric oxide formation. *Ann NY Acad Sci,* 1996; 777: 3 56-361.
13. Snaedal J, Johannesson T, Jonsson JE, Gylfadottir G: The effects of nicotine in dermal plaster on cognitive functions in patients with Alzheimer's disease. *Dementia,* 1996; 7(l): 47-52.