

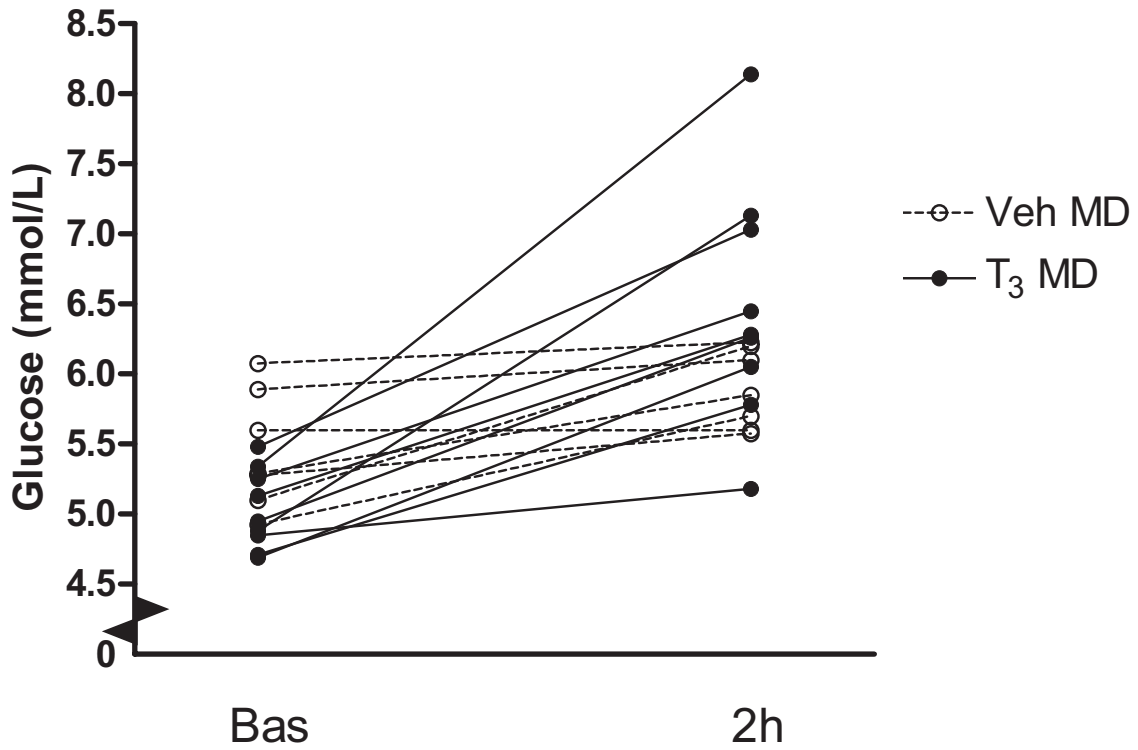
# Supporting Information

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## SI Materials and Methods

**Plasma Hormone and Isotope Analyses.** Plasma concentrations of the thyroid hormones T<sub>3</sub> and T<sub>4</sub> were determined by in-house RIA, with inter- and intra-assay coefficient of variation (CV) of 7 to 8% and 3 to 4% (T<sub>3</sub>), and 3 to 6% and 2 to 4% (T<sub>4</sub>), respectively. Detection limits for T<sub>3</sub> and T<sub>4</sub> were 0.3 nmol/L and 5 nmol/L, respectively. Plasma TSH concentrations were determined by a chemiluminescent immunoassay (Immulite 2000, Diagnostic Products Corp.), using a rat-specific standard. The inter- and intra-assay CV for TSH were less than 4% and 2% at ± 3.5 mU/L, respectively, and the detection limit was 0.20 mU/L. Plasma insulin concentrations were measured using a commer-

cially available Elisa kit (Mercodia). The inter- and intra-assay CVs were 4% and 2%, detection limit 13 pmol/L. Plasma glucagon and corticosterone concentrations were measured using a commercially available RIA (RIA, LINCO Research, and ICN Biomedicals, respectively). All samples were measured in duplicate (e.g., 2 tubes were analyzed per plasma sample). Glucose enrichment was measured as described earlier (35). The [6,6-<sup>2</sup>H<sub>2</sub>]-glucose enrichment (tracer/ tracee ratio) inter-assay CV was 1%, the intra-assay CV 1%, and the detection limit 0.04%.



**Fig. S1.** The relation between basal glucose concentration and the progression of plasma glucose during MD. Note that basal plasma glucose was not a determinant of the plasma glucose response to T<sub>3</sub> MD (Spearman correlation  $P = 0.546$  for basal glucose vs. glucose delta between Bas and 2 h). In addition, when the animals in the T<sub>3</sub> MD group that had lower basal glucose concentrations than the Veh-treated animal with the lowest basal-glucose value were excluded from the analysis, the relative increase in plasma glucose was still be significantly higher in T<sub>3</sub> MD as compared with Veh MD animals ( $n = 5$  vs.  $n = 7$ , respectively,  $P = 0.004$ ).