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Thyroxine (T₄) transfer from blood to cerebrospinal fluid in sheep isolated perfused choroid plexus: Role of multidrug resistance-associated proteins and organic anion transporting polypeptides (Article)

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Abstract

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Thyroxine (T₄) enters the brain either directly across the blood - brain barrier (BBB) or indirectly via the choroid plexus (CP), which forms the blood - cerebrospinal fluid barrier (B - CSF - B). In this study, using isolated perfused CP of the sheep by single - circulation paired tracer and steady - state techniques, T₄ transport mechanisms from blood into lateral ventricle CP has been characterized as the first step in the transfer across the B - CSF - B. After removal of sheep brain, the CPs were perfused with ¹²⁵I - T₄ and ¹⁴C - mannitol. Unlabeled T₄ was applied during single tracer technique to assess the mode of maximum uptake (U_{max}) and the net uptake (U_{net}) on the blood side of the CP. On the other hand, in order to characterize T₄ protein transporters, steady - state extraction of ¹²⁵I - T₄ was measured in presence of different inhibitors such as probenecid, verapamil, BCH, or indomethacin. Increasing the concentration of unlabeled - T₄ resulted in a significant reduction in U_{max}%, which was reflected by a complete inhibition of T₄ uptake into CP. In fact, the obtained U_{net}% decreased as the concentration of unlabeled - T₄ increased. The addition of probenecid caused a significant inhibition of T₄ transport, in comparison to control, reflecting the presence of a carrier mediated process at the basolateral side of the CP and the involvement of multidrug resistance-associated proteins (MRPs: MRP1 and MRP4) and organic anion transporting polypeptides (Oatp1, Oatp2, and Oatp14).

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