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HIV-LIPODYSTROPHY IS CHARACTERIZED BY INSULIN RESISTANCE FOR LEUCINE AND GLUCOSE METABOLISM: DISSIMILAR TO TYPE 2 DIABETES

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BACKGROUND: Type 2 diabetes is characterized by impaired glucose tolerance and insulin resistance with respect to glucose metabolism, but not amino acid metabolism ([Diabetes. 2002 Aug;51\(8\):2395-404](#)).

OBJECTIVES: To examine whether HIV-associated impaired glucose tolerance (IGT) and insulin resistance extends to amino acid metabolism.

METHODS: Glucose disposal rate and plasma leucine rate of appearance (Leu R_a = whole-body proteolysis rate) were measured during the post-absorptive state and euglycaemic-hyperinsulinaemia using primed constant infusions of 6,6-²H₂-glucose and ¹³C-leucine in three groups of subjects: eight seronegative control (three women, five men; BMI=28 ±1 kg/m²), 18 HIV+ non-lipodystrophic (two women, 16 men; BMI=26 ±1, HIV RNA=6361 ±3817 copies/ml, CD4=521 cells/μl), and 19 HIV-lipodystrophic (Carr et al., [Lancet. 2003 Mar 1;361\(9359\):726-35](#)) subjects (four women, 15 men; BMI=26 ±1, HIV RNA=1704 ±951, CD4=554). Glucose and Leu kinetics were examined at insulin infusion rates of 20 and 50 mU/m²/min, which produced plasma insulin levels of 240–280 and 570–670 pM. Fat-free mass (FFM) was measured using dual energy X-ray absorptiometry.

RESULTS: At the highest insulin level, glucose disposal rate was lower ($P=0.002$; ANOVA) in HIV lipodystrophy (42 ±3; mean ±SEM) and HIV non-lipodystrophy (56 ±5), than in controls (69 ±7 μmol/kg FFM/min). Contrary to type 2 diabetes, whole body proteolysis rate was higher ($P<0.001$) at all insulin levels in HIV lipodystrophy (baseline 163 ±4; low insulin 147 ±4 and high insulin 139 ±4 μmol/kg FFM/hr) and HIV+ non-

lipodystrophy (146 ±4, 132 ±4, 123 ±3) than in controls (138 ±3, 121 ±3, 115 ±3). Plasma interleukin-6 (IL-6) levels tended to be higher ($P=0.016$) in HIV lipodystrophy (1.9 ±0.3) and HIV+ non-lipodystrophy (1.1 ±0.2) than in controls (0.9 ±0.2 pg/dl).

CONCLUSIONS: These findings suggest that both whole-body glucose and amino acid (Leu) metabolism are insensitive to the anabolic actions of hyperinsulinaemia in HIV, especially in HIV lipodystrophy. Increased inflammatory cytokine (IL-6) levels may contribute to the failure of hyperinsulinaemia to suppress whole-body proteolysis in HIV-infected people.

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9

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