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PARKINSON DISEASE

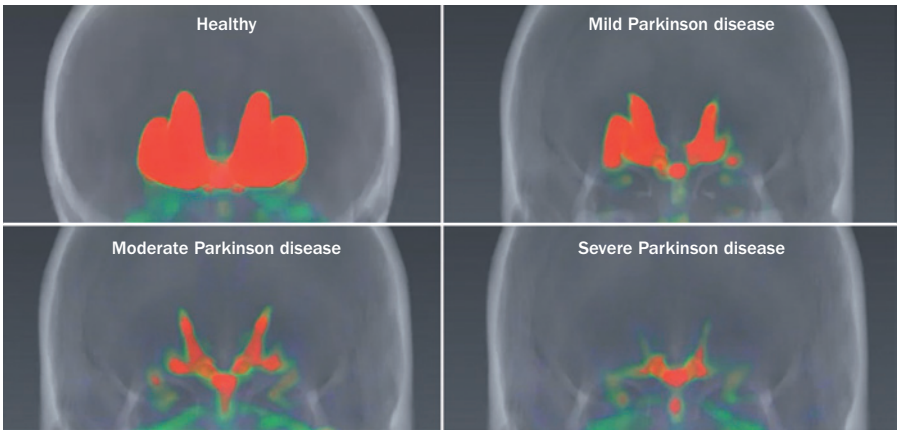
^{18}F-DTBZ PET tracks dopaminergic degeneration in patients with Parkinson disease

Parkinson disease (PD) is difficult to diagnose definitively during life, as it shares many clinical features with other movement disorders, such as multiple system atrophy, corticobasal degeneration and progressive supranuclear palsy. To address this problem, neuroimaging approaches are being developed that enable the disease process to be visualized in the living brain. As recently reported in *JAMA Neurology*, researchers in Taiwan have demonstrated that binding of a novel PET radioligand in the brains of patients with PD correlates inversely with the severity of dopaminergic neurodegeneration.

"Currently, the Unified PD Rating Scale (UPDRS) is commonly used by neurologists to follow the longitudinal course of PD," explains lead investigator Kun-Ju Lin. "Our group at the Neuroscience Research Center of Chang Gung Memorial Hospital has been searching for additional biomarkers for this task since 2000."

The new radioligand, ^{18}F-9-fluoropropyl-(+)-dihydrotetrabenazine (^{18}F-DTBZ), binds to vesicular monoamine transporter type 2 (VMAT2), which is known to be a reliable marker of dopaminergic neuronal integrity. Using ^{18}F-DTBZ, Lin and colleagues found that a PET scan could be accomplished in just 10 min, compared with the 40–60 min scan times usually required for imaging approaches of this type.

The investigators recruited 17 healthy controls and 53 patients with PD, who were further subdivided into mild PD ($n = 22$), moderate PD ($n = 20$) and severe PD ($n = 11$) on the basis of UPDRS and modified Hoehn and Yahr Scale scores. In each participant, a single 10 min PET scan was performed 90 min after injection of ^{18}F-DTBZ. To avoid artefacts caused by interference of dopaminergic drugs with VMAT2 availability, the patients were taken off their medication at least 12 h before the scans were performed.



Maximum intensity projection of ^{18}F-DTBZ PET in brains of healthy individuals and patients with Parkinson disease (anterior view). Image courtesy of K.-J. Lin.

The scans revealed reduced VMAT2 availability in the striatum and substantia nigra in patients with PD, which correlated closely with the clinical severity of the condition. "We also proved that the mesolimbic pathway and extrastriatal regions, including the hippocampus, amygdala and raphe nuclei, were still preserved in advanced stages of disease," adds Lin.

The data indicated asymmetric loss of dopaminergic neurons, especially in the early stages of PD. In patients with mild PD, the decline in VMAT2 availability was most marked in the posterior putamen contralateral to the limbs that were predominantly affected by the disease. Previous imaging studies in patients with PD have demonstrated a similar phenomenon.

"Our findings suggest that ^{18}F-DTBZ PET imaging is a potential imaging biomarker for measuring dopaminergic degeneration *in vivo* and monitoring the severity of disease in PD," concludes Lin. The authors acknowledge, however, that their study was limited by small sample sizes and a lack of longitudinal data.

If the results can be validated in future studies, ^{18}F-DTBZ PET could have a number of possible applications. As well as enabling monitoring of disease progression in patients who have already received a PD diagnosis, the technique might enable the identification of individuals who are at risk of developing PD or are in the preclinical phase of the disease. ^{18}F-DTBZ PET might also help to reduce the rates of misdiagnosis of PD, which can reach 20–30% in the early stages of the condition.

"Neuromodulatory therapy that can slow down the progression of PD is an unmet need in PD treatment," says Lin. "An objective tool to monitor severity and progression of PD is critical for developing clinical trials of these therapies." As the results of the current study indicate, ^{18}F-DTBZ PET has the potential to be developed for this purpose.

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Original article Hsiao, I.-T. *et al.* Correlation of Parkinson disease severity and ^{18}F-DTBZ positron emission tomography. *JAMA Neurol.* doi:10.1001/jamaneurol.2014.290

Further reading Lin, K. J. *et al.* Whole-body biodistribution and radiation dosimetry of ^{18}F-FP-(+)-DTBZ (^{18}F-AV-133): a novel vesicular monoamine transporter 2 imaging agent. *J. Nucl. Med.* **51**, 1480–1485 (2010) | Lin, S. C. *et al. In vivo* detection of monoaminergic degeneration in early Parkinson disease by ^{18}F-9-fluoropropyl-(+)-dihydrotetrabenzazine PET. *J. Nucl. Med.* **55**, 73–79 (2014)