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RESPONSE to Plasma fasting cholesterol profiles and age at onset in Parkinson's Disease

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We thank Mählknecht and coauthors¹ for their interest in our study. We were interested in their findings with respect to HDL's lack of correlation with age at onset in Parkinson's disease in their cohort, as it echoes our experience with cohorts of patients other than the very early patients in the PPMI cohort. For example, we have found in the Columbia University cohort of 237 patients, with an average disease duration of 6 years, that HDL does not show a significant association with age at PD onset (two-tailed $p=0.34$ in linear regression model adjusted for age and sex). This data has not been previously published, so we are happy for this opportunity to provide it.

We suspect there may be at least two different reasons for the differences between their observations with HDL and our observations with ApoA1, one of which does correlate with age at PD onset (ApoA1), whereas the other one may or may not (HDL). First, HDL and ApoA1, while correlated with each other, are not the same. In our recent paper, we find an R^2 value of 0.8 between the two measures in 254 PPMI subjects, which is remarkably similar to the R^2 of 0.79 reported in our first ApoA1 publication² using a different measurement platform for ApoA1 and only 17 samples. If ApoA1 is the true driver behind the association with age at PD onset, then one would expect a lesser degree of association with HDL, in which signal is diluted by noise by ~20%. Second, individual cohorts differ, for reasons that are not always clear. For example, in the meta-analysis performed in our recent paper, one can see that the Columbia University cohort, unlike the other four cohorts, does not show a statistically significant association (only a trend) between age at PD onset and ApoA1 levels. This cohort-by-cohort heterogeneity was precisely the reason that we ended up evaluating 5 different cohorts, spanning >20 clinical sites and >1000 individual PD patients, to understand whether our ApoA1 association was robust enough.

With respect to the authors' point that more experimental and epidemiological studies are needed prior to consideration of ApoA1/HDL-elevating drugs as neuroprotective agents for PD, we point out two intriguing studies by Gao and coauthors³ and by Lee and colleagues⁴, both of which provide epidemiological data suggesting that statin users are less likely to develop PD. At the same time, however, we absolutely agree with Mählknecht and

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colleagues¹ that mechanistic studies are needed to determine the direction of correlation prior to embarking on clinical trials of ApoA1-elevating drugs. We hope these studies are performed, and quickly.

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References

1. Mählken P, Sprenger F, Seppi K, et al. Plasma fasting cholesterol profiles and age at onset in Parkinson's disease. *Mov. Disord.* (ahead of print).
2. Qiang JK, Wong YC, Siderowf A, et al. Plasma apolipoprotein A1 as a biomarker for parkinson's disease. *Ann Neurol.* 2013; 74:119–127. [PubMed: 23447138]
3. Gao X, Simon KC, Schwarzschild MA, Ascherio A. Prospective study of statin use and risk of Parkinson disease. *Arch Neurol.* 2012; 69:380–384. [PubMed: 22410446]
4. Lee YC, Lin CH, Wu RM, Lin MS, Lin JW, Chang CH, Lai MS. Discontinuation of statin therapy associates with Parkinson disease: A population-based study. *Neurology.* 2013; 81:410–416. [PubMed: 23884037]