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The Future of Statins: Essential Tremor?

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Essential tremor (ET) is a progressive condition that is clinically heterogeneous, as it may be associated with a spectrum of clinical features with both motor and nonmotor elements [1, 2]. The risk and etiological factors for ET have not been clearly established; however, recent research suggests that several environmental factors [3], including neurotoxins (e.g. lead and harmaline) [4], cigarette smoking [5, 6], high levels of ethanol consumption [7], shorter sleep duration [8], or head trauma [9] may play an etiological role in ET, whereas other studies demonstrate genetic causes [10]. These findings may not be mutually exclusive; indeed, environmental factors might work in concert with underlying susceptibility genotypes [11]. Although the biological mechanisms that underlie ET are not completely understood, there is an open and active dialogue in the medical community as to whether ET is a neurodegenerative disease, with considerable evidence in favor of this [12, 13]. Published studies have demonstrated that oxidative stress plays a central role in a common pathophysiology of neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease (PD) [14]. In addition, a number of authors have reviewed the role of statins in these 2 neurodegenerative diseases [15, 16]. Among the recognized pleiotropic effects of statins are their anti-inflammatory and antithrombotic activities, as well as their antioxidant, profibrinolytic, or antiproliferative properties [15].

Despite the links between ET and other neurodegenerative diseases [17–20], and an increasing appreciation that ET itself may be a neurodegenerative disease [13], an association between statin use and the odds of ET had not been formally assessed.

In this issue of *Neuroepidemiology*, Shalaby and Louis [21] probe whether statin use differed in ET cases vs. controls and PD cases vs. controls. The results confirm a marginally significant inverse association between PD and statin use. In addition, although in primary analyses there was no evidence that statin use was protective in ET, there was an inverse association in analyses that assessed longer-term use of statins.

The study had several strengths, including the large sample size, the fact that cases had all received a diagnosis of ET or PD that was carefully assigned by a movement disorder neurologist, the inclusion of a disease group (PD) with a well-known inverse

association with statin use, and a well thought-out approach to the statistical analyses. The study was not without limitations. As noted by the authors, this was a case-control study rather than a cohort study, and hence, this precludes direct inferences about causality in the relationship between statin use and neurological diseases. Second, statin use was assessed by self-report, rather than pharmacy records. Finally, the study was powered to detect a doubling in the proportion of statin users across diagnostic groups; subtler group differences might not have been detected. The authors were aware of the limitations and, to their credit, provided a thoughtful discussion of these issues, indicating why they thought these issues were of less concern in this study.

Leaving aside issues of strengths and limitations, the study suggests for the first time that there is an inverse association between longer-term use of statins and ET and this is an important discovery. A better understanding of the anatomical and pathological bases of this disorder will lead to advances in the development of more effective symptomatic treatments, and also possibly neuroprotective treatments.

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