IN VIVO OXIDATIVE CAPACITY VS. MITOCHONDRIAL VOLUME DENSITY IN SKELETAL MUSCLE OF AGE-MATCHED, ELDERLY ATHLETES AND SEDENTARY SUBJECTS – A MATTER OF FUNCTION AND CONTENT

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PURPOSE: Ageing is associated with a loss of both mitochondrial content and function[1]. However, chronic training may, at least partially, alleviate the decline in oxidative capacity[2]. We determined the rate of phosphocreatine (PCr) recovery after exercise to assess in vivo oxidative function and mitochondrial volume density (mitoVD; using muscle biopsies), a measure of mitochondrial content, in elderly (60-80y) endurance-trained athletes (A) vs. sedentary (S) subjects. This allows addressing the question if the muscular oxidative capacity is increased in A and if this is associated with an increase of the mitochondrial content and/or function.

METHODS:

Subjects were allocated to A or S based on their level of self-reported physical activity (A: 3 and more structured aerobic exercise sessions/week; S: one or less days per week of structured exercise sessions). 11 athletes (4f) and 13 sedentary (6f) subjects were included in this study. All subjects were in general good health, non-diabetic and non-smoker. While PCr recovery was analyzed in all subjects, mitoVD was available from 7 subjects in A and 10 subjects in S.

VO_{2peak}: VO_{2peak} was determined by a cycle ergometer maximal graded exercise test adapted to this population[3]. VO_{2peak} is expressed relative to lean body mass (assessed using DEXA).

PCr recovery: Experiments were performed on a 3T MR-system (VERIO, Siemens, Erlangen Germany). A double-tuned $^{31}P/^{1}H$ surface coil (RAPID Biomedical, Rimpar Germany) was placed on the center of the thigh and FIDs (adiabatic excitation pulse) were collected with a TR of 2s, averaged over 2 spectra, resulting in a time resolution of 4s. Exercise: dynamic knee extensions against a rubber band (supine position, 1 extension/s, different resistance levels, adapted to each subject's strength) were used. Default exercise duration was 28s, spectra were obtained before, during and for 9min after the end of exercise. If the decrease of PCr was outside the target of 20 to 40%, exercise duration was changed to 22s, 36s, or 44s; otherwise it was unchanged for a 2nd repetition. Since pH did not decrease below 6.8 in any experiment, and because the recovery rates of experiment 1 and 2 were not significantly different from each other (p=0.13), the results are shown as average of the 2 experiments. Post-processing: Spectra were analysed with jMRUI, using AMARES for quantitation. The recovery of PCr was fitted to the formula $PCr(t)= PCr0 + \Delta PCr\cdot(1-e^{-k\cdot t})$; with PCr0: PCr-intensity at the beginning of recovery; ΔPCr: exercise-induced decrease of the PCr-signal. pH was calculated from the chemical shift between inorganic phosphate and PCr.

MitoVD: Muscle biopsy samples were obtained from m. vastus lateralis. Twenty micrographs of the intramyofibrillar region were taken per subject with a transmission electron microscope (FEI CM100) with 33000x. A point counting technique was used with grids composed of 500nm squares, allowing computing the percentage of the image covered by mitochondria[3].

Data analysis: T-tests and linear regression were performed. Results are expressed as mean ± 1 standard deviation.

RESULTS:

Table 1 displays the anthropometric data, the results of the PCr recovery experiment, and MitoVD. The rate constant k was significantly higher in A than in S, while end-exercise pH, minimum pH, and relative decrease of PCr were not different between the 2 groups. MitoVD was significantly higher in A vs. S, while the ratio k to MitoVD was not significantly different between the 2 groups (**Table 1**). The rate constant k correlated with mitoVD over the 2 groups (r^2=0.46, p<0.003; **Figure 1**), but not within the groups (r^2=0.08, p=0.5 and r^2=0.16, p=0.2 for A and S respectively). The rate constant k was not significantly correlated with VO_{2peak}, neither over the 2 groups, nor within the groups.

	A (N=11, 4f)	S (N=13, 6f)	*p-value*
Age [y]	69 ± 5	66 ± 2	*0.07*
BMI [kg·m^{-2}]	21.5 ± 1.5	28.0 ± 4.8	*<0.001*
VO_{2peak} [ml·min^{-1}·kg$_{LBM}^{-1}$]	47 ± 6	38 ± 7	*0.002*
k [min^{-1}]	2.34 ± 0.33	1.92 ± 0.41	*0.01*
$pH_{end\ exercise}$	7.11 ± 0.03	7.12 ± 0.02	*0.2*
pH_{min}	6.94 ± 0.04	6.96 ± 0.04	*0.2*
Decrease of PCr [%]	29 ± 7	32 ± 6	*0.3*
MitoVD [%] *	7.4 ± 1.5	4.9 ± 1.1	*0.02*
k /MitoVD [min^{-1}·%$^{-1}$]*	0.34 ± 0.07	0.39 ± 0.10	*0.3*

Table 1: Anthropometric data, PCr recovery rate, and MitoVD in athletes (A) and sedentary (S). *: Obtained from 7 A and 10 S; LBM: lean body mass

DISCUSSION AND CONCLUSION:

A reduction of oxidative capacity and mitochondrial density with age has been reported in literature[1]. This study, however, is now investigating the effect of chronic training on the ageing metabolism. The main finding was that in elderly volunteers, endurance-trained subjects display a greater in vivo oxidative capacity, as determined by the rate of PCr recovery, compared to age-matched sedentary subjects. This is paralleled by a ~50% greater mitoVD in the trained. Furthermore, the ratio k to mitoVD was not different between athletes and sedentary subjects, indicating that the increased oxidative capacity in our trained elderly subjects is due to elevated mitochondrial volume, while there is no evidence of increased function per mitochondrial volume. This is further supported by the observed strong correlation of k and mitoVD over the 2 groups. Of note, k was not significantly correlated with VO_{2peak}, possibly indicating that at least in some volunteers of this population, VO_{2peak} might be limited by other factors (e.g. cardiovascular limitation).

An intervention study in elderly subjects is required to further elucidate the effects of endurance training on oxidative capacity, mitoVD, and function per mitochondrial volume unit.

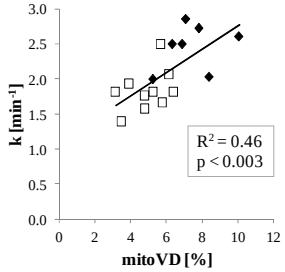

Figure 1: The rate constant k of PCr recovery vs. mitochondrial volume density (mitoVD)

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