UHASSELT

Ketones in exercise, training and rehabilitation

Prof. Dr. Chiel Poffé
Exercise and muscle physiology
Rehabilitation Research Center
UHasselt (Belgium)

KU LEUVEN

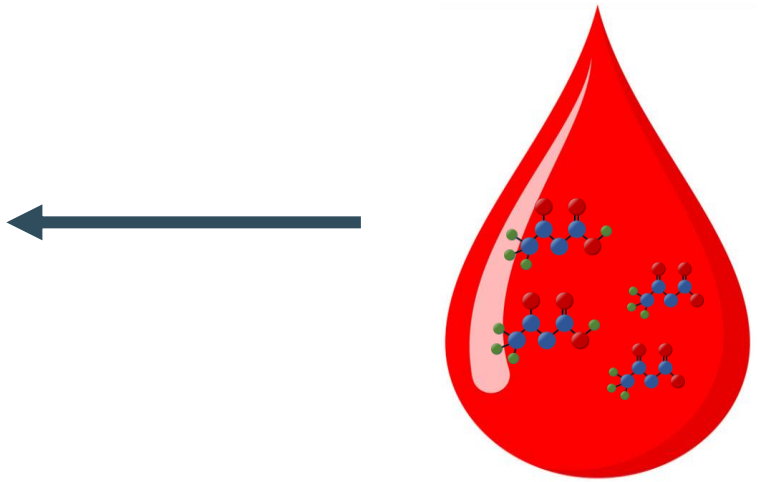
fwo

Danish Cardiovascular Academy

Why ketones during exercise & training? (in 2014)

Energy substrate

“The fourth fuel”



Ketosis

Signalling molecule

Erythropoiesis (1)

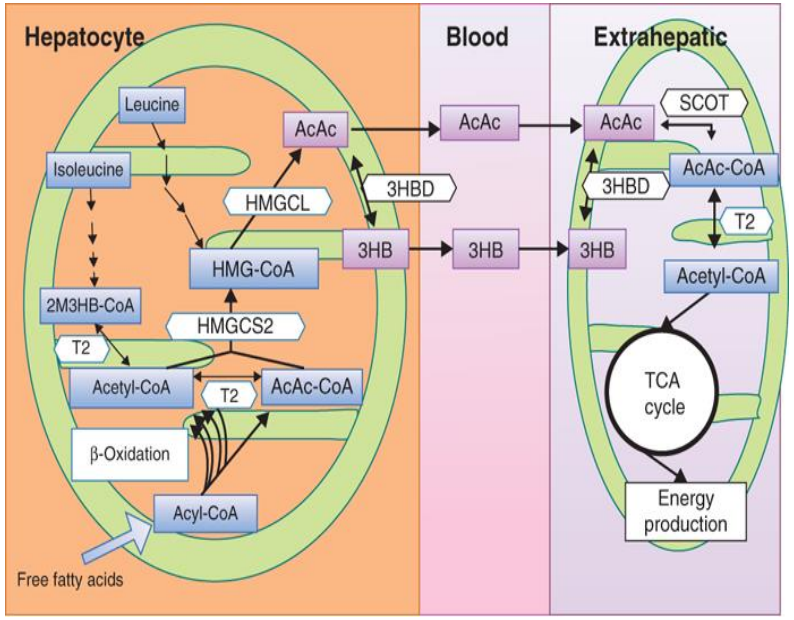
Angiogenesis (2)

Sympathetic activity (3)

...

(1) Evans, E. et al. Am. J. Physiol. Endocrinol. Metab. 324, E56–E61 (2023)
(2) Poffé, C. et al. J. Physiol. 12, 2345–2358 (2023)
(3) Robberechts, R. et al. J. Appl. Physiol. 449–460 (2022)

Ketones: a “superfuel” for athletes?



Sparing other energy sources (e.g., muscle glycogen)

Higher “metabolic efficiency” (1)

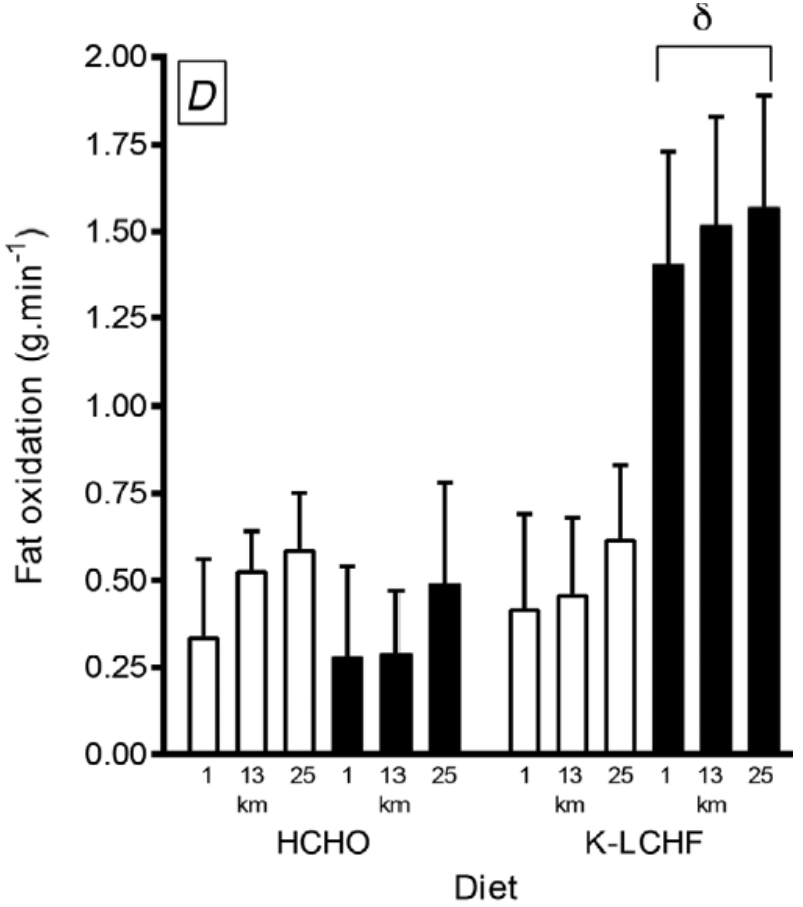
	Control, n = 8	Insulin,[b] n = 5	Ketones,[c] n = 5	Ketones and insulin, n = 5
Hydraulic work, J·min^{-1}·g wet wt^{-1}	0.30 ± 0.01	0.34 ± 0.01[d]	0.37 ± 0.01[d]	0.32 ± 0.01
O_2 consumption, μmol·min^{-1}·g wet wt^{-1}	6.5 ± 0.1	5.6 ± 0.1[d]	6.0 ± 0.2[d]	5.4 ± 0.4[d]
Cardiac efficiency, %	10.5 ± 0.3	13.4 ± 0.6[d]	13.0 ± 0.2[d]	14.3 ± 1.3[d]

