Increased Amino Acid Turnover and Net Protein Breakdown but Preserved Muscle and Cognitive Function in Obese Middle-Age Adults

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Objectives: Skeletal muscle weakness has been observed in obese patients despite preserved or even greater lean body mass. Additionally, the presence of obesity-related comorbidities is a recognized risk factor for cognitive dysfunction and mood disturbances. Metabolism of several amino acids (AAs) including the Branched-chain Amino Acids (BCAAs) is altered in obesity but whether these disturbances are associated with muscle and cognitive dysfunction remain underexplored.

Methods: 159 subjects were divided, using the BMI cut-off of 30 kg/m^2, into two groups: 79 non-obese (32 males/47 females, age 48.5 [43.3, 53.7], BMI 25.2 [24.6, 25.7] kg/m^2) and 80 obese (31 males/49 females, age 54.3 [51.0, 57.6], BMI 38.3 [36.9, 39.6] kg/m^2). Postabsorptive whole-body production (WBP) rates of several AAs were measured by IV pulse of stable isotopes including BCAAs, Phenylalanine (Phe), Tyrosine (Tyr), Glutamate (Glu), and Tryptophan (Trp). Plasma amino acid enrichments and concentrations were analyzed by LC-MS/MS. Large Neutral Amino Acids (LNAA) was calculated as the sum of BCAAs, Phe, and Tyr. Body composition (DXA), hand and leg peak strength and endurance (isokinetic dynamometer), cognitive function (Stroop, TMT), and mood (POMS, HADS) were assessed. Statistics performed by ANCOVA with age, gender, and lean body mass as covariates. Significance at $P < 0.05$. Results expressed as means [95% CI].

Results: Obese subjects had higher concentrations of plasma Leu (12%, $P = 0.0097$), Ile (7%, $P = 0.0310$), Tyr (23%, $P < 0.0001$), and Glu (40%, $P = 0.0001$). The obese group was also characterized by elevated WBP of BCAAs (8%, $P = 0.0343$), Phe (12%, $P = 0.0003$), Tyr (18%, $P = 0.0005$) and increased whole-body net protein breakdown (Phe to Tyr conversion, 11%, $P = 0.0212$). Both groups had similar muscle and cognitive functions but obese individuals had greater scores for self-reported depressive symptoms ($P = 0.0273$), anger ($P = 0.0234$), fatigue ($P = 0.0098$), and tension ($P = 0.0158$). No changes in Trp metabolism were found but obese subjects had elevated LNAA (7%, $P = 0.0170$) resulting in increased systemic Trp availability to the brain ($P = 0.0014$).

Conclusions: Obese subjects have preserved muscle and cognitive function despite greater whole-body net protein breakdown and increased turnover of several AAs involved in muscle metabolism and serotonin synthesis.

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