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Imaging in the dopaminergic pathway using three different positron emission tomography radiotracers in Parkinson's disease

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Introduction: It is well known that the dopaminergic system plays an important role in neurodegenerative disorders such as Parkinson's, Alzheimer's and Huntington's diseases. Nowadays, technological advances in molecular imaging have made it possible to obtain, in vivo and non-invasively, information on alterations in dopamine synthesis, integrity of dopaminergic terminals and receptor densities, invaluable information to understand the mechanisms underlying pathogenesis and efficacy of treatments for these diseases Positron emission tomography (PET) provides these characteristics, provided that adequate tracers are available to investigate presynaptic and postsynaptic function. The objective of this research is to evaluate the utility of the combined use of presynaptic and post-synaptic PET radiopharmaceuticals to evaluate Parkinson's disease (PD) and correlate the analysis of the simple uptake rate in striatal subregions (SSR) with the unified qualification scale of Parkinson's disease (mUPDRS

Methods: The radiopharmaceuticals evaluated were 6-[18F] Fluoro-L-DOPA (FDOPA), [11C] Raclopride (RAC) and (+) - alpha- [11C] Dihydrotetrabenazine (DTBZ). We included eight patients diagnosed with PD (2f, 6m, 43-74y, mean 56y) and 4 healthy voluntary male controls (30-72y, mean 53.8y). All patients underwent DTBZ-PET scans and an additional study with FDOPA or RAC, at least a week apart. The controls were studied with a single tracer. The scans were acquired in a Siemens Biograph 64 PET / CT after the intravenous administration of radiopharmaceuticals (185-370 MBq). Brain emission scans of 30 minutes 20 minutes after the DTBZ and RAC injection were obtained, while scans of 15 minutes were acquired after 75 minutes after the injection for FDOPA. All subjects studied with FDOPA received 150 mg of carbidopa to block peripheral decarboxylation. The images were reconstructed using an OSEM-2D algorithm and analyzed with OsiriX v. 6.0 of 32 bits. The regions of interest (0.5 cm2) were drawn in caudate, putamen (anterior, medial and posterior), and the occipital cortex was used as a reference region. Striatal to occipital relationships (SOR) were obtained for each Ssr and correlated with the mUPDRS score. Statistical analysis (Pearson correlation, $\alpha = 0.05$) was performed with GraphPad Prism 5.

Results: The typical images of PET for controls and patients with PD with each radiopharmaceutical are shown in Fig. 1 and Fig. 2. FDOPA measures the synthesis of dopamine through the expression of DDC, DTBZ is a marker of activity of VMAT2 and RAC evaluates the density of D2 receptors. Note the coincidence between the images with DTBZ and FDOPA (reduced uptake in the putamen) and the corresponding lack of coincidence with the RAC images (increased absorption in the putamen) in patients with PD.

Conclusions: To our knowledge, this is the first report that uses 3 different radiopharmaceuticals in a single study in humans. The trackers studied in this investigation showed all the tools for evaluating PD and the information obtained with each radiopharmaceutical is complementary as a key final measure of the efficacy of clinical treatments. The correlations between the mUPDRS score and the SOR values for the different Ssr for DTBZ were all statistically significant ($\alpha = 0.05$), specifically for the putamen subregions, suggesting that this method could be useful for staging, following the evolution and compare intrasubjects and, in addition, intersubjects in the evaluation of PD. Given that FDOPA and DTBZ show similar information, a combination of RAC-DTBZ or RAC-FDOPA could be the best option if it is necessary to choose two radiopharmaceuticals.

Biography

Aylin Akbulut has completed her fellowship on Nuclear Medicine at the age of 30 years from Gazi University and she had postdoctoral studies at Geneva University, Switzerland with Prof O Ratib, Prof Korkmaz, MD, PhD is the founding director of Nuclear Medicine Department in University of Health Sciences, Ankara Training and Research Hospital. After her fellowship on Nuclear Medicine, she had her Postdoctoral studies on radio-peptides at University of Texas MD Anderson Cancer Center, USA. She has published more than 50 papers in reputed journals and has been serving as an editorial board member of repute.

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