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PET analysis of mitochondria in living brain for dementia diagnose

Statement of the Problem: FDG-PET is a well-established technique, however [^{18}F]FDG was taken up into not only normal tissues but also inflammatory regions with microglial activation. We developed a novel PET probe, [^{18}F]BCPP-EF, for quantitative imaging of mitochondrial complex 1 (MC-1) activity in vivo, and aging effects on MC-I activity was investigated in the living brains of monkeys using animal PET scanner. The present study was aimed to assess the effects of amyloid-β (Aβ) deposition on rCMRglc, translocator protein (TSPO) activity, an established marker of microglial activation, and MC-I activity in aged monkey brain. Methodology & Theoretical

Orientation: PET scans using [^{11}C]PIB for Aβ, [^{11}C]DPA-713 for TSPO, [^{18}F]FDG for rCMRglc, and [^{18}F]BCPP-EF for MC-1 were performed under conscious states in aged animals. Scans of [^{18}F]FDG and [^{18}F]BCPP-EF were conducted with arterial blood sampling. Binding of [^{18}F]BCPP-EF to MC-I was analyzed as total distribution volume (VT). Energy metabolism was calculated using [^{18}F]FDG as rCMRglc. Aβ deposition and TSPO activity were determined as SUV of [^{11}C]PIB and [^{11}C]DPA-713, respectively.

Findings: When plotted VT of [^{18}F]BCPP-EF against SUVR of [^{11}C]PIB in the cerebral cortical regions, it showed a significant reverse correlation between them. Plotting of SUV of [^{11}C] DPA-713 against SUVR of [^{11}C]PIB resulted in a significant positive correlation, suggesting that Aβ deposition-induced inflammatory effects with microglial activation. In contrast, plotting of rCMRglc against SUVR of [^{11}C]PIB did not reach statistically significant level. Plotting of rCMRglc against SUV of [^{11}C]DPA-713 revealed a significant positive correlation. Furthermore, when plotted VT of [^{18}F]BCPP-EF in olfactory bulb against SUVR of [^{11}C]PIB in the limbic system, it showed a significant reverse correlation between them, suggesting the deficit mechanism of olfactory identification ability in dementia patients.

Conclusion & Significance: The present study demonstrated that rCMRglc measured using [^{18}F]FDG could not always reflect normal neuronal/astroglial activity disturbed by inflammatory microglial activation. In contrast, [^{18}F]BCPP-EF could be a potential PET probe for quantitative imaging of age-related neurodegenerative alterations as a change in MC-1 activity in the living brain using PET.

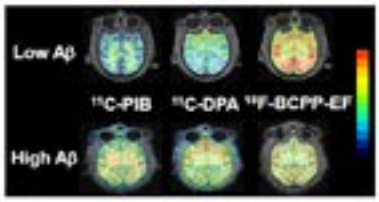

Figure 1: Effects of amyloid β deposition on inflammation and mitochondria complex-I in aged monkey brains

Biography

Hideo Tsukada received PhD from Shizuoka College of Pharmacy, Japan. He was visiting researcher in Uppsala University PET Center, directed by Professor Bengt Langstrom, from 1990 to 91. At present, he is the senior manager of PET Center, Central Research Laboratory, Hamamatsu Photonics, Japan, and conducting PET researches in preclinical to clinical stages. He has published more than 250 papers, being awarded by the Society for Nuclear Medicine (2009), and Japan Molecular Imaging Award (2010). He is serving as the visiting professor in Hamamatsu University School of Medicine, and University of Shizuoka, School of Pharmaceutical Sciences.

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