Functional analysis of P-glycoprotein using 5-HT_{2A} ligand [^{18}F]MH.MZ

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Introduction:
[^{18}F]altanserin is the most frequently used tracer to image the 5-HT_{2A} receptor status *in vivo*. However, [^{18}F]altanserin is a P-gp substrate as reported by Palner et al.[1] and very similar in structure to [^{18}F]MH.MZ, a very promising 5-HT_{2A} antagonistic tracer recently developed.[2] The objective of this study was to determine the influence of the receptor binding of [^{18}F]MH.MZ regarding P-gp activity

Methods:
[^{18}F]MH.MZ was applied as a putative substrate to measure changes in 5-HT_{2A} receptor binding in transgenic P-gp KO and wild-type mice. µPET was used to study the uptake profile of [^{18}F]MH.MZ in various brain areas. Brain to plasma concentrations of [^{18}F]MH.MZ and MH.MZ were determined *ex vivo*.

Results:
Highest uptake of [^{18}F]MH.MZ was identified in the frontal cortex and in regions that agree with 5-HT_{2A} receptor distribution.

Conclusion:
In summary, the brain to plasma concentration ratios was higher in P-gp KO transgenic mice treated with MH.MZ vs. wild-type mice. Imaging studies provide evidence for the use of [^{18}F]MH.MZ as a tool to measure not only changes in 5-HT_{2A} receptor density, but possibly in P-gp function, too.

References
1)Herth, Debus et al. (2008), Bioorg Med Chem Lett; 18:1515-1519
2)Palner et. Al (2007), Brain and Mind Forum, Abstracts)

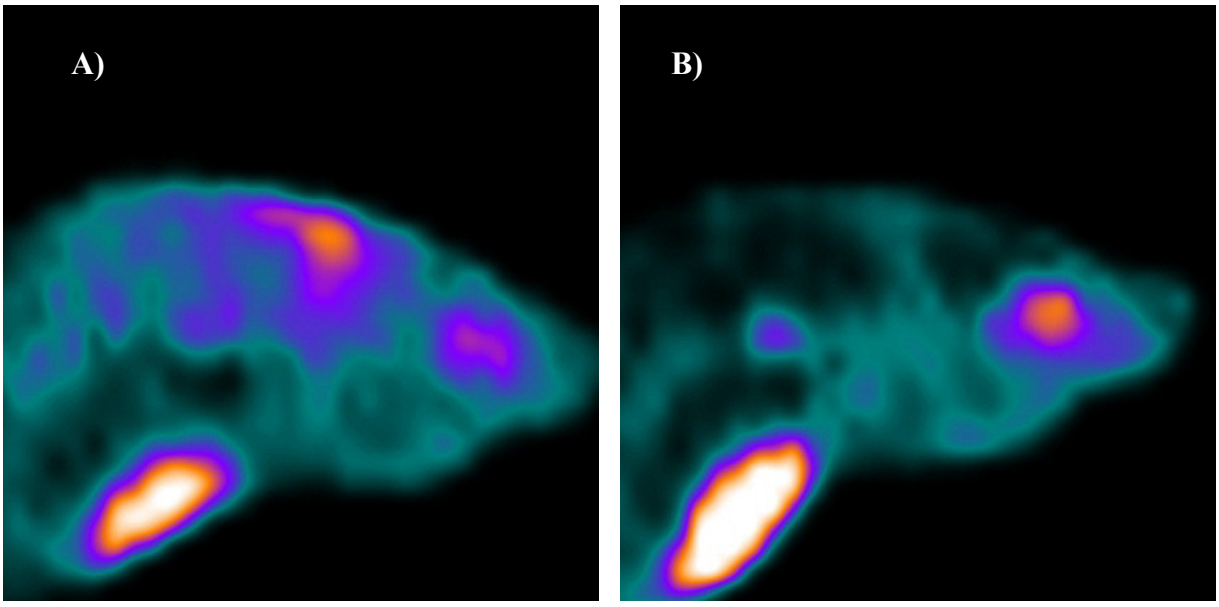

Fig. 1: [^{18}F]MH.MZ PET scan of a A) P-gp k.o. and B) wild type mouse brain. Images derive from a 10 min. static scan 45 min. after i.p. injection of ~ 12 MBq. The imaging was performed with the Focus 120 microPET scanner