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Presentation Abstract

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Presentation Title: [Sickness behaviors \(reduced social interaction and aggression\) induced by in a rat model of overuse are attenuated by anti-inflammatory drugs that reduce overuse-induced systemic inflammation](#)

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Abstract: We have shown in a rat model of overuse that prolonged performance of repetitive tasks increases serum inflammatory cytokines. Systemic inflammation is known to exaggerate sickness behaviors, e.g. decreased social interaction and increased aggression. We examined these behaviors in our rat model, and the effectiveness of anti-inflammatory treatments. A total of 92 young adult female Sprague-Dawley rats trained for 4 wks for 10 min/day, 5 days/wk to a high force level (TRHF; 60% max force). 49 rats went on to perform a high repetition high force (HRHF) task of 8 reaches/min, 60% max force, for 2 hrs/day, 3 days/wk for 5-12 wks. In wk 4, the HRHF rats either continued to wk 12 with no treatment (n=31), received oral ibuprofen (40 mg/kg body wt) for 8 wks (HRHF+IBU, n=18), or received anti-TNFalpha (8 mg/kg body wt, i.p; n=6). Thirteen TRHF rats received anti-TNFalpha (8 mg/kg body wt, i.p) prophylactically during training; 21 TRHF rats were euthanized immediately after training (TRHF wk0); 10 rested until euthanasia 6 wks later (TRHF+REST). Duration of social interaction with novel juvenile rats was assessed every 3 wks, as was incidence of aggression. Results were compared to naïve data, food-restricted controls (FRC, n=23), or normal controls +/- ibuprofen for 8 wks, or after saline injection (n=8, 41, & 4, respectively). Following euthanasia, serum was collected and analyzed for inflammatory cytokines. There was

no evidence of sickness behaviors in any NC or FRC group. TRHF wk 0 rats had decreased duration of social interaction ($p < 0.01$ compared to naive); rest somewhat attenuated this increase. Prophylactic anti-TNFalpha prevented the decrease in social interaction. Untreated HRHF rats showed decreased social interaction after training ($p < 0.01$) and until euthanasia in wk 12 ($p < 0.05$). Treatment of HRHF rats with ibuprofen and anti-TNFalpha was effective in attenuating the decrease in social interaction. Regarding aggression, untreated HRHF rats showed increased aggression ($p < 0.0001$ Chi square), with the greatest increases immediately after training and in HRHF wk 3 and 6. Ibuprofen and anti-TNFalpha treatment of HRHF rats attenuated the aggression by wk 6. TRHF-anti-TNFalpha rats did not display aggression, nor did NC or FRC rats. TRHF wk 0 and HRHF rats showed increased serum TNFalpha, IL-1beta, & MIP2. Prophylactic treatment of TRHF rats with anti-TNFalpha prevented these increases in serum cytokines. Secondary treatment of HRHF rats with ibuprofen or anti-TNFalpha also effectively attenuated the increased serum cytokines. Thus, sickness behaviors induced by overuse are attenuated by primary and 2nd interventions that also reduced systemic inflammation.

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