SEX DIFFERENCES IN SKELETAL MUSCLE-AGEING TRAJECTORY: SAME PROCESSES, BUT WITH DIFFERENT MAGNITUDES

Jelle CBC de Jong[1,2], Brecht J Attema[1], Marjanne D van der Hoek[1,3,4], Lars Verschuren[5], Martien PM Caspers[5], Robert Kleemann[2], Feike R van der Leij[4,6], Anita M van den Hoek[2], Arie G Nieuwenhuizen[1] and Jaap Keijer[1]

1. Human and Animal Physiology, Wageningen University, Wageningen, the Netherlands
2. Department of Metabolic Health Research, The Netherlands Organization for Applied Scientific Research (TNO), Leiden, the Netherlands
3. Applied Research Centre Food and Dairy, Van Hall Larenstein University of Applied Sciences, Leeuwarden, the Netherlands
4. MCL Academy, Medical Centre Leeuwarden, Leeuwarden, the Netherlands
5. Department of Microbiology and Systems Biology, The Netherlands Organization for Applied Scientific Research (TNO), Zeist, the Netherlands
6. Research and Innovation Centre Agri, Food & Life Sciences, Inholland University of Applied Sciences, Delft and Amsterdam, the Netherlands

J.dejong@tno.nl

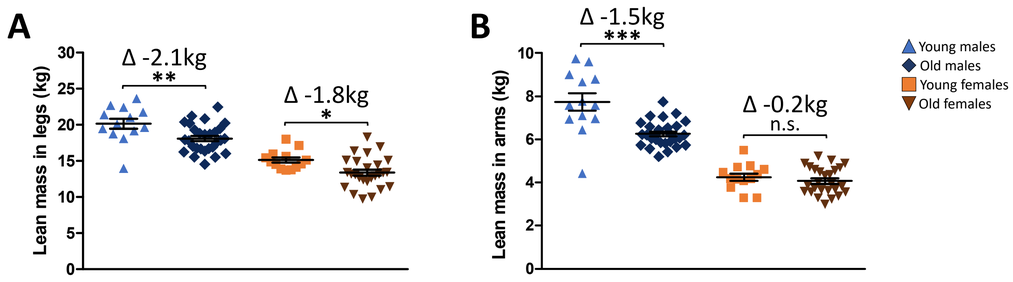
INTRODUCTION AND AIM

- Sex differences in muscle-ageing are incompletely understood and could be crucial for the optimalisation of sarcopenia-related interventions.
- Therefore, we performed an observational trial to gain insight in potential sex differences in processes involved in human muscle-ageing.

METHODS

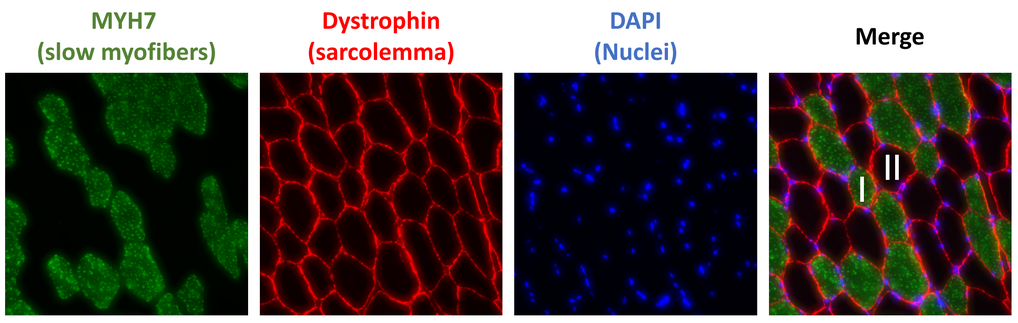
Old (80 ± 3.5 yrs, 26 males and 28 females) and young (23 ± 2.0 yrs, 13 males and 13 females) participants were compared for each sex separately. Males and females were highly matched regarding age, BMI and old participants for Fried frailty score as well. Lean mass, *vastus lateralis* muscle transcriptome and histological analyses were performed.

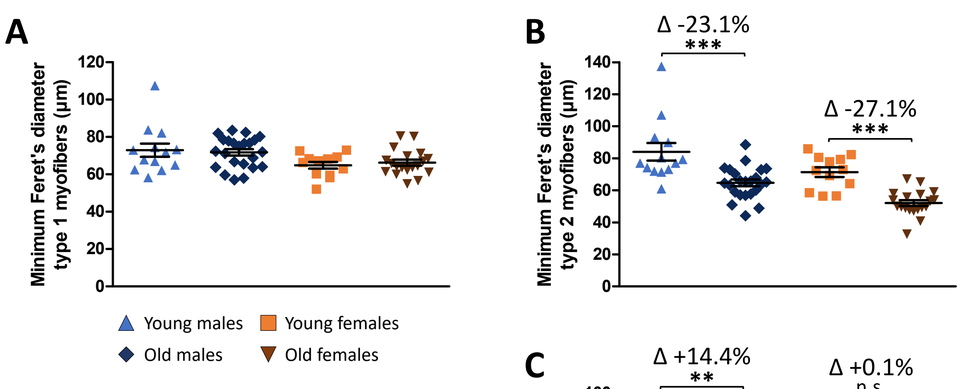
OLD GROUPS HAD LESS LEAN MASS IN LEGS THAN YOUNG GROUPS, BUT ONLY AGED MALES HAD LESS LEAN MASS IN ARMS

