Alzheimer's disease (AD) is the leading cause of dementia and the most common form of amyloidosis in humans. Extensive extracellular deposition of amyloid-β (Aβ), a 40-42 amino acid degradation product of APP, is considered a hallmark feature of AD. Our attention is focused on the highly heterogeneous biochemical nature of the brain Aβ species, delving beyond Aβ40 and Aβ42, likely reflecting a complex balance between amyloidogenic and clearance pathways. We have fractionated water-soluble, detergent-soluble and formic acid soluble Aβ species from brains of transgenic mouse models of amyloid deposition and AD cases. Subsequently, we applied a combination of biochemical techniques including immunoprecipitation followed by identification of Aβ species with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Our biochemical data on the Aβ species present in sporadic AD cases and in transgenic mouse models highlight the presence of similar N- and C-terminally truncated fragments-likely reflecting the ability of multiple proteases to degrade Aβ in situ- and several post-translational modifications with still unclear roles in the amyloidogenesis mechanism. Notably, not all the brain Aβ peptides have identical solubility properties; whereas many of them are highly soluble in water-based physiologic solutions others require mild detergents or strong acids for extraction, suggesting their differential involvement in catabolic and fibrillogenic processes.