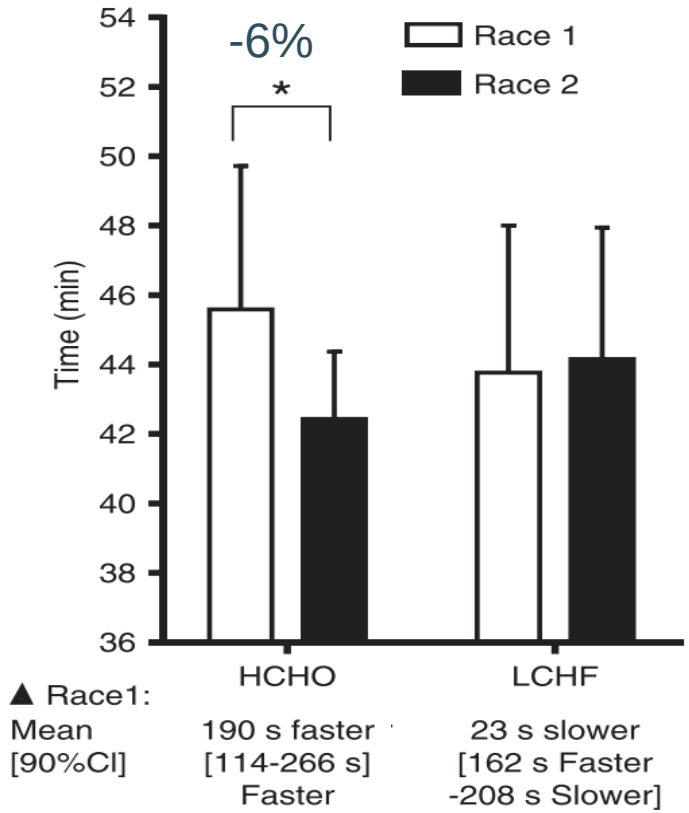
[a]Data are means ± SE. Control = 10 mM glucose perfusion. [b]Insulin: 100 nM. [c]Ketone bodies: 4 mM D-β-hydroxybutyrate + 1 mM acetoacetate. [d]$P < 0.05$ compared to control, determined using the Mann-Whitney U test.

+24% +36%

Saraflogou et al. (2017)
(1) Sato et al., *FASEB* (1995)

Endogenous ketosis not suitable for most athletes



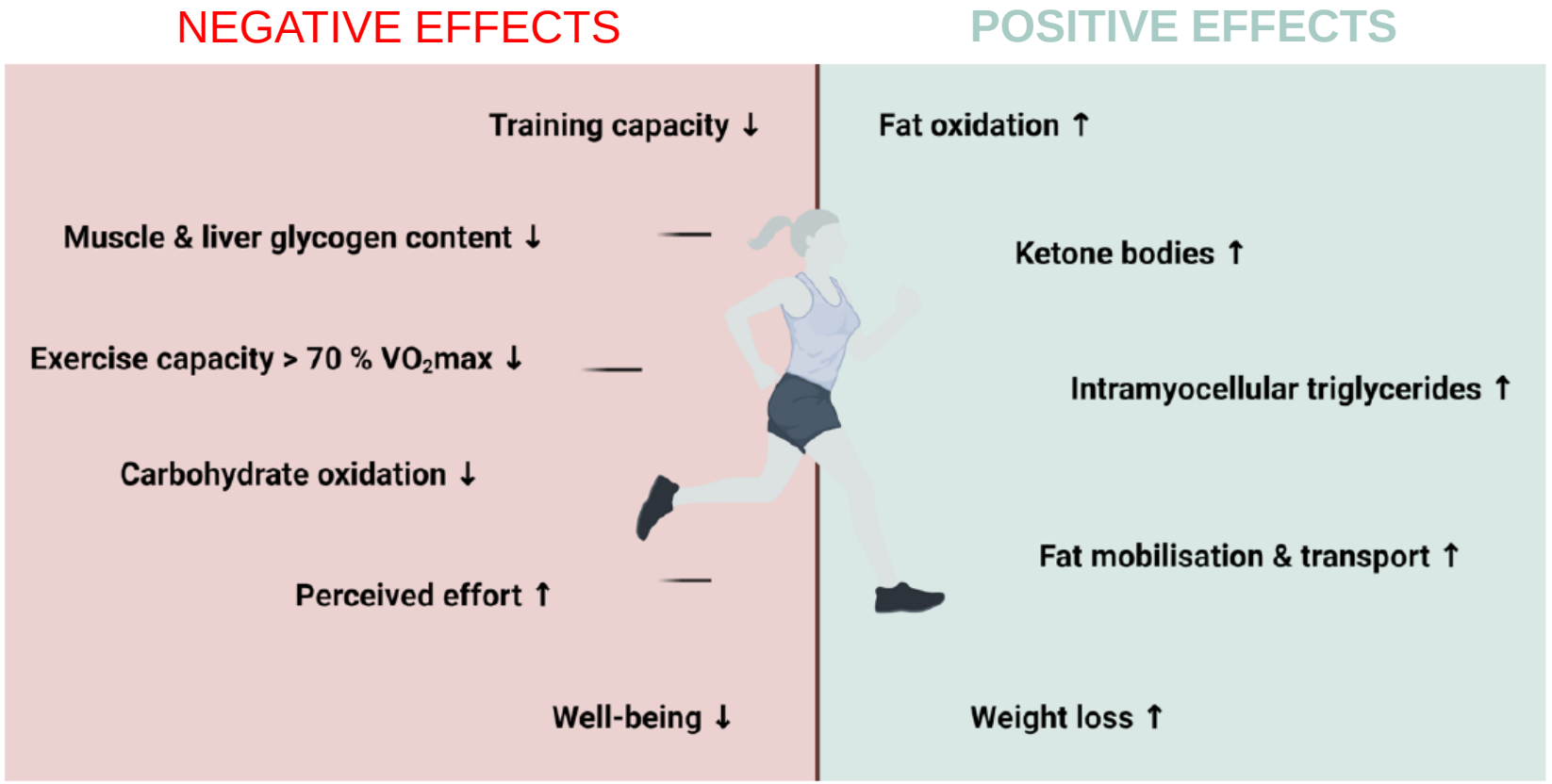


For each mole O_2 **6% more ATP with CHO vs. FAT**

Burke et al., *J Physiol* (2017)