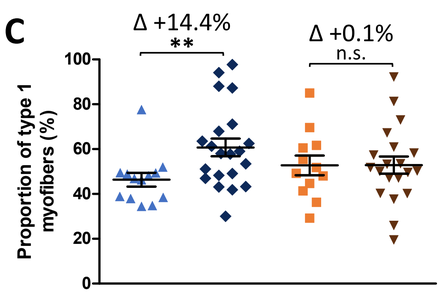


A. Old males, but not old females, had less absolute lean mass in upper arms compared to young controls.
B. However, in the legs, both old males and females had less absolute lean mass compared to young controls.

DIAMETER OF TYPE 2 MYOFIBERS DECREASED IN BOTH SEXES, BUT PROPORTION OF TYPE 1 MYOFIBERS INCREASED IN MALES ONLY

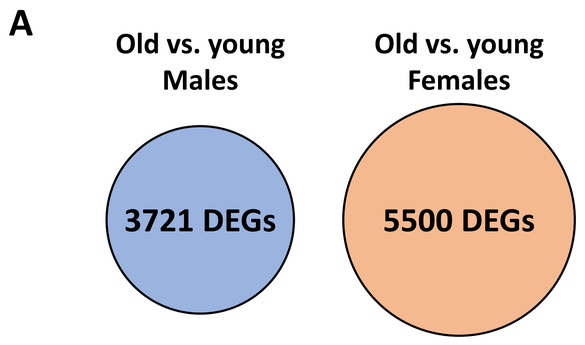


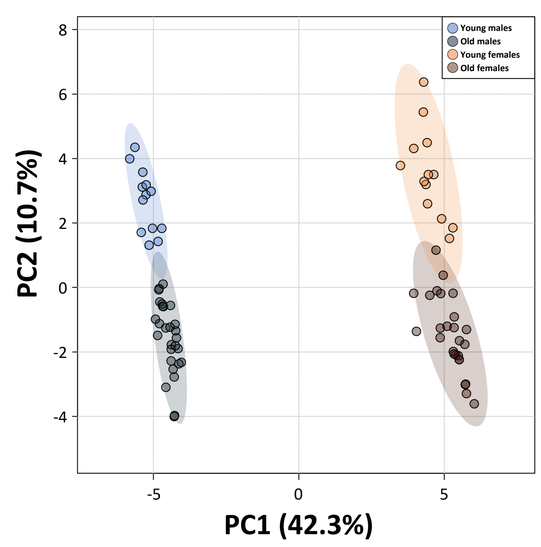




A. Diameter of type 1 (slow) myofibers was similar between old vs. young groups.
B. Diameter of type 2 (fast) myofibers was smaller in both old vs. young groups.
C. The proportion of type 1 myofibers was higher in old vs. young males, but not in old vs. young females.

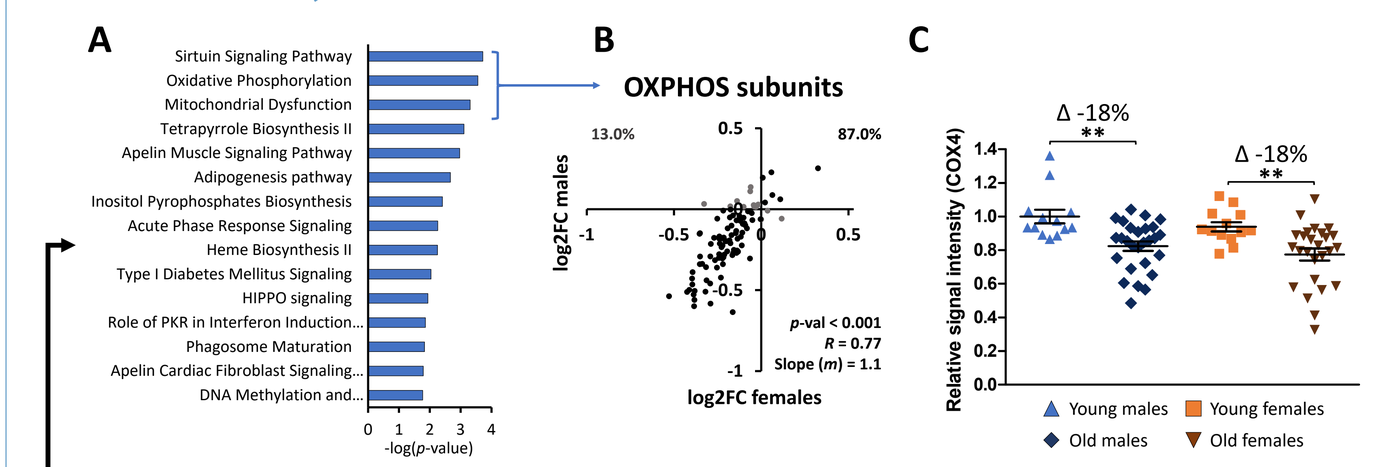
TRANSCRIPTOME PROFILES OF MALES AND FEMALES WERE DIFFERENT, BUT AGEING-TRAJECTORY WAS LARGELY SHARED



