

A brain uptake study of [1-¹¹C]hexanoate in the mouse: The effect of hypoxia, starvation and substrate competition

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We evaluated the potential of sodium [1-¹¹C]hexanoate (¹¹C-HA) as a radiopharmaceutical with which to assess oxidative metabolism of the brain by PET. ¹¹C-HA, sodium [1-¹⁴C]acetate and [³H]deoxyglucose were simultaneously injected into mice under control, hypoxic and starving conditions. In the control, the brain uptake of ¹¹C was maximal at 3 min (% ID/g = 2.2–2.5), being twice as high as that of ¹⁴C, followed by a gradual clearance. The time-radioactivity curve of ¹¹C was similar to that of ¹⁴C. Hypoxia enhanced the brain uptake of ³H, but not of either ¹¹C or ¹⁴C. Starvation enhanced the brain uptake of ³H and ¹¹C. The clearance rate of ¹¹C was not significantly affected by either condition. In the control brain at 3 min postinjection of HA, 65% of the total radioactivity was detected as labeled glutamate and glutamine, which was gradually decreased by 47% at 30 min. The brain to blood ratios of ¹¹C-HA at 3 min were significantly reduced by butyrate, hexanoate and octanoate loading but not by that with other monocarboxylic acids or ketone bodies.

Key words: [1-¹¹C]hexanoate, brain, oxidative metabolism, β -oxidation, PET