UHASSELT

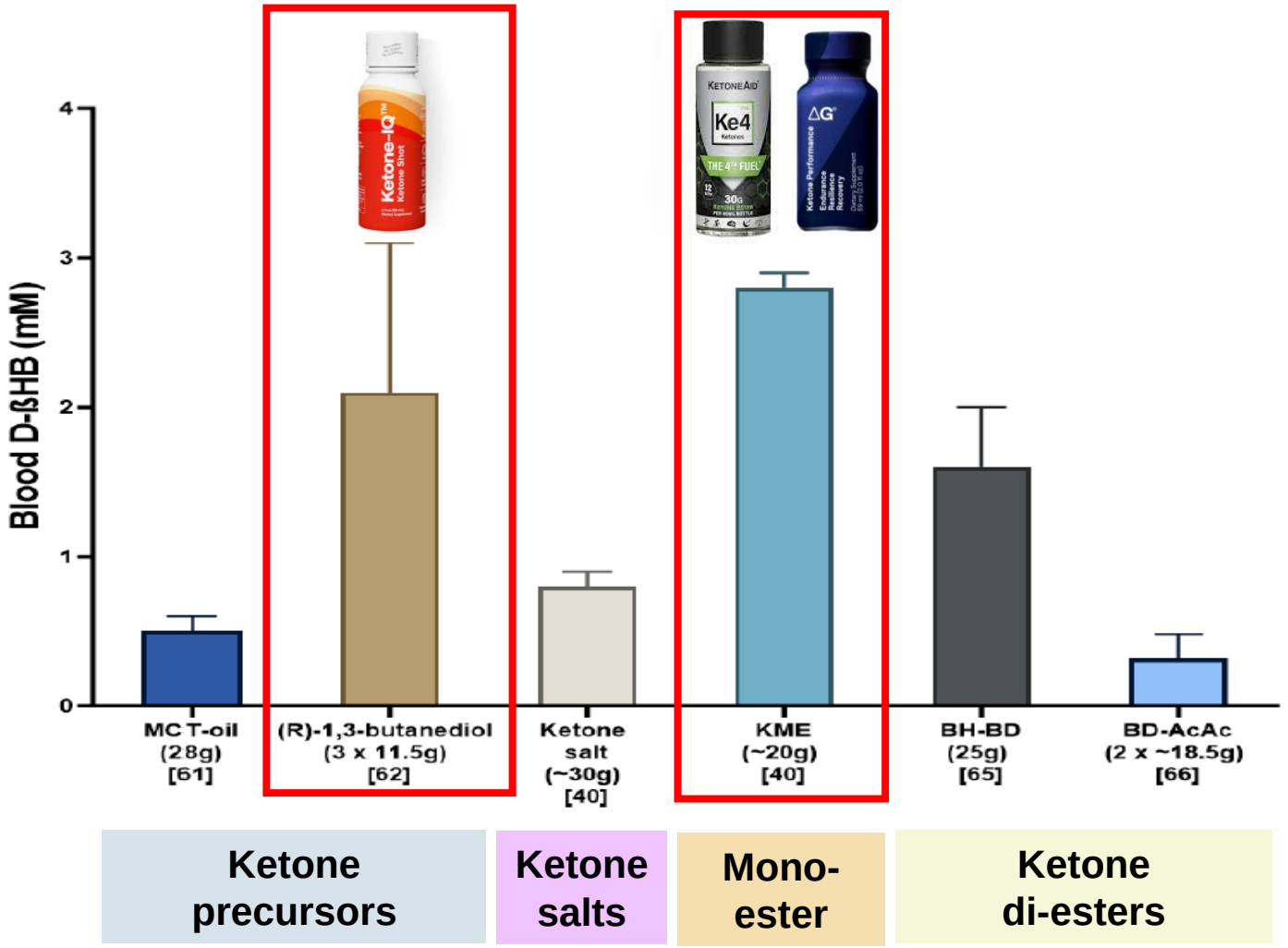
Endogenous ketosis not suitable for most athletes



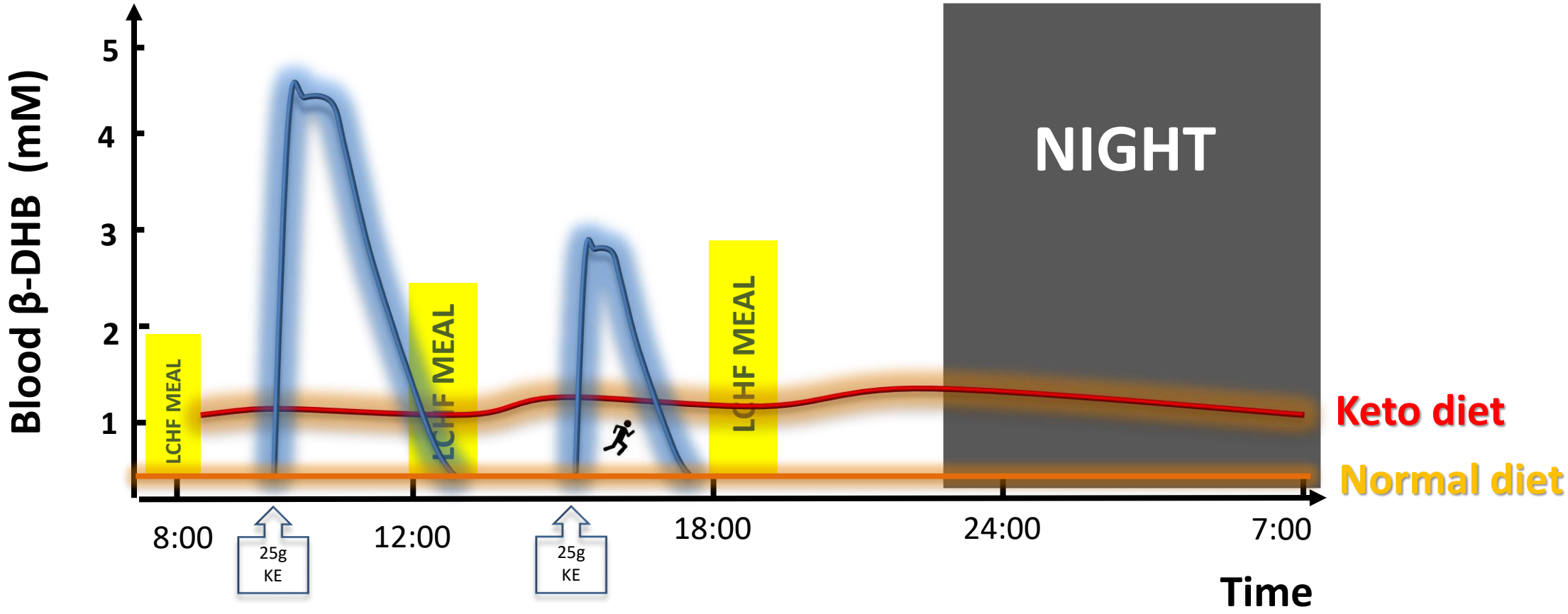
Ruben Robberechts, *PhD thesis* (2024)

