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Lewy bodies in essential tremor are no different than in controls

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We are writing to respond to the recent publication entitled "The relationship between essential tremor and Parkinson's disease", authored by Thenganatt and Jankovic[1]. We have several points we would like to raise regarding the section on pathology of essential tremor (ET). In this section, the authors cite evidence published by the group at Columbia suggesting that a high percentage of ET subjects harbor Lewy Bodies (LBs), to a significantly greater degree than controls. However, when one reviews these papers carefully, as we have done in previous publications[2], one will conclude that that the prevalence of LBs in prospectively ascertained ET subjects is no greater than that found in clinically normal subjects of the same age range, where the presence of LBs is termed incidental Lewy body disease (ILBD). The authors then go on to discount our studies as flawed because 1) we studied an older age ET onset and 2) we excluded those with clinically evident PD in addition to ET. Regarding age, it is well known that the prevalence of ET, PD and ILBD increases with advancing age. However, ET, unlike PD and ILBD, often begins in young adulthood, while LBs are extremely rare at these ages. Admittedly, more neuropathological studies of young adults with ET are needed but autopsies with full neuropathological exams in this age group are infrequently done. In our studies, we have found that LBs are no more frequent in older subjects with ET than in older subjects without ET, and conversely, action tremor is not more common in subjects with ILBD than it is in older subjects without LBs [3]. We and others have also shown that subjects with ILBD have about a 50% reduction in striatal dopaminergic markers as well as anosmia, suggesting that they would have imminently developed classic motor signs of PD had they lived longer[4, 5]. If this is true, why would those harboring LBs since young adulthood not develop PD for decades or never? Alternatively, perhaps the authors speculate that longstanding ET somehow causes LB formation rather than the other way around? If so, what is the mechanism that might do this? Finally, the reason we excluded those with PD was so that it would have been possible to know whether observed LBs were due to PD or ET. Adding those with PD into our analysis would only have obscured any possible relationship between LBs and ET.

We continue to accrue autopsied cases of ET at the Arizona Study of Aging and Neurodegenerative Disorders, an IRB approved study based in Sun City, AZ. As of July

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2015, we compared 67 ET to 43 Controls with a mean age of 87 years. Neither group had parkinsonism or dementia. The frequency of ILBD was 21% in ET (14/67) and 19% (8/43) in controls, which was not significantly different.

In summary, pathological studies of the relationship between ET and PD go far to exclude, rather than support, a link between the two disorders. We acknowledge that does not completely exclude the possibility that there are genetic factors that might increase risk for both disorders in some families, however, this is likely rare given the preponderance of evidence.

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