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Presentation Abstract

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Presentation Title: [Sickness behaviors \(reduced social interaction and increased aggression\), serum and brain IL6, increase with performance of high demand tasks in a rat model of overuse](#)

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Abstract: We have shown in a rat model of work-related overuse that prolonged performance of repetitive tasks increases serum inflammatory cytokines that correlate with sensorimotor declines. Since virally-induced increases in serum inflammatory cytokines also correlate with increased brain cytokines and sickness behaviors, e.g. decreased social interaction and increased aggression, we now examined these in our rat model. 168 young adult (n=96) and aged (n=72) female Sprague-Dawley rats trained for 4-5 wks for 10 min/day, 5 days/wk at either a low force (TRLF; 15% max force) or a high force (TRHF; 60% max force) task level. The rats then performed a high repetition low force task (HRLF) of 8 reaches/min, 15% max force, for 2 hrs/day, 3 days/wk, for 9-24 wks. Duration of social interaction and incidence of aggression with novel juvenile rats were assessed every 3 wks. Results were compared to age-matched food-restricted controls (FRC). Following euthanasia, serum and brains were collected and analyzed for inflammatory cytokines. Behaviorally, at end of initial training period, both aged TRHF and TRLF rats had decreased social interaction with juvenile rats than at naïve (p=0.05 each), and FRC (p<0.0001 and p=0.01, respectively). Only a trend towards decreased social interaction was observed in young adult TRHF rats (p=0.08). Both aged and young TRHF

rats had increased displays of aggression towards the juveniles than at naïve ($p=0.05$ each), behavior not observed in aged or young TRLF or FRC rats. These behavioral changes in aged TRHF rats did not resolve until week 9 of the HRLF task (termed TRHF-HRLF), but resolved by week 3 in the young adult TRHF-HRLF and in aged TRLF-HRLF rats. These behaviors were not observed in young adult TRLF-HRLF rats, even those performing the HRLF task for 24 weeks. There was an increase of serum interleukin 6 (IL-6) in aged and young TRHF ($p=0.01$ and $p=0.05$, respectfully) and in aged TRHF-HRLF rats that performed the task for 3 weeks; this increase resolved in these aged rats thereafter. No increase in serum cytokines was detected in young adult TRLF or TRLF-HRLF rats. Increased IL-6 and IL-6 receptor was also detected immunohistochemically in brains of aged rats with these sickness behaviors, specifically in the anterior cingulate cortex and paraventricular nuclei ($p<0.05$ each). No increase of IL6 or IL-6 receptor was observed in aged TRLF-HRLF rats or any young adult rats. Thus, training to high force, even for a short time period, induced increased serum IL6 and sickness behaviors. Aging also contributed to increased sickness behaviors and brain IL6 and IL-6 receptor.

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