Frailty is increased in aging mice with lower urinary tract dysfunction

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Introduction

Benign prostatic hyperplasia (BPH) is a prototypic aging disease confined to the transition zone of the prostate that occurs in 50% of men in their 50s but dramatically increases to 90% of men in their 80s. The aging prostate invariably undergoes pathological changes, often leading to lower urinary tract symptoms (LUTS), including urinary frequency, urgency, and retention, significantly increasing risks of falls (frailty) and decreasing quality of life in aging men. Our lab and others have developed several rodent models that recapitulate the lower urinary tract dysfunction associated with human disease. In this study, we examine young and aging male mice for changes in frailty and urinary function. Additionally, we begin to assess the alterations to voiding after exercise, as administered by running wheel.

Hypothesis

We hypothesize that frailty is increased while anxiety and social interactions with female mice decrease in aging mice with lower urinary tract dysfunction (LUTD).

Materials and Methods

- *Young (2 months) and old (24 months) C57Bl6 mice were obtained from Jackson Laboratory.*
  - *All mice were singly housed throughout the experiment.*
- *LUTD was assessed using void spot assays and analyzed with Void Whizzard [1].*
- *A 31-item frailty assessment was used to evaluate overall health [2].*
- *Grip strength was assessed using a digital force transducer.*
  - *Each mouse was tested five times and the min/max readings discarded.*
  - *Remaining measurements were averaged for final grip strength measurement.*
- *Locomotive ability and anxiety were evaluated using an open field test.*
  - *Mice are placed individually into a brightly lit, open field apparatus for 30 minutes.*
  - *Activity is measured in 10 minute increments.*
- *Social investigation and ultrasonic vocalizations between male (young/old) and female (random controlled) mice were examined to assess social behavior.*
- *Exercise was administered to each mouse using a traditional exercise wheel.*
  - *Each wheel is electronically monitored to collect times of running as well as distance run per mouse/per day through the duration of the experiment.*

Results

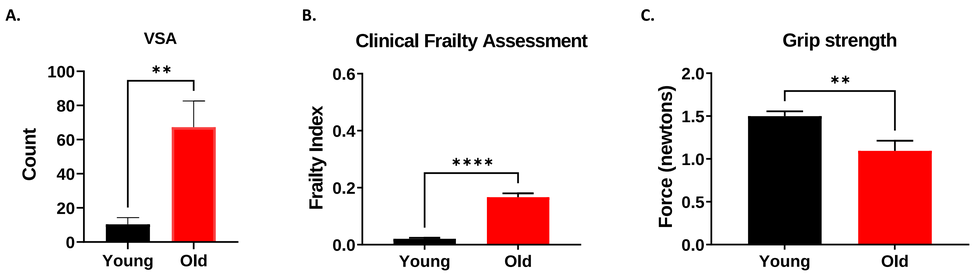

Figure 1. Urinary dysfunction and frailty increase in aged mice. A. Urinary dysfunction increases in 24-month old mice compared to 2-month old mice. **B.** Frailty as measured by a 31-point clinical assessment increases in 24-month old mice compared to 2-month old mice [2]. **C.** Forelimb grip strength decreases with age.
**, p-value < 0.01; ****, p-value < 0.0001

