Universität Basel

Research Project

Studies on the role of OATP1A2 and OATP2B1 in dopamine-agonist and -antagonist transport across the blood-brain barrier

Project funded by own resources

Project title Studies on the role of OATP1A2 and OATP2B1 in dopamine-agonist and -antagonist transport across the blood-brain barrier
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Organisation / Research unit
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Project start 01.08.2018
Probable end 31.08.2020
Status Completed

In order to enter the brain a compound has to cross the blood brain barrier (BBB), which efficiently protects the central nervous system from xenobiotic exposure. However, the protection is substrate specific as there are some compounds, which exert their pharmacological effect in the brain and are certainly able to cross the membrane, while others do not even if they are structurally related. It is widely known that membrane proteins are involved in cellular efflux and uptake, whereby influencing transcellular transport. The family of Organic Anion Transporting Polypeptides plays a pivotal role in cellular uptake. In this project we will focus on two OATPs namely OATP1A2 and OATP2B1 and the aim will be to evaluate whether dopamine-agonists and dopamine-antagonists are transported by OATP1A2 and OATP2B1, and whether there are differences explaining their differential CNS exposure profile currently explained by limited brain entry.

At first, we are going to validate the localization of OATP1A2 and OATP2B1 in the BBB by immunofluorescent staining in human tissue samples. Then we will test whether the transport of the known endogenous substrate estrone 3-sulfate by OATP2B1 and OATP1A2 is influenced by the dopamine-agonists bromocriptine and cabergoline as well as the dopamine-antagonists domperidone and metoclopramide. For compounds exerting an impact on transport rate the respective inhibitory potency will be determined. Transport by OATP2B1 and OATP1A2 will be validated applying either the recently established competitive counterflow protocol or using radiolabeled tracers.

Keywords OATP2B1, Blood-brain barrier, transport, dopamine-agonists, dopamine-antagonists
Financed by
University funds

Add publication

Published results

4602107, Schäfer, Anima M; Meyer zu Schwabedissen, Henriette E; Bien-Möller, Sandra; Hubeny, Andrea; Vogelgesang, Silke; Oswald, Stefan; Grube, Markus, OATP1A2 and OATP2B1 Are Interacting with Dopamine-Receptor Agonists and Antagonists., 1543-8392, Molecular pharmaceutics, Publication: JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

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