Abstract

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ALZGHOOL OBADA: Characterisation of the novel tau PET radiotracer [^{18}F]-*S*-THK5117 in APP/PS1-21 transgenic mouse model of Alzheimer's disease

Master's Thesis, 37 p, 3 appendices

Drug Discovery and Development

June 2017

Purpose: The novel radiotracer [^{18}F]-*S*-THK5117 is recently synthesised at Turku PET Centre. [^{18}F]-*S*-THK5117 is an imaging agent for hyper-phosphorylated tau fibrils. Preliminary testing revealed high [^{18}F]-*S*-THK5117 binding in the brain of APP/PS1-21 transgenic mouse model of Alzheimer´s disease (AD). This is a discrepancy considering that [^{18}F]-*S*-THK5117 is a tau selective radiotracer, and that this mouse model mostly mimics amyloid pathology and to much less extent tau pathology in AD. This observation led to conduct this thesis. **Methods:** In the APP/PS1-21 mouse model, [^{18}F]-*S*-THK5117 binding selectivity to hyper-phosphorylated tau fibrils was investigated by *in vivo* PET/CT imaging, *ex vivo* brain autoradiography and immunohistochemical staining. [^{18}F]-*S*-THK5117 organ uptake was quantified to evaluate the radioactivity distribution in brain and peripheral organs. [^{18}F]-*S*-THK5117 and its radioactive metabolites were studied with radio-TLC. **Results:** [^{18}F]-*S*-THK5117 bound to both Aβ-peptide plaques and paired helical filaments of hyper-phosphorylated tau, with very minor off-target binding to the white matter. [^{18}F]-*S*-THK5117 quantification revealed high uptake in gallbladder, intestine, eyes, and liver, with no defluorination *in vivo*. In the brain only one minor radioactive metabolite of [^{18}F]-*S*-THK5117 was observed at any time point studied. **Conclusions:** [^{18}F]-*S*-THK5117 binds to both hyper-phosphorylated tau fibrils and Aβ-peptide plaques in the APP/PS1-21 mice. Further studies are needed to confirm the specificity of [^{18}F]-*S*-THK5117.

Key words: [^{18}F]-*S*-THK5117, APP/PS1-21, tau, PET