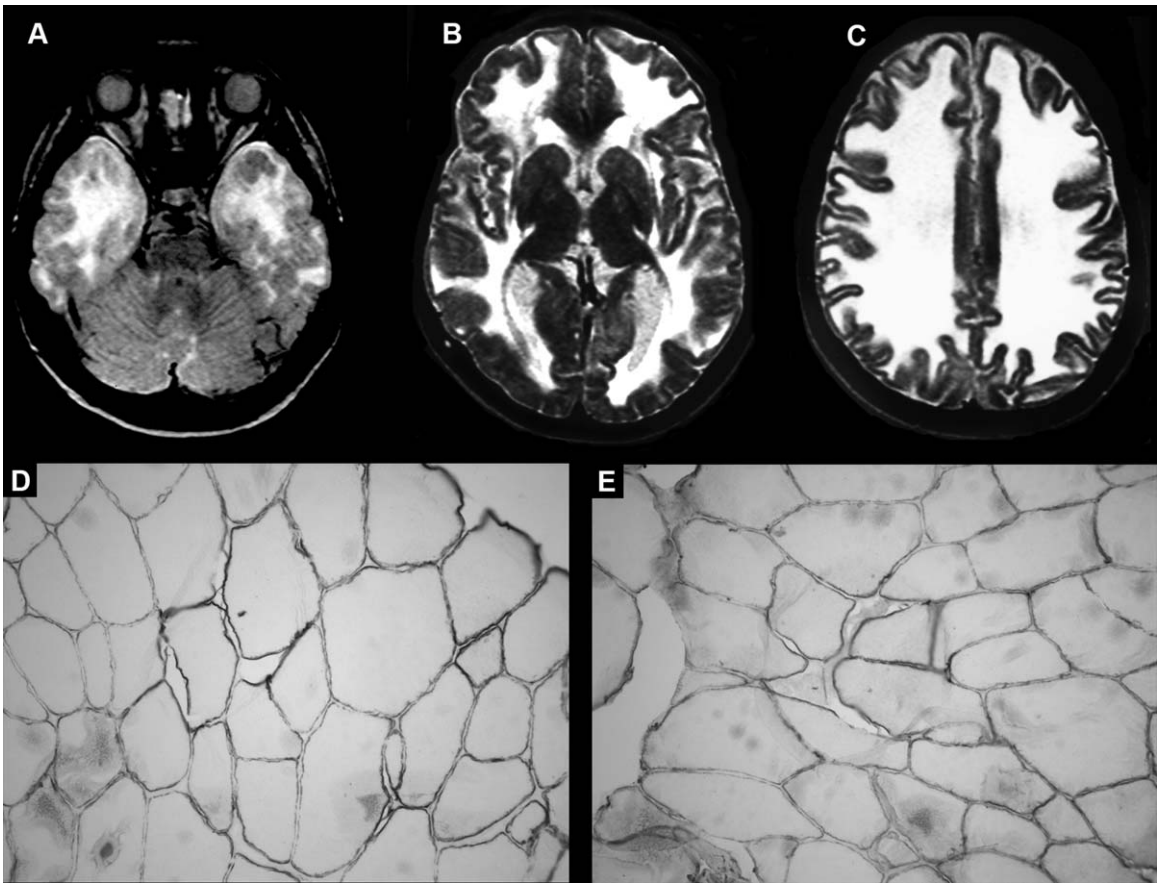

FIGURE 1. Brain MRI **(A–C)** shows diffuse cerebral white matter abnormalities with mild swelling of the abnormal white matter **(C)**. The cerebellar white matter **(A)** and corpus callosum **(B)** are spared. Immunocytochemical labeling of spectrin as control and laminin-α2 in the muscle biopsy (collected in 2001) from a patient **(D, E)**. Note the normal level of laminin α2 expression using an antibody directed against merosin (clone Mer2/22B2; Novocastra) **(E)** as compared with the control **(D)**. Original magnification: $\times$125.