Fake ‘keto’ supplements

Ketone supplements



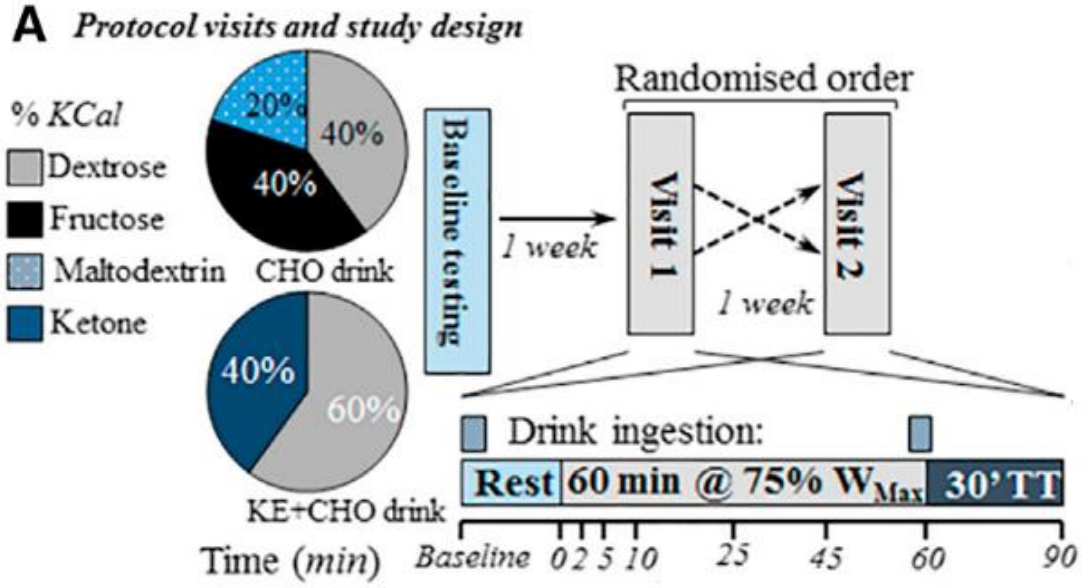
Ketone supplements *vs.* ketogenic diet

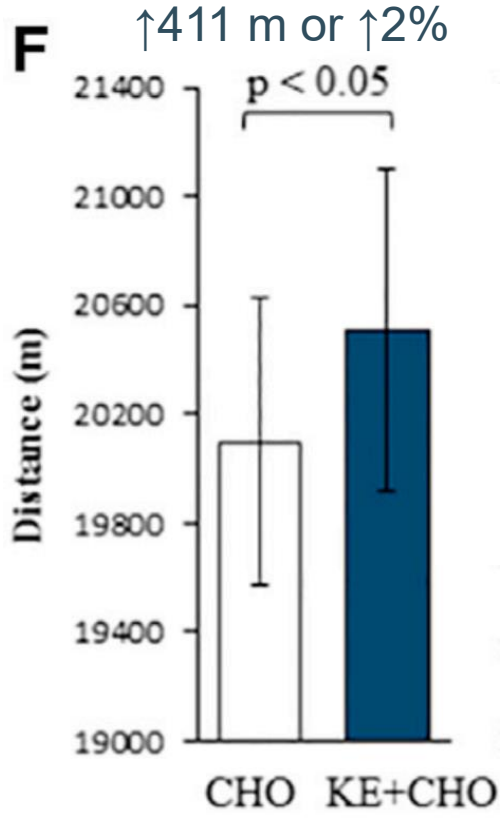


How to use ketones to improve performance?

During exercise
to improve
endurance exercise performance

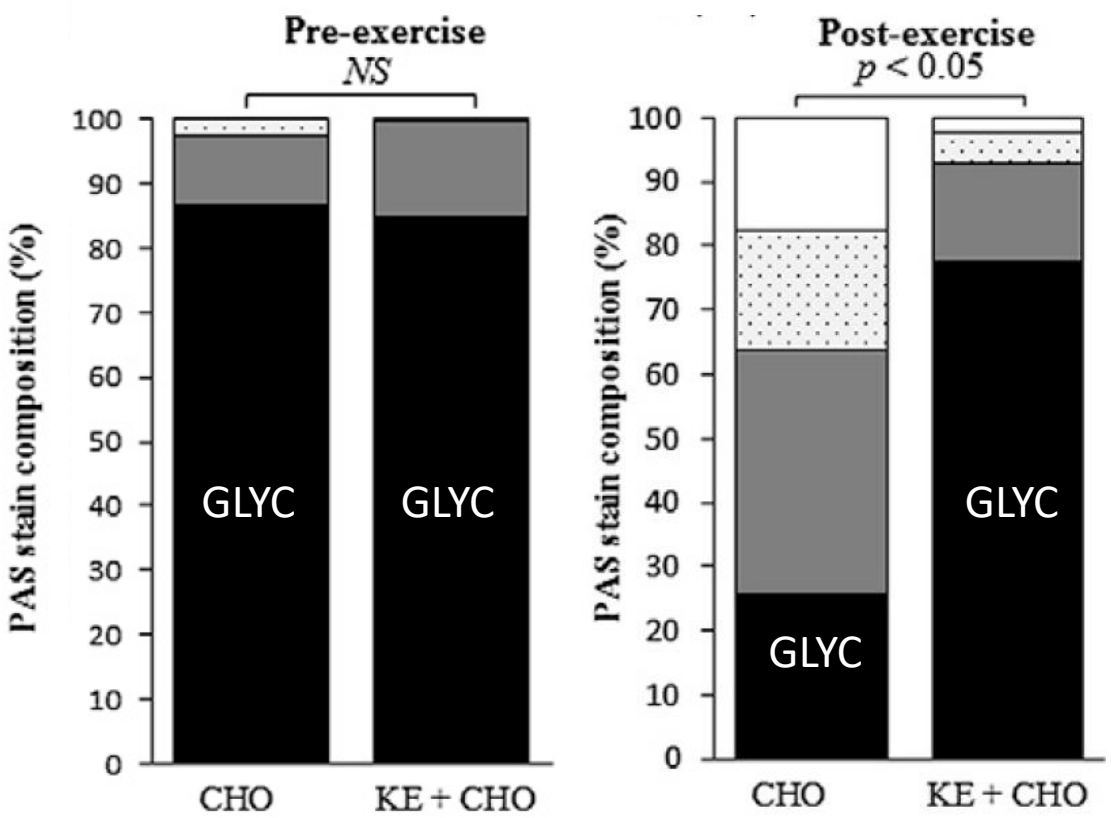
KE improved cycling time-trial performance

