Correspondence on Caffeine intake interacts with Asian gene variants in Parkinson's disease: author's reply

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Dear Editor,

We thank Tsai and colleagues for their interest in our study.[1] They have asked if there are biologically plausible mechanisms for the interaction between caffeine and LRRK2.

To our knowledge, the mechanistic link between the Asian LRRK2 variants and caffeine has yet to be elucidated in any experimental models. However, neuroprotection by caffeine (blocks adenosine A2A receptor) and similar compounds have been shown to be protective in animal models of Parkinson's disease (PD).[2] Two of the Asian variants are located in the WD 40 (G2385R) and COR domain (R1628P) of the LRRK2 protein, and these may disrupt protein-protein interactions, and/or kinase and GTPase activity. It is possible that the downstream effect of adenosine A2A receptor blockage somehow modulates these functions. Other postulated mechanisms could involve the neuroinflammatory and antioxidant pathways.[3] Interestingly, in a clinical study, caffeine and its metabolites have been shown to be markers of resistance to LRRK2-linked PD. Dietary caffeine was lower in PD LRRK2 carriers compared to LRRK2 controls, with significant interaction with LRRK2 mutation.[4] These are indirect corroborative evidence supporting a potential mechanistic link between LRRK2 mutations/variants and caffeine pathways.

In our population, coffee and tea constitute the major source of caffeine intake,[5] and we have shown the test-retest repeatability of our evaluation tool previously,[5] and data of our subjects were collected over a period of a few years. However, we do agree the annual fluctuations of caffeine intake and other individual factors can potentially be confounders.

Last, we will also try to use a system science approach to further evaluate how best to apply and implement a strategic change in managing subjects at risk of PD in a clinical setting.

Perhaps 2–3 cups of tea and coffee a day with regular physical activity/exercise and other dietary monitoring can be explored. Certainly, a long term longitudinal follow up will be able to provide better clarity on the cause and effect relationship between LRRK2 mutations/variants and caffeine intake.

Contributors

EK-Tan and LL-Chan drafted and approved the manuscript.

Declaration of interests

No conflict of interest to declare. EK-T and LL-Chan are supported by National Medical Research Council. EK-Tan received honoraria from Eisai and Elsevier for editorial and academic activities.

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