Development and Application of Beta-Amyloid Imaging Agents

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Imaging agents capable of assessing amyloid in Alzheimer’s disease (AD) subjects are of critical importance to test the amyloid cascade hypothesis, as AD diagnostic agents, and as surrogate markers of a variety of anti-amyloid therapeutic drugs currently under intense development. We have determined that neutral analogues of thioflavin-T possess the properties required of radiotracers to image amyloid. PET imaging studies using one of these agents, carbon-11-labeled Pittsburgh Compound B (PIB), are currently underway in AD, mild cognitively impaired (MCI), and elderly control subjects. We have extended the original SUV analysis of PIB binding by using more quantitative methods that involve arterial blood sampling and reference tissue measures. Analysis methods included compartmental modeling, Logan analysis with either arterial or cerebellar inputs, simplified reference tissue method, or carotid input. All data analysis methods provided qualitatively similar results in AD, MCI, and controls. PIB imaging studies consistently revealed markedly increased PIB outcome measures (1.5-3.0-fold) in AD, relative to controls, in brain areas known to contain amyloid. Heterogeneous PIB outcome measures were observed in MCI subjects, which ranged from AD-like to control-like values. PET imaging studies using PIB as an agent to test the amyloid cascade hypothesis, as a diagnostic agent for AD, and as a surrogate marker to assess the efficacy of anti-amyloid therapeutics are ongoing.