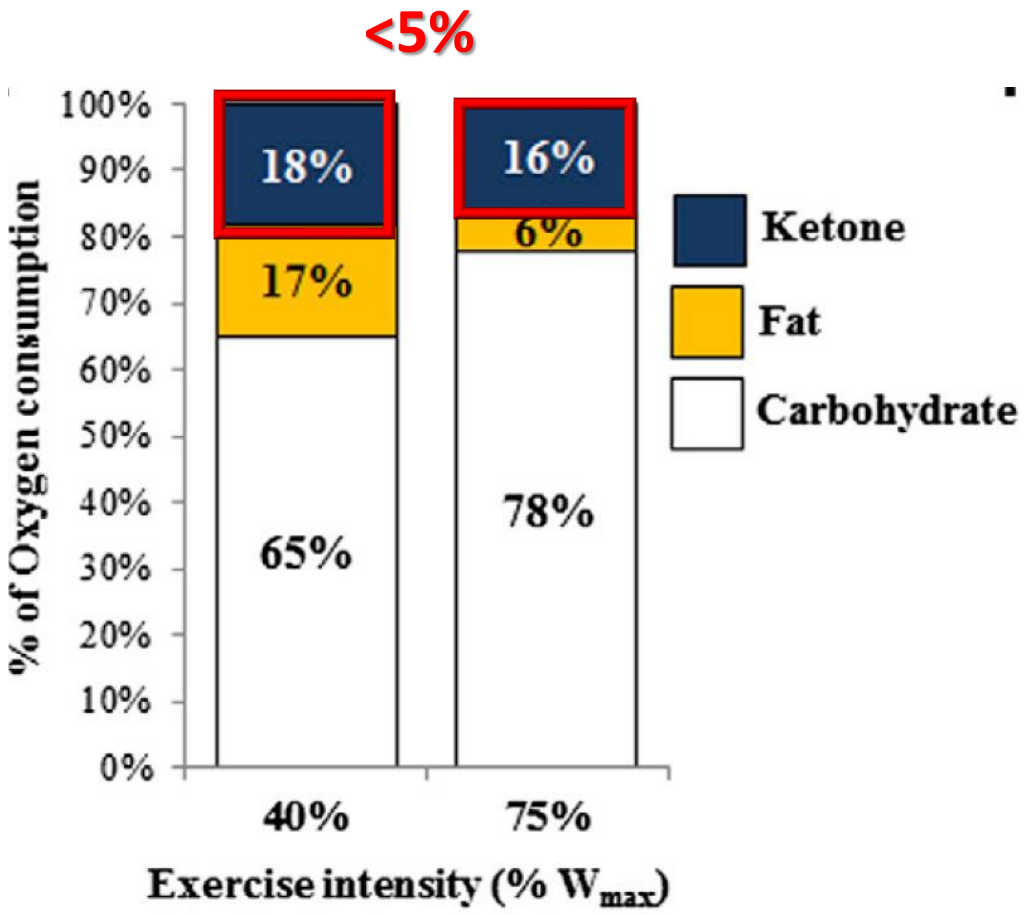




Cox et al., *Cell Metabolism* (2016)

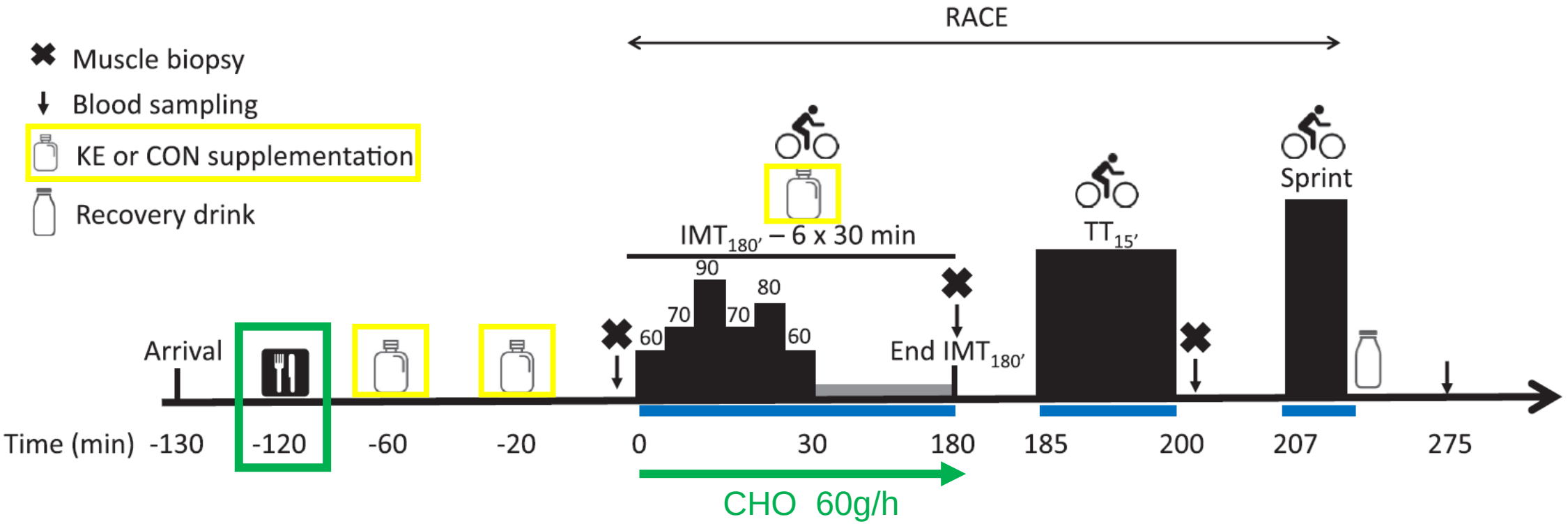
Mechanism: glycogen sparing + extra energy source