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ULNAR NEUROPATHY AT THE ELBOW

I read with interest the study by Frost et al.[1] and the associated editorial[2] regarding smoking and ulnar neuropathy at the elbow (UNE). The main findings suggest that UNE is a disease of the left upper limb in middle aged men who smoke. Furthermore, the likelihood of UNE increases with greater tobacco exposure. We found nearly identical results in 2004 and 2009 using smaller numbers of subjects and a population from the United States rather than Denmark.[3,4] We also found an exposure-response effect in that pack-years of smoking inversely correlated with the ulnar compound muscle action potential amplitude when stimulating above the elbow. This finding was present for ever-smokers and

even remote smokers, who were defined as having discontinued smoking 10 or more years before the study.

I offer 2 points for discussion. The first is that my primary motivation for investigating the relationship between UNE and tobacco use relates to having been an expert witness for a case of bilateral severe UNE in a middle-aged man who performed light manual labor. His examination revealed that, although his hand intrinsic muscle atrophy was impressive, the most prominent finding was the intense tobacco staining of both hands. The patient confirmed that he smoked 3–4 packs of cigarettes per day and had done so for many years. My suspicion at that time was that the patient's smoking was primarily responsible for the UNE; however, the literature offered nothing to support this conclusion. I reluctantly concluded that the man's work habits were primarily to blame for his UNE. Since that time, research suggests that extreme tobacco use is more likely the cause. Although the combined works provide another reason not to smoke, it is uncertain whether the public will be swayed by the risk of a numb hand if cancer, vascular disease, premature aging, and lung disease have not done so. However, the impact on Workers' Compensation cases may be significant, as UNE is very likely related to smoking as much or more as it is to repetitive upper limb use.

A second point concerns the pathophysiology of UNE in relation to smoking. The mechanical demands placed on the ulnar nerve are unique. The elbow is the only joint taken routinely through 130 degrees of motion, a maneuver that produces substantial ulnar nerve stretch and recoil. Although the nerve itself may not become less elastic with smoking, the arteries and arterioles which serve the nerve in the region may. In support of this hypothesis, nicotine impairs dilation of large peripheral arteries and resistance arterioles and increases myointimal hyperplasia.[5,6] Should these changes diminish the ability of the intraneural arteries to stretch and recoil, then inefficient or incomplete repair following trauma is likely. This mechanism would explain the effect of smoking on ulnar nerve function even when it occurred 10 or more years before patient examination.

In closing, I offer the authors my congratulations on their work which more convincingly demonstrates what we had suspected.

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REPLY: LIFESTYLE RISK FACTORS FOR ULNAR NEUROPATHY AND ULNAR NEUROPATHY-LIKE SYMPTOMS

We thank Dr. Richardson for his interest in and points for discussion of our recently published work on lifestyle and risk of ulnar neuropathy.[1]

Two important points for discussion are raised. The first concerns causal inference in individual cases of ulnar neuropathy, e.g., in connection with Workers' Compensation claims. In an earlier report, we identified work with high hand force requirements as a strong risk factor for ulnar neuropathy, while repetitive work was not a risk factor.[2] In a case of nontraumatic ulnar neuropathy in a patient who has both been smoking and exposed to forceful work, the neuropathy may have been caused by either smoking or occupational exposure, combinations of these factors, or unknown factors, and it is not possible to reach a causal conclusion. However, as suggested by Richardson, knowledge of risk factors may help to judge which of these possibilities is more likely. In our opinion, knowledge of risk factors is also important to identify potential preventive measures, but as pointed out by Richardson, the public may not decide to stop smoking because of a risk of ulnar neuropathy. A relatively strong incentive to stop smoking may occur later in life when the patient has developed symptoms, as we have also found that smoking is a negative prognostic factor among patients who have developed symptoms of ulnar neuropathy.[3]

The second point raised concerns the pathophysiology of ulnar neuropathy in relation to smoking. Richardson suggests mechanisms which include mechanical stretch/recoil of the nerve with elbow movement in combination with smoking, which may damage intraneural arteries so that the nerve becomes more vulnerable to occupational exposure. We think that the question about pathophysiology is relevant, and we welcome studies which explore hypotheses of possible links between smoking, nerve stretch/recoil (as well as nerve compression) and the development of ulnar neuropathy.

Once again, we thank Dr. Richardson for the interesting points for discussion of our work.

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