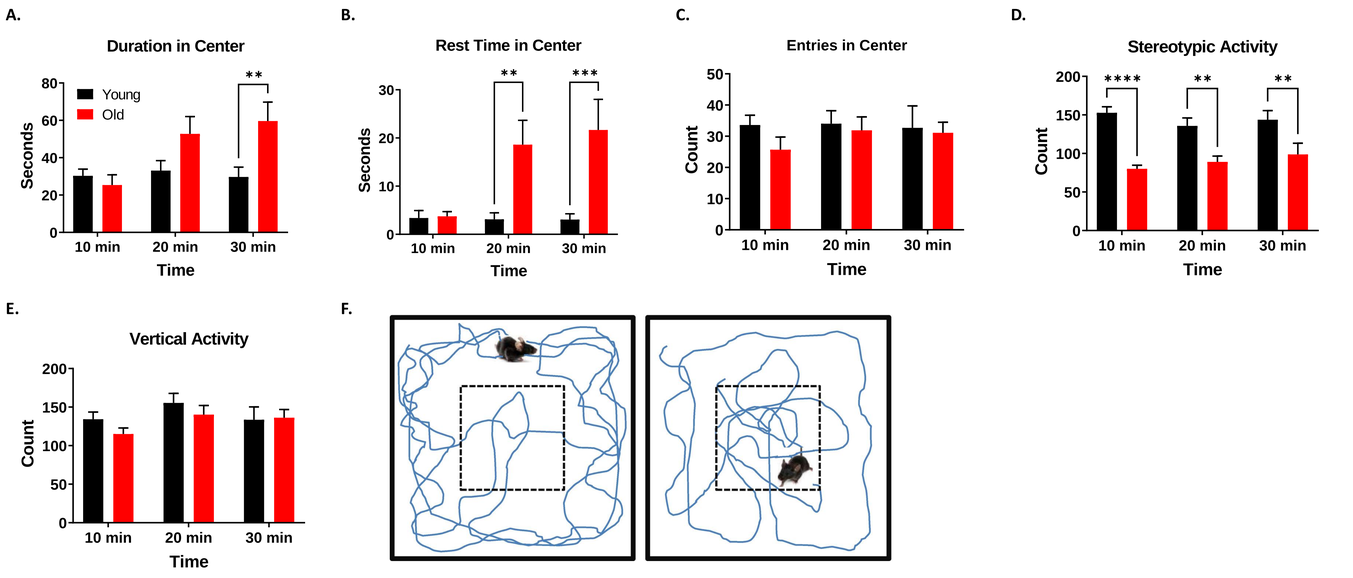

Figure 2. Aging alters anxiety behaviors but not movement in male mice as measured by open field testing. A. Aging mice spend more time in the center portion of the open field. **B.** Aging mice spend more time resting in the center portion of the open field. **C.** Entries into the center portion of the open field is unchanged between young and aging mice. **D.** Young mice demonstrate more repetitive, purposeless activity throughout the test. **E.** Rearing ability was unchanged with age. **F.** Representative diagram of open field testing [3].
**, p-value < 0.01; ****, p-value < 0.0001

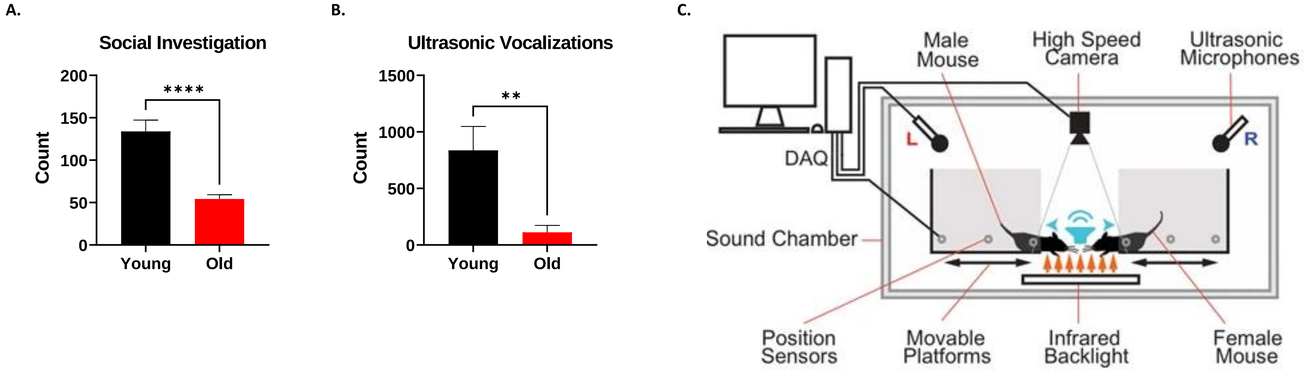

Figure 3. Aging alters social interactions in male mice as measured by an audio-tactile interaction setup. A. Social investigation of the female mouse decreases with aging. **B.** Ultrasonic vocalizations by male mice decrease with aging. **C.** Diagram of audio-tactile interaction chamber [4]. **, p-value < 0.01; ****, p-value < 0.0001

Results (cont.)

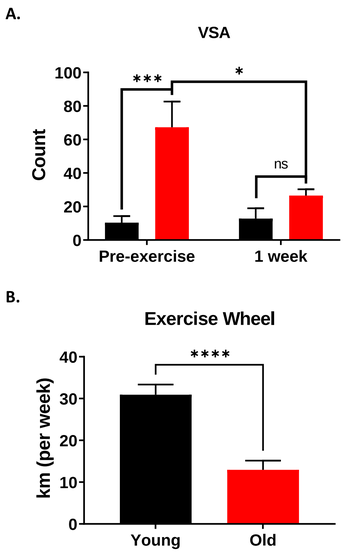

Figure 4. Exercise decreases the age-mediated lower urinary tract dysfunction in aging mice. A. One week of exercise significantly decreases void spot count in aging mice with no change in young. **B.** Compared to young mice, aging mice run significantly less overall.
*, p-value < 0.05; ***, p-value < 0.001; ****, p-value < 0.0001

Conclusions

- Age significantly increases voiding dysfunction and frailty in male mice.
- Aging male mice experience less fear and anxiety as measured by open field testing.
- Aging male mice were overall less interested in young female mice compared to young male counterparts.
- Exercise decreases urinary dysfunction in aging male mice.

References

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