be rare (e.g. Yoruba, Met frequency 0.0004 in a group of 226 sampled; African Americans 0.05 in a group of 90) so that a genetic association analysis with depression would require very large samples.

Although we would anticipate the functional impact of being a Met carrier to be similar across population groups, we agree with Yeebo that this would warrant further investigation.

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Relevance of ^{123}I-FP-CIT SPECT brain scans in routine clinical settings

The findings from Walker *et al*'s study[1] do not come as a surprise. The high sensitivity and specificity of ^{123}I-ioflupane injection (^{123}I-FP-CIT) single photon emission computed tomography (SPECT) in diagnosing dementia with Lewy bodies (DLB) relate to a highly selected group of individuals, where underlying vascular pathology, severe mental and physical illness (including delirium) as well as medication interference were excluded. The working group also based their findings on a large group of patients with DLB, in comparison to rather modest size groups previously reported.

How relevant is this study to those of us working in a routine clinical setting? What is the sensitivity and specificity of the ^{123}I-FP-CIT SPECT brain scan in differentiating DLB from other dementia syndromes – and pseudodementia in our patients with more advanced age – with polypharmacy, polycomorbidity or recovering from a prolonged spell of acute confusion? Our own clinical experience working with older people with mental and medical health problems suggests that patients can be easily misdiagnosed as having DLB based on their ^{123}I-FP-CIT SPECT scans, and this includes individuals with major depression, severe brain trauma accompanied by widespread vascular white matter changes and small vessel disease, HIV encephalopathy, and even an older adult with mild intellectual disability with frontal lobe syndrome and extensive hypoperfusion as demonstrated on the SPECT brain scan. This is another confirmation of the clinician's gullibility when faced with ^{123}I-FP-CIT SPECT altered scans, as confirmed by Walker *et al*.[1]

With the availability of ^{123}I-FP-CIT SPECT scans, it is unclear what we have learned from the use of this imaging technique: do we use them for DLB diagnosis – based on their abnormal findings alone – or do we put them in the wider context of our patients' clinical symptomatology and medical history? There is a well-documented inverse relationship between vascular lesions and Lewy body pathology;[2] 30% of patients with frontotemporal lobe dementia have abnormal scans and a significant reduction in uptake in the putamen and the caudate[3] (also highlighted by Walker *et al*[1]). About 5% of people diagnosed with DLB in fact have vascular dementia[4] and altered suspected ^{123}I-FP-CIT SPECT are also found in Creutzfeldt–Jakob disease.[5] It is of note that the influence of antipsychotic[6] and antidepressant medication[7] in older adults has largely been neglected in research studies in the public domain. The evidence from a limited number of animal[8] and human[9] studies clearly indicates that medication (e.g. haloperidol, citalopram, sertraline) reduces ^{123}I-FP-CIT dopamine binding to the dopaminergic transporter. However, there is an overwhelming lack of evidence for the most frequently used drugs in the older population, including a number of dopaminergic antagonists, the influence of polypharmacy, the effect of chronic administration of these drugs and modifying effects of advanced age. Until such data are available, it is not surprising that clinicians would be inclined to diagnose and/or accept the diagnosis of DLB based on the evidence of a dopaminergic abnormality. Even in their strictly controlled study, Walker *et al*[1] report 5.4% mismatch between ^{123}I-FP-CIT SPECT scan findings and clinical DLB diagnosis. It is now the responsibility of the DLB research community to provide us with further clarification of clinical situations and exclusion criteria when using ^{123}I-FP-CIT SPECT scans to diagnose DLB in busy clinical settings.

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Authors' reply: The data presented were the culmination of a well-designed European multicentre study which adds a valuable data-set on the clinical usefulness of ^{123}I-FP-CIT SPECT (DaTSCAN). Although it is correct that the participants in the study were a selected group, as is the case in all clinical trials and similar studies, the sample overall was probably not significantly different in terms of general comorbidities and

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