Dearlove et al., *MSSE (2020)*

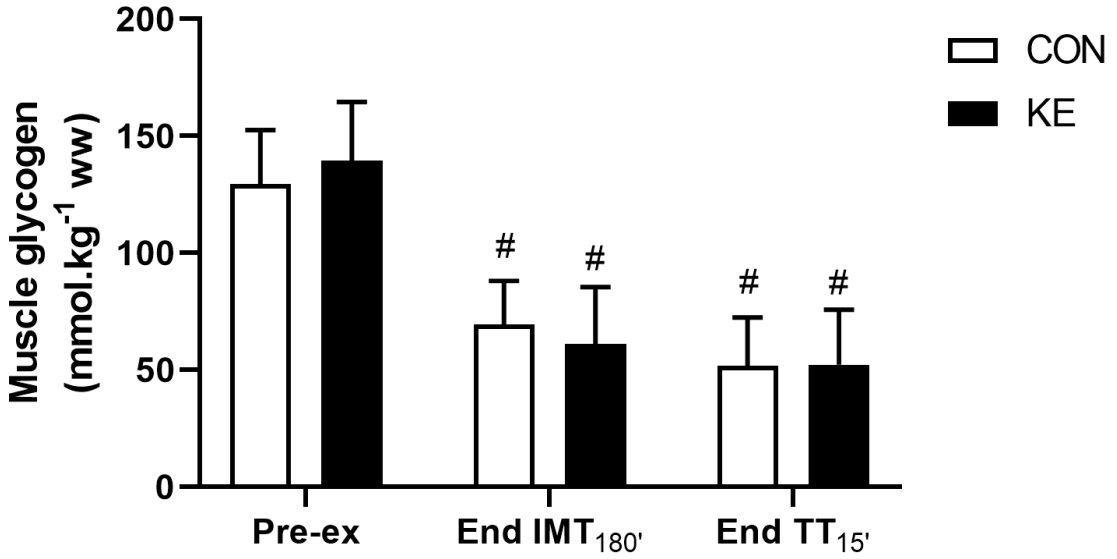
Glycogen sparing in simulated cycling race?

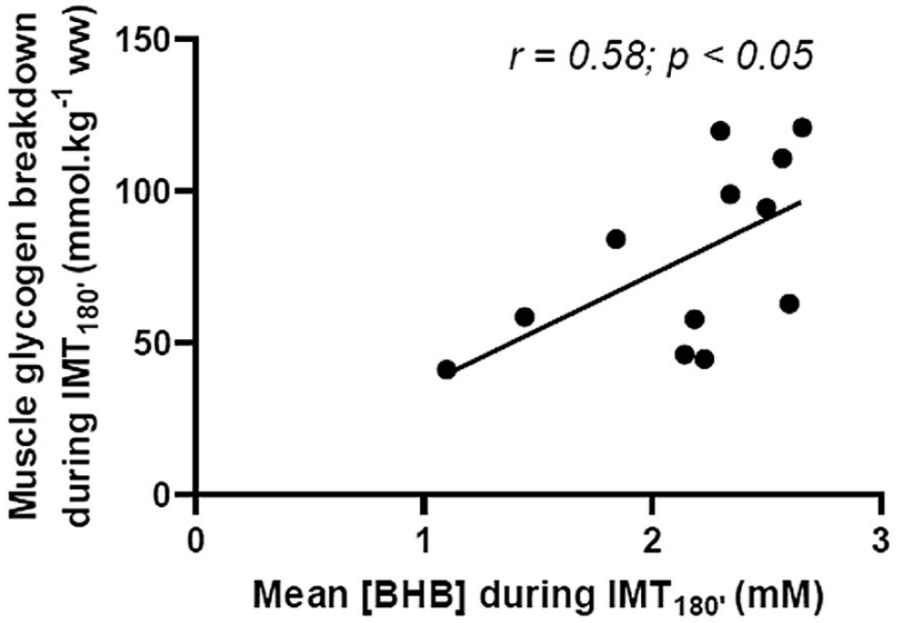


Poffé et al., J Appl Physiol (2020)

