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Reply: Plasma cholesterol and Parkinson's disease: is the puzzle only apparent?

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Our first publication in *Movement Disorders*¹ reporting an “association” between lower cholesterol and Parkinson’s disease (PD) noted the limitations of case-control analysis. It cautioned the readers that “*we could not make a causal inference between LDL-C, and/or statin use and risk of PD*”¹. To reduce the possibility of reverse causality, we subsequently studied a prospective cohort² and found a similar association. Similar findings were also reported in two other prospective cohorts^{3,4}. Interestingly, Scigliano and colleagues themselves found “*the association of untreated IPD with reduced vascular diseases risk(s)*” including higher cholesterol⁵. There has been one inconsistent report⁶ in which the cases were identified from a National Insurance Register that entitles patients to medication free of charge.

Therefore, the overall evidence to date favors an association between higher cholesterol and lower PD occurrence. The three prospective cohorts cited above^{2–4} have generated some useful insight on PD etiology. Rigorous diagnostic criteria⁷ were applied in the Honolulu Asia Aging Study, and of 25 cases that had autopsy, PD was confirmed pathologically in 21. Further, the age of onset in any study population is bounded by its age distribution. The average age at cholesterol assay in the Honolulu cohort was 77 years old², thus it is not surprising that the onset of incident cases was also higher in this cohort. Given the consistency of this association across prospective studies, it seems to us that more, not less, research should be conducted to understand the nature of this finding and its medical ramifications, if any. Thus, we disagree with Scigliano et al.’s notion that future studies should simply be abandoned. It is both inconsistent with the weight of available evidence, and contrary to the scientific method.

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