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# Rate of small-molecular drug transport across the blood-brain barrier in a pericyte-deficient state

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**Abstract**

Close interactions between pericytes and brain endothelial cells are essential for keeping the blood-brain barrier (BBB) functional and to restrict the transport of various xenobiotics from blood circulation to the brain parenchyma. Profound understanding of pericyte roles at the BBB and underlying mechanisms for the regulation of BBB transport are important as a potential strategy to improve drug delivery in treatment of CNS disorders. The aim of the present study was to investigate pericyte role in the rate of small-molecular drug transport across the BBB, by examining three model compounds in a pericyte-deficient state. Diazepam, oxycodone and paliperidone were selected for this purpose based on utilization of different transport mechanisms at the BBB. The rate of brain uptake was assessed by implementing the trans-cardiac *in situ* brain perfusion technique. Radiolabeled $^{14}$C-sucrose was used as a vascular marker. Pericyte-deficient mice (*Pdgfb*$^{ret/ret}$) exhibited significantly larger brain vascular volumes ($V_{vasc}$) 1.72 ± 0.13 mL/100g brain, compared to littermate controls with normal pericyte coverage (*Pdgfb*$^{ret/+}$) 1.15 ± 0.13 mL/100g brain ($p < 0001$). However, the unidirectional transfer coefficient $K_{in}$ , which describes the rate of brain uptake, was not different between *Pdgfb*$^{ret/ret}$ and *Pdgfb*$^{ret/+}$ mice for all three tested compounds. Taken together the present results indicate no pericyte influence in the rate of small-molecular drug transport at the BBB, despite the larger brain vascular volumes that were observed in a pericyte-deficient state.

**Key words**: Blood-brain barrier, Pericytes, Drug delivery, Rate of transport, *In situ* brain perfusion