UHASSELT

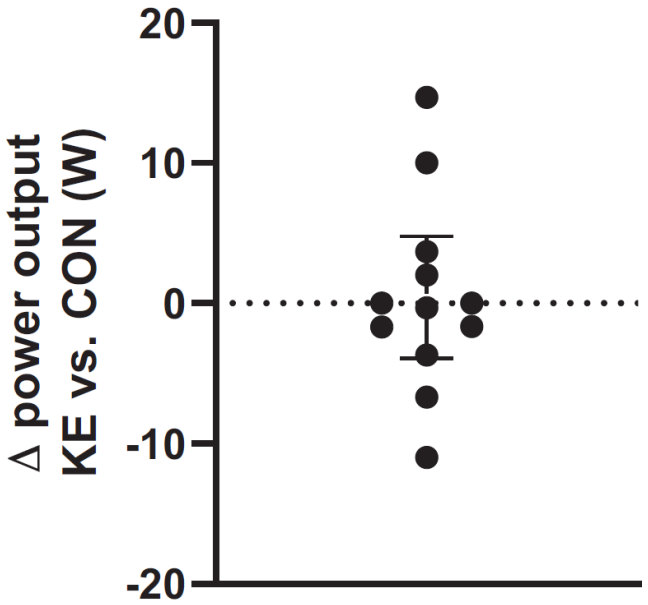
No glycogen sparing effect



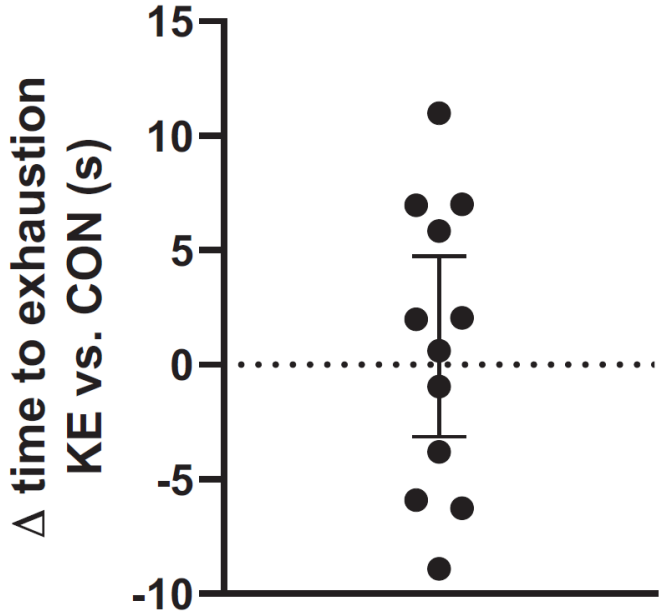


No performance effect

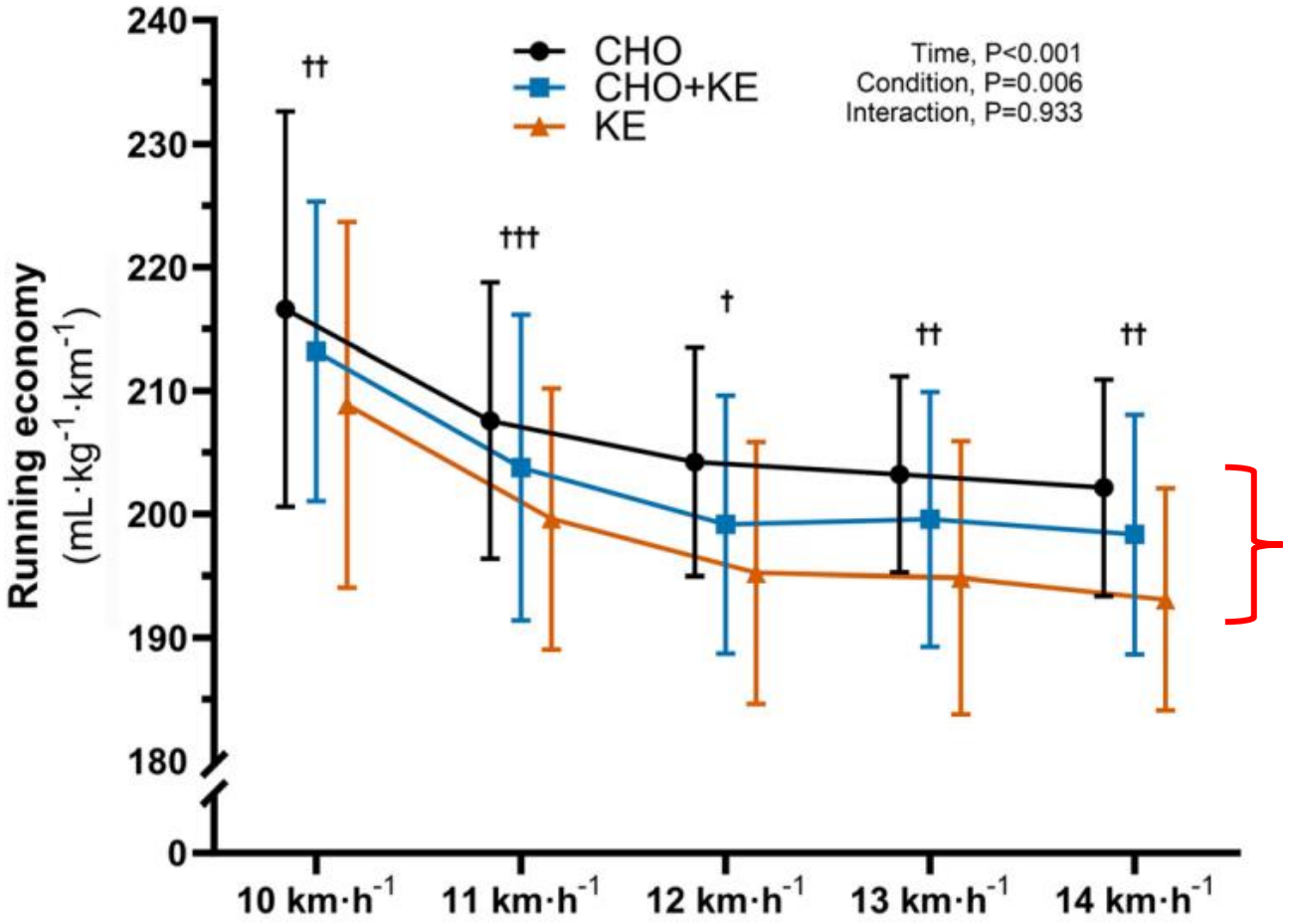
15-min TT



Sprint



Carbohydrates negate the KE-induced increase in exercise efficiency

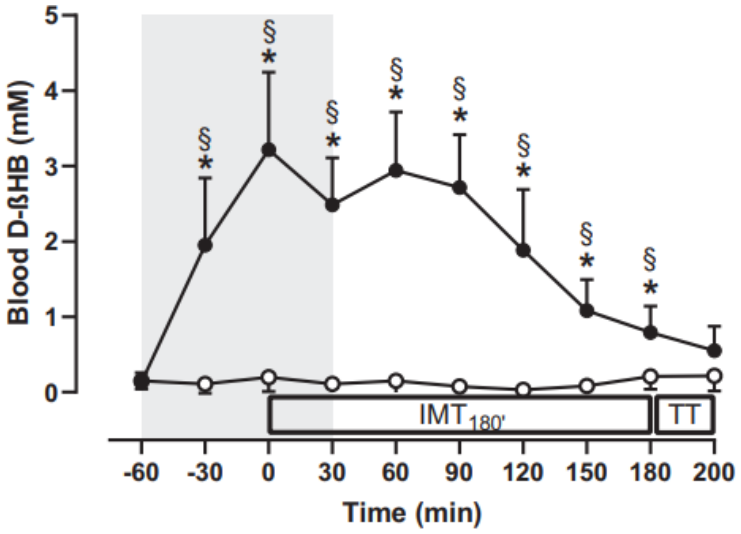


P < 0.05
KE *vs.* CHO

Brady & Egan, *MSSE* (2023)

