Milk consumption and the risk of nigral degeneration

In the era of genetic research for neurodegenerative diseases, less attention has been paid to epidemiologists’ search for potential environmental risk factors for Parkinson disease (PD). Epidemiologic evidence suggests that cigarette smoking is associated with about 50% lower risk of PD and exposure to certain pesticides such as rotenone and paraquat is associated with doubled risk. Recent studies also suggest that higher concentration of serum urate, an endogenous antioxidant, is associated with a lower risk of PD. Compared with these observations, another epidemiologic finding has been largely neglected. Several prospective studies, including the Honolulu-Asia Aging Study (HAAS), have reported that higher consumption of dairy products, or milk alone, was associated with higher risk for PD.

A new study in the current issue of Neurology® may offer a potential clue that links these seemingly unrelated epidemiologic findings. Using data from the HAAS, Abbott et al. report that consumption of more than 2 cups of milk per day in midlife was associated with approximately 40% fewer neurons in the ventrolateral, ventromedial, and dorsolateral quadrants of the substantia nigra, as measured at autopsy, among individuals who were followed longitudinally and never developed PD. This association was observed only among nonsmokers. Higher milk consumption was also associated with the detection of heptachlor epoxide in the brains of decedents without PD, again only in nonsmokers. Heptachlor is an organochlorine insecticide that had been used in the Hawaii pineapple industry for decades prior to 1980. Contamination of milk with heptachlor, probably via cattle feed, was identified in Hawaii in 1981–1982 as part of routine state inspections. No one knows for sure how long or widespread milk contamination was present before it was detected.

The current study makes heptachlor contamination a plausible culprit for higher PD risk among frequent milk drinkers in HAAS. This study may not offer a good explanation for the association of milk or dairy consumption and PD in other cohorts, where evidence of milk contamination is lacking. Another potential explanation for the milk and PD relationship may be that milk consumption lowers plasma urate, which in turn leads to a higher risk for PD over time. However, serum uric acid concentration was not related to substantia nigra neuronal density in the current study.

The HAAS was launched in 1991 as an extension of the Honolulu Heart Program (HHP), which enrolled 8,006 Japanese American men, aged 45–68 years, from 1965 to 1968. A dietary assessment was conducted at HHP enrollment using a 24-hour dietary recall. The mean age of the study population at the time of the dietary assessment was 51.4 ± 4.9 years. Death occurred on average at age 85.7 ± 5.2 years, approximately 30 years after the assessment. Neuropathologic assessment was conducted blinded to clinical information. The HAAS has an exceedingly long follow-up that allows examinations of midlife risk factors for late-life neurodegenerative diseases. More importantly, the rich data collection over time on diet, lifestyle, environmental factors, prodromal symptoms (e.g., sense of smell), and brain pathology has enabled the HAAS to make a number of important contributions to our understanding of the natural history and etiology of PD.

Although the results are exciting, they should be interpreted within context. First, the accelerated neuron loss was observed only among nonsmokers who drank more than 2 cups of milk per day. The sample size is relatively small (n = 12 for this category), and there was minimal or no neuron loss for nonsmokers who drank less than 2 cups of milk per day. Therefore the possibility of chance association cannot be excluded. In addition, milk consumption was assessed only once at enrollment, and we have to assume that this measurement represented participants’ dietary habits over time. Further, it is unclear whether milk consumption is related to incidental Lewy bodies or prodromal symptoms, such as the sense of smell, among individuals without clinical PD. Affirmative findings would strengthen the authors’ claim that
milk consumption is an early to midlife risk factor for PD. Finally, although contamination of milk with heptachlor is a reasonable explanation for the findings, the study did not directly show that the brain heptachlor was from milk rather than from other sources.

Nevertheless, this study sets an excellent example of how epidemiologic studies can contribute to the search for causal mechanisms underlying PD. It further challenges others to adapt existing cohorts with extensive nongenetic data for PD research, a cost-effective approach. It also challenges ongoing large clinical studies of PD to collect environmental data so they are better able in the future to address critical questions such as these. Brain donation should also be considered in these valuable cohorts. This life-course approach to unveiling the complicated process of neurodegeneration should be encouraged.

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REFERENCES