

Effect of tracer metabolism on PET measurement of [¹¹C]pyrilamine binding to histamine H₁ receptors

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The present study was carried out to investigate the time course of [¹¹C]pyrilamine metabolism and the degree of entry of metabolites into the brain. PET studies were performed in seven healthy volunteers and arterial plasma concentrations of [¹¹C]pyrilamine and its labeled metabolites were determined. After intravenous injection, [¹¹C]pyrilamine metabolized gradually in the human body, with less than 10% of plasma activity being original radioligand at 60 min. Tracer metabolism markedly affected the input function and the calculated impulse response function of the brain. Rat experiments demonstrated that although metabolites of [¹¹C]pyrilamine might enter the brain, they were not retained for prolonged periods of time. At 30–90 min after injection of [¹¹C]pyrilamine, less than 1% of the radioactivity in the brain was originating from metabolites of [¹¹C]pyrilamine. Based on the rat data, the contribution of ¹¹C-labeled metabolites to total [¹¹C]pyrilamine radioactivity in the human brain was estimated and found to be negligible. These results suggest that the metabolites of [¹¹C]pyrilamine do not accumulate within the cerebral extravascular space and that there is minimal metabolism of [¹¹C]pyrilamine by brain tissue itself. Therefore, [¹¹C]pyrilamine metabolites can be neglected in kinetic analysis, using either a compartmental or a noncompartmental model, of the [¹¹C]pyrilamine binding to histamine H₁ receptors.

Key words: histamine H₁ receptor, [¹¹C]pyrilamine, tracer metabolism, positron emission tomography