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[^{11}C]PK11195-PET Brain Imaging of the Mitochondrial Translocator Protein in Mitochondrial Disease

Jelle van den Ameele, PhD, Young Hong, PhD, Roido Manavaki, PhD, et al.

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Correspondence
Dr. Chinnery
pfc25@cam.ac.uk

Study Question

Can radioligands for the mitochondrial outer membrane translocator protein (TSPO) serve as biomarkers for mitochondrial disease?

What Is Known and What This Paper Adds

Researchers have historically used PET imaging with TSPO radioligands as a tool for assessing neuroinflammation and microglial activation. This investigation's results indicate that PET imaging with TSPO radioligands can serve as a tool for assessing mitochondrial pathology in the brain.

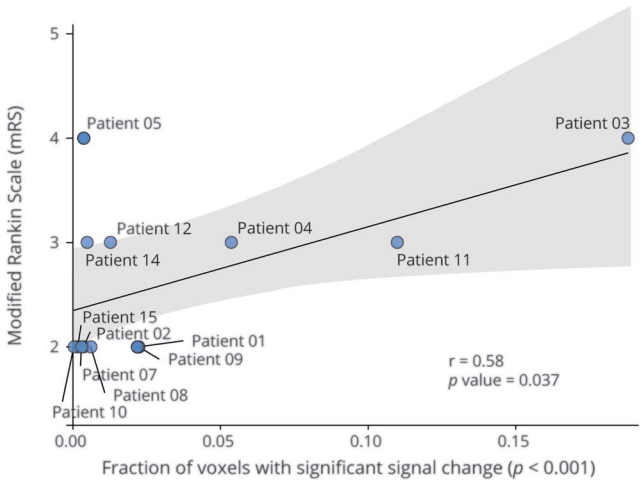
Methods

For this case-control study, the investigators recruited 14 patients with genetically confirmed mitochondrial disease through a specialty clinic. The control group consisted of 33 healthy age- and gender-matched volunteers that were recruited as part of 2 other PET-MR studies at the same facility. The participants underwent combined 3T MRI brain scans and PET imaging with the TSPO radioligand [^{11}C]PK11195. Human phenotype ontology (HPO) terms for each patient were assigned based on electronic health records. Modified Rankin Score (mRS) and Ataxia Scale (SARA) were calculated based on available clinical examinations in the electronic health records. The present study's primary outcomes were between-group comparisons of regional [^{11}C]PK11195 binding levels.

Results and Study Limitations

Between-group comparisons of [^{11}C]PK11195 binding data revealed that 46% of the patients with mitochondrial disease had volumes of abnormal radiotracer binding that were greater than the 95th percentile value observed in the control group. In general [^{11}C]PK11195 binding levels were elevated in the gray matter and reduced in the white matter, and this pattern was most pronounced in the patients with nuclear *TYMP* or mitochondrial m.3243A > G *MT-TL1* mutations in keeping with differences in mitochondrial density seen postmortem. Some regional binding patterns corresponded to clinical presentations and underlying mutations even in the absence of structural changes in MRI scans. Overall, there was a correlation between aberrant [^{11}C]PK11195 binding levels and clinical severity. This study provides Class III evidence that PET-MR brain imaging with TSPO radioligands identifies mitochondrial pathology. The present study's limitations include the small and heterogeneous group of patients with mitochondrial disease.

Figure [^{11}C]PK11195 Binding and Disease Severity



Correlation between change in [^{11}C]PK11195 binding potential and clinical severity as measured by the modified Rankin Scale.

Study Funding and Competing Interests

This study was funded by the Wellcome Trust, the UK Medical Research Council, the UK National Institute for Health Research, the European Research Council, the Newton Fund, Fight for Sight, the Isaac Newton Trust, the Addenbrookes Charitable Trust, the UK National Eye Centre, the Evelyn Trust, the Leverhulme Trust, and the Alzheimer's Society. The authors report no competing interests. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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CORRECTION

[^{11}C]PK11195-PET Brain Imaging of the Mitochondrial Translocator Protein in Mitochondrial Disease

In the Article "[^{11}C]PK11195-PET Brain Imaging of the Mitochondrial Translocator Protein in Mitochondrial Disease" by van den Ameele et al.[1], panels E, H, K, and N of Figure 4 should be labeled "Patient<controls." A corrected version of Figure 4 is available at [URL http://links.lww.com/WNL/B478]. The editorial staff regret the error.

REFERENCE

[1]van den Ameele J, Hong YT, Manavaki R, et al. [^{11}C]PK11195-PET brain imaging of the mitochondrial translocator protein in mitochondrial disease. *Neurology*. 2021;96(22):e2761-e2773.