Autoradiographic investigation of α7 nACh-receptor expressionin the Alzheimer brain

Großmann, U.[1], Zeisig V[1], Brust P.[2], Deuther- Conrad W.[2], Patt M.[1], Schildan A.[1], Sabri O.[1], Barthel H.[1]

1 Department of Nuclear Medicine, University of Leipzig, Leipzig, Germany
2 Helmholtz-Zentrum Dresden-Rossendorf, Institute of Radiopharmaceutical Cancer Research, Research Site Leipzig, Germany

Research question and background

During the past decade the search for novel radiotracers for the imaging of alpha7 nicotinic acetylcholine receptors (α7 nAChRs) has been intensified in parallel with the development of novel therapeutic approaches. The diverse physiological functions modulated by α7 nAChR are relevant in many neurological disorders, like Alzheimer`s disease (AD). So far, both in vivo and in vitro studies indicated an unexpected radiotracer uptake by white and grey matter structures. In this context, autoradiographic methods offer excellent potential to evaluate and validate radiotracer binding in vitro, due to a high spatial resolution. In this study we therefore used the ex vivo nuclear medicine technique of autoradiography to validate [^{18}F]DBT10, as a new PET radioligand, with regard to its binding to α7 nAChRs.

Methods and tissues used

Experiments were performed on post mortem human brain material (hippocampus, frontal cortex) originated from one AD patient and one healthy control (HC) and received from the Netherlands Brain Bank.

The cryoconservated tissue was cut into 20 µm sections and mounted onto glass slides. [^{18}F]DBT10 autoradiography was performed according to Perry and Kellar (1995) with minor modifications. Briefly, slidemounted sections were thawed and dried for 15 min at room temperature, and incubated in assay buffer (50 mM TRIS-HCl, pH 7.4) for 10 min at room temperature. Slices were then incubated in assay buffer containing the respective ligands with 5 Bq/µl for 30 min. Nonspecific binding was determined in the presence of 50 nm NS6730 as α7 nAChR antagonist. Afterwards, slides were washed twice in 50 mM TRIS-HCl (pH 7.4), air-dried and exposed to imaging plates (Fuji Film, Tokyo, Japan) along with [^{18}F]DBT10 standards which were prepared according to Gatley et al. (1998). Imaging plates were analyzed using a BAS-5000 system and computer assisted microdensitometry (MCID, Raytest, Germany). Binding of [^{18}F]DBT10 was evaluated in white and grey matter regions of frontal cortex and hippocampus of the AD patient and the HC.

Results and conclusion

A higher specific binding of [^{18}F]DBT10 was found in white and grey matter of frontal cortex of the AD patient as compared to the HCs. These autoradiographic data show the potential of [^{18}F]DBT10 to potentially visualize α7 nAChRs, justifying its further testing as a potential in vivo PET imaging tracer.