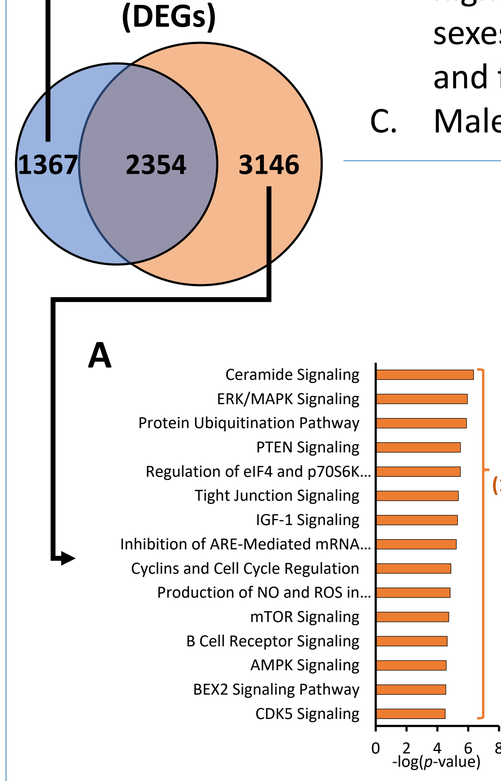


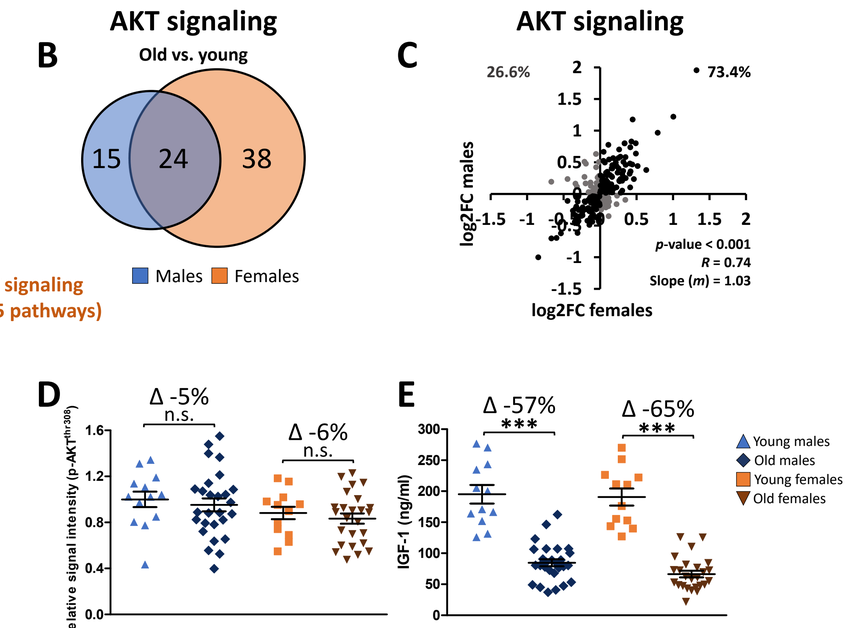
A. In males 3721 differentially expressed genes (DEGs) were found, whilst in females more DEGs were found, namely 5500.
B. PCA revealed clear separation of males and females, but young and old groups of males and females were orientated in a parallel manner, suggesting that ageing-related gene expressions patterns were shared between males and females.

HIGHEST RANKED PROCESSES IN MALES OR FEMALES WERE NOT SEX-SPECIFIC, BUT CHANGED WITH A DIFFERENT MAGNITUDE



A. Top pathways of male-specific DEGs were related to OXPHOS.
B. A correlation plot of genes encoding OXPHOS subunits revealed highly similar fold change values in old vs. young groups of both sexes. This indicated a similar loss of OXPHOS subunits in males and females during ageing.
C. Males and females displayed similar ageing-related loss of COX4.





A. AKT signaling was a common feature in top pathways of female-specific DEGs.
B. Females displayed more DEGs related to AKT signaling than males.
C. However, fold change values of genes involved in AKT signaling were highly similar in old vs. young males and females.
D. No differences in p-AKT^{thr308} were measured between old vs. young groups.
E. Males and females displayed similar ageing-related loss of circulating IGF-1.

CONCLUSIONS

Highest ranked processes differ between males and females, but were present and altered in the same direction in both sexes. We conclude that similar processes are associated with skeletal muscle-ageing in males and females, but the magnitude of differential expression in old vs. young participants is sex specific.

Acknowledgements: Reckitt / Mead johnson Nutrition Institute, Calico Life sciences, HistoIndex, dietician Berbée and InHolland University of Applied Sciences