Letters

COMMENT & RESPONSE

Observations on a 2-Step Approach to Screening for Parkinson Disease

To the Editor We read with interest the report from Jennings et al.[1] The study showed that, among hyposmic individuals, a dopamine transporter (DAT) deficit at baseline identified those with a high relative risk of conversion to clinical Parkinson disease (PD) after 4 years of follow-up.[1]

Power calculations for randomized clinical trials of disease-modifying therapy in prodromal PD suggest that sample sizes will need to include hundreds to thousands of participants to achieve sufficient statistical power.[2] Using the numbers at each stage from this study and a previous Parkinson's Associated Risk Study (PARS) report, we observed that 9400 participants were sent a $30 smell test (including postage), which would have cost approximately $280 000. Among these, there were around 200 participants with hyposmia who consented to have a DaTscan (approximately $1000 for the tracer and single-photon emission computed tomography scan), which would have cost approximately $200 000. This approach identified around 20 participants that had hyposmia and a DAT deficit. This means that identifying a sufficient number of participants with hyposmia and a DAT deficit, to power a clinical trial with 500 participants in each arm and incident PD as the outcome, would cost approximately $24 million.

These costs, while substantial, may be justifiable if disease-modifying therapy were shown to delay conversion to clinical PD and progression to advanced PD. However, the lack of information on incident PD in participants who were not hyposmic and/or underwent scanning means that only the effect of a DAT deficit in those with hyposmia can be evaluated, and not the strengths of the 2-step process.

An interesting finding was the presence of subtle motor dysfunction at baseline in those with a DAT deficit. We too have observed subtle motor dysfunction among at-risk participants in the PREDICT-PD study.[3] Given the lack of association with hyposmia at baseline,[4] subtle motor dysfunction may be an important, independent predictor of those who go on to develop clinically defined PD.

We agree that the PARS approach probably identifies Parkinson disease, as opposed to other atypical parkinsonian syndromes or Parkinson-dementia syndromes, and that DAT single-photon emission computed tomography will play an important role as an imaging marker of the prodromes of PD. Perhaps exploring the role of DAT single-photon emission computed tomography as a progression marker for randomized clinical trials among those estimated to be at high risk (which the authors allude to), rather than as a predictive marker, would maximize benefit and use. There is also a strong argument for an additional low-cost screening step before smell testing, along with an assessment of subtle motor dysfunction, to enrich and engage participants from the outset.

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