A brain uptake study of [1-\textsuperscript{13}C]hexanoate in the mouse: The effect of hypoxia, starvation and substrate competition

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We evaluated the potential of sodium [1-\textsuperscript{13}C]hexanoate (\textsuperscript{13}C-HA) as a radiopharmaceutical with which to assess oxidative metabolism of the brain by PET. \textsuperscript{13}C-HA, sodium [1-\textsuperscript{14}C]acetate and [\textsuperscript{1}H]deoxyglucose were simultaneously injected into mice under control, hypoxic and starving conditions. In the control, the brain uptake of \textsuperscript{13}C was maximal at 3 min (% ID/g = 2.2-2.5), being twice as high as that of \textsuperscript{14}C, followed by a gradual clearance. The time-radioactivity curve of \textsuperscript{13}C was similar to that of \textsuperscript{14}C. Hypoxia enhanced the brain uptake of \textsuperscript{1}H, but not of either \textsuperscript{13}C or \textsuperscript{14}C. Starvation enhanced the brain uptake of \textsuperscript{1}H and \textsuperscript{13}C. The clearance rate of \textsuperscript{13}C 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 \textsuperscript{13}C-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-\textsuperscript{13}C]hexanoate, brain, oxidative metabolism, \textsuperscript{\beta}-oxidation, PET