

SFB 35 Colloquia in Membrane Transport

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"The Binding Site for Dopamine and Cocaine on the Dopamine Transporter are Overlapping"

Cocaine is a widely abused substance with psychostimulant effects attributed to inhibition of the dopamine transporter. It has been debated whether or not the cocaine binding site overlaps with that of dopamine. If the binding sites were separate, it would be possible, at least in theory, to generate a cocaine antidote that did not influence the transport of dopamine. Here we present molecular docking models of the dopamine- and cocaine binding site showing an almost complete overlap. The models were validated experimentally using site-directed mutagenesis, Zn²⁺-site engineering, and chemical cross-linkers. These data argue against the possibility of creating such a cocaine antagonist. However, there might be hope for the cocaine addicts after all...