constituent of solanaceous plants other than nicotine that affect PD risk. Although plant viruses are not believed to replicate in animals or humans, they may induce immune responses, which may contribute to pathogenesis or disease prevention.[6] The role of plant viruses in human disease deserves further consideration.

Potential Conflicts of Interest

Nothing to report.

Department of Neurology, University of Louisville School of Medicine, Louisville, KY

References

1. Searles Nielsen S, Franklin GM, Longstreth WT, et al. Nicotine from edible Solanaceae and risk of Parkinson disease. Ann Neurol 2013; 74:472–477.
2. Liu R, Vaishnav RA, Roberts AM, Friedland RP. Humans have antibodies against a plant virus: evidence from tobacco mosaic virus. PLoS One 2013;8:e60621.
3. Hu Q, Niu Y, Zhang K, et al. Virus-derived transgenes expressing hairpin RNA give immunity to tobacco mosaic virus and cucumber mosaic virus. Virol J 2011;8:41.
4. Balique F, Colson P, Raoult D. Tobacco mosaic virus in cigarettes and saliva of smokers. J Clin Virol 2012;55:374–376.
5. Schapira AH. Mitochondrial diseases. Lancet 2012;379:1825–1834.
6. Friedland RP, Tedesco JM, Wilson AC, et al. Antibodies to potato virus Y bind the amyloid beta peptide: immunohistochemical and NMR studies. J Biol Chem 2008;283:22550–22556.

DOI: 10.1002/ana.24041

Reply

Susan Searles Nielsen, PhD,[1] Gary M. Franklin, MD, MPH,[1] W. T. Longstreth Jr, MD, MPH,[2,3] Phillip D. Swanson, MD, PhD,[2] Harvey Checkoway, PhD[4]

Dr Liu and colleagues propose an interesting hypothesis in response to our finding that pepper consumption is associated with a reduced risk of Parkinson disease.[1] Although we had examined this association because tobacco family (*Solanaceae*) edibles contain nicotine, which appears neuroprotective in animal models, we noted that other shared constituents of tobacco and peppers might also be relevant. Among the candidates we mentioned were anatabine and capsaicin. Like nicotine, they readily cross the blood–brain barrier[2,3] and then presumably reach dopaminergic neurons in the substantia nigra.

A thorough examination will indeed include other possible agents. These include tobacco mosaic virus (TMV) as these authors suggest, although our data do not fully support it. Edible cucumbers and other *Cucurbitaceae* for which we have data (cantaloupe, zucchini, and yellow winter squash) are susceptible to TMV,[4] but their combined consumption is not associated with Parkinson disease (relative risk = 1.00, 95% confidence interval = 0.72–1.38 per time per day, adjusted for *Solanaceae*, other vegetables, age, sex, race/ethnicity, tobacco use, and caffeine, not shown). In addition, the smoking–TMV antibody association recently observed by Liu et al[5] was present in African Americans but not Caucasians, and overall, 30% of the smokers but none of the nonsmokers worked with tobacco products. Even in the absence of confounding by occupational TMV exposure, it is not yet clear that these intriguing results[5] apply to our largely Caucasian[1] population (or pepper eaters compared to noneaters). We look forward to continued research by this group and others to explore this and the many other possible alternative hypotheses for the inverse association between Parkinson disease and both tobacco use and consumption of peppers.

Potential Conflicts of Interest

S.S.N., G.M.F., W.T.L., P.D.S., H.C.: grants/grants pending, NIH.

[1]*Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA*
[2]*Department of Neurology, University of Washington, Seattle, WA*
[3]*Department of Epidemiology, University of Washington, Seattle, WA*
[4]*Department of Family and Preventive Medicine, University of California, San Diego, La Jolla, CA*

References

1. Searles Nielsen S, Franklin GM, Longstreth WT Jr, et al. Nicotine from edible *Solanaceae* and risk of Parkinson disease. Ann Neurol 2013;74:472–477.
2. Paris D, Beaulieu-Abdelahad D, Bachmeier C, et al. Anatabine lowers Alzheimer's Aβ production in vitro and in vivo. Eur J Pharmacol 2011;670:384–391.
3. Güler AD, Rainwater A, Parker JG, et al. Transient activation of specific neurons in mice by selective expression of the capsaicin receptor. Nat Commun 2012;3:746.
4. Brunt AA, Crabtree K, Dallwitz MJ, et al, eds. Plant viruses online: descriptions and lists from the VIDE database. 1996 onwards. Available at: http://pvo.bio-mirror.cn/refs.htm Accessed August 17, 2013.
5. Liu R, Vaishnav RA, Roberts AM, Friedland RP. Humans have antibodies against a plant virus: evidence from tobacco mosaic virus. PLoS One 2013;8:e60621.

DOI: 10.1002/ana.24033

Treatment of Intractable Epilepsy in Tuberous Sclerosis Complex with Everolimus Is Not Yet Evidence-Based

Iris E. Overwater, MSc, André B. Rietman, MSc, Ype Elgersma, PhD, Marie-Claire Y. de Wit, MD, PhD

We read with great interest the article by Krueger et al,[1] reporting the outcome of their clinical trial of patients with tuberous sclerosis complex (TSC) and intractable epilepsy. The authors