Effects of neutralizing IL-6 on glucocorticoid action in rat tissue after exposure to short-term intermittent mild psychological stress.

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Glucocorticoids (GCs), such as cortisol and corticosterone, are known mediators of both the stress and anti-inflammatory responses to stress. As part of the metabolic response to stress GCs stimulate the expression of GC-inducible enzymes, such as tyrosine aminotransferase (TAT) and glutamine synthetase (GS). This effect is mediated by glucocorticoid receptors (GRs), the levels of which are in turn also regulated by GCs. GCs mediate the anti-inflammatory response to stress by down-regulation of pro-inflammatory cytokines such as interleukin-6 (IL-6). We investigated the effects of blocking IL-6 in vivo on GC action in skeletal muscle and liver in response to mild immobilization stress.

Forty (40) mature, male Wistar rats were divided into four groups (n=10 per group): (A) Control Placebo (CP, non-stressed, i.p. saline injection); (B) Control Antibody (CA, non-stressed, i.p. anti-IL-6-antibody injection); (C) Immobilization Placebo (IP, subjected to immobilization stress, i.p. saline injection) and (D) Immobilization Antibody (IA, subjected to immobilization stress, i.p. anti-IL-6-antibody injection). The mild stress response was achieved by immobilizing the rats for 2h/day for 4 consecutive days. The levels of TAT (in skeletal muscle and liver) and GS (in skeletal muscle) were measured by colorimetric enzymatic assays. Serum corticosterone levels were measured by enzyme-linked immunosorbent assays (ELISA) and cytosolic GR levels (in skeletal muscle and liver) were determined by radioligand binding assays.

Our main findings were (i) a significant loss of body mass in response to short-term intermittent mild psychological stress (groups A and B vs C and D); (ii) immobilization-induced increases in corticosterone secretion (groups A and B vs C) that were at least partially dependent on IL-6 (group D not different from groups A, B or C); (iii) immobilization-induced increases in expression of GS and TAT (groups A and B vs C and D) and (iv) immobilization-induced decreases in GR expression in both liver and muscle (groups A and B vs C and D).

Although effects seen on enzymes and GR could be interpreted that IL-6 had no modulating effects, it must be considered within the context of no significant increase in corticosterone itself in group D. Our results indicate that IL-6 antagonizes the intramuscular effects of corticosterone since less corticosterone results in the same downstream effect on glucocorticoid responsive metabolic enzymes in the absence of IL-6.