Neurochem Int. 2009 Jan;54(1):28-36. doi: 10.1016/j.neuint.2008.10.001. Epub 2008 Oct 15.

A comparative autoradiography study in post mortem whole hemisphere human brain slices taken from Alzheimer patients and age-matched controls using two radiolabelled DAA1106 analogues with high affinity to the peripheral benzodiazepine receptor (PBR) system.

Gulyás B, Makkai B, Kása P, Gulya K, Bakota L, Várszegi S, Beliczai Z, Andersson J, Csiba L, Thiele A, Dyrks T, Suhara T, Suzuki K, Higuchi M, Halldin C.

Source

Karolinska Institutet, Department of Clinical Neurosciences, Psychiatry Section, S-171 76 Stockholm, Sweden. balazs.gulyas@ki.se

Abstract

The binding of two radiolabelled analogues (N-(5-[125I]Iodo-2-phenoxyphenyl)-N-(2,5-dimethoxybenzyl)acetamide ([125I]desfluoro-DAA1106) and N-(5-[125I]Fluoro-2-phenoxyphenyl)-N-(2-[125I]Iodo-5-methoxybenzyl)acetamide ([125I]desmethoxy-DAA1106) of the peripheral benzodiazepine receptor (PBR) (or TSPO, 18kDa translocator protein) ligand DAA1106 was examined by in vitro autoradiography on human post mortem whole hemisphere brain slices obtained from Alzheimer's disease (AD) patients and age-matched controls. Both [(125)I]desfluoro-IDAA1106 and [(125)I]desmethoxy-IDAA1106 were effectively binding to various brain structures. The binding could be blocked by the unlabelled ligand as well as by other PBR specific ligands. With both radiolabelled compounds, the binding showed regional inhomogeneity and the specific binding values proved to be the highest in the hippocampus, temporal and parietal cortex, the basal ganglia and thalamus in the AD brains. Compared with age-matched control brains, specific binding in several brain structures (temporal and parietal lobes, thalamus and white matter) in Alzheimer brains was significantly higher, indicating that the radioligands can effectively label-activated microglia and the up-regulated PBR/TSPO system in AD. Complementary immunohistochemical studies demonstrated reactive microglia activation in the AD brain tissue and indicated that increased ligand binding coincides with increased regional microglia activation due to neuroinflammation. These investigations yield further support to the PBR/TSPO binding capacity of DAA1106 in human brain tissue, demonstrate the effective usefulness of its radio-iodinated analogues as imaging biomarkers in post mortem human studies, and indicate that its radiolabelled analogues, labelled with short half-time bioisotopes, can serve as prospective in vivo imaging biomarkers of activated microglia and the up-regulated PBR/TSPO system in the human brain.

PMID:
18984021
[PubMed - indexed for MEDLINE]