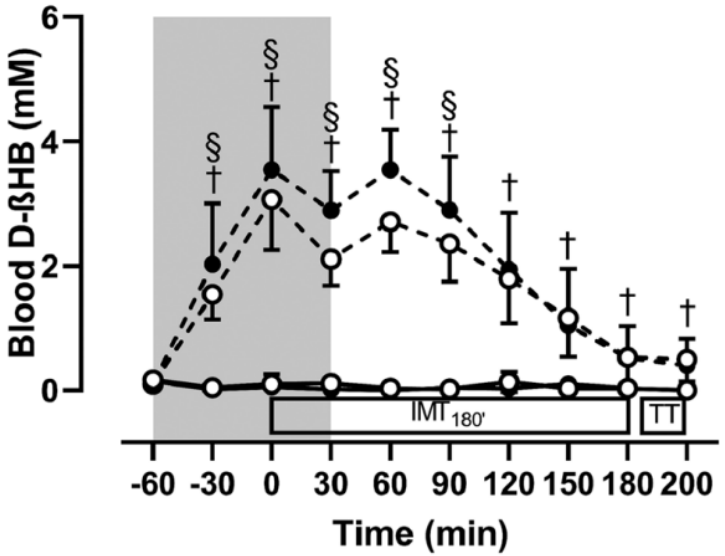
UHASSELT

No (positive) performance effect



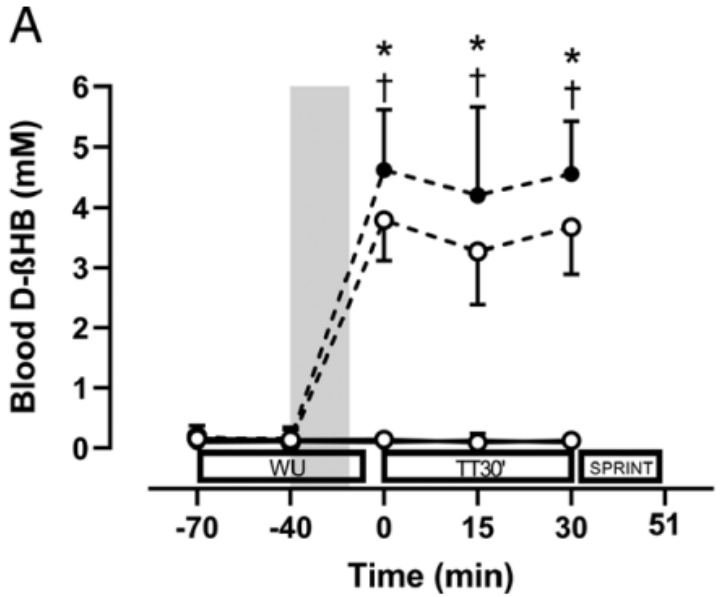
Poffé et al., *JAP* (2020)

No effect



Poffé et al., *MSSE* (2021)

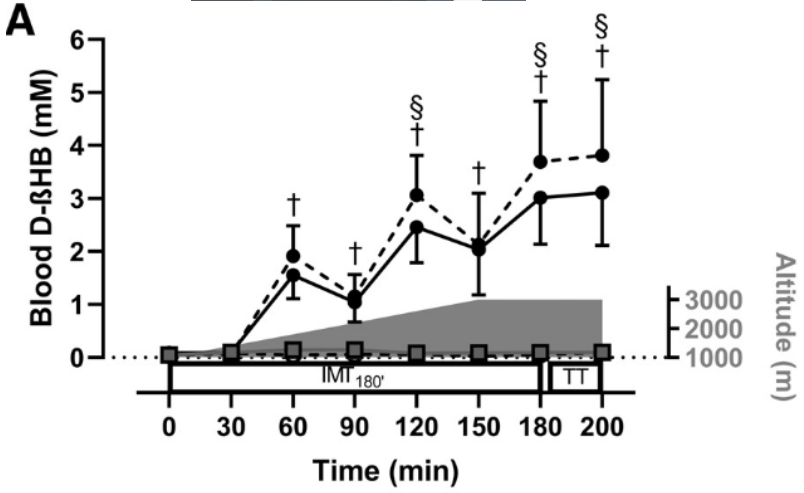
No effect



Poffé et al., *MSSE* (2021)

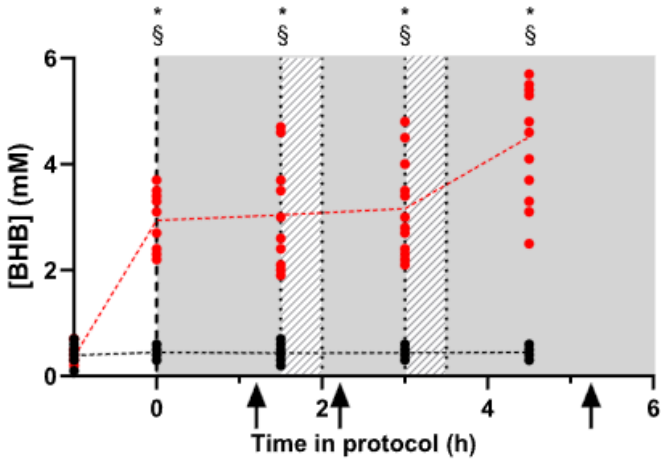
-1.5% (30 min TT)

No (positive) performance effect



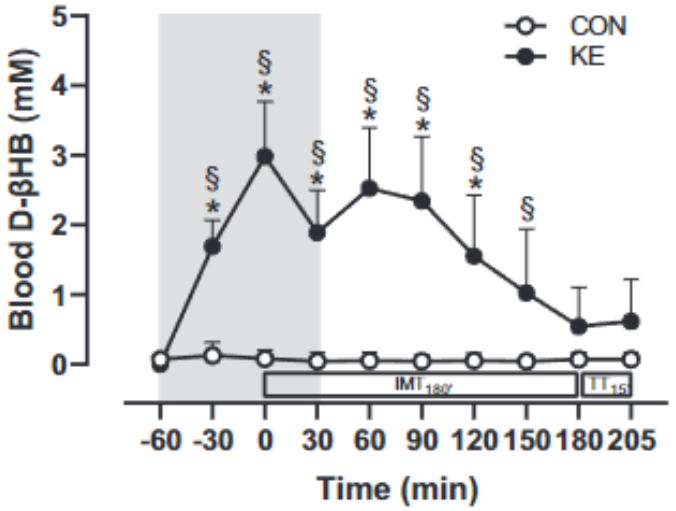
Poffé et al., *AJP* (2021)

No effect



Stalmans et al., *unpublished*

-3.5% (30 min TT)



Robberechts et al., *JAP* (2022)

No effect

Should you take ketones during exercise?

15s | 20 min | 60 min | 3h + 15 min TT

Evans et al., *MSSE* (2018)
Waldman et al., *Appl Physiol Nutr Metab* (2018)

Leckey et al., *Front Physiol* (2017)
Poffé et al., *MSSE* (2020)
McCarthy et al., *Int J Sport Nutr Exerc Metab* (2023)

Poffé et al., *J Appl Physiol* (2020)
Poffé et al., *MSSE* (2021)
Robberechts et al., *J Appl Physiol* (2022)

When CHO intake is adequate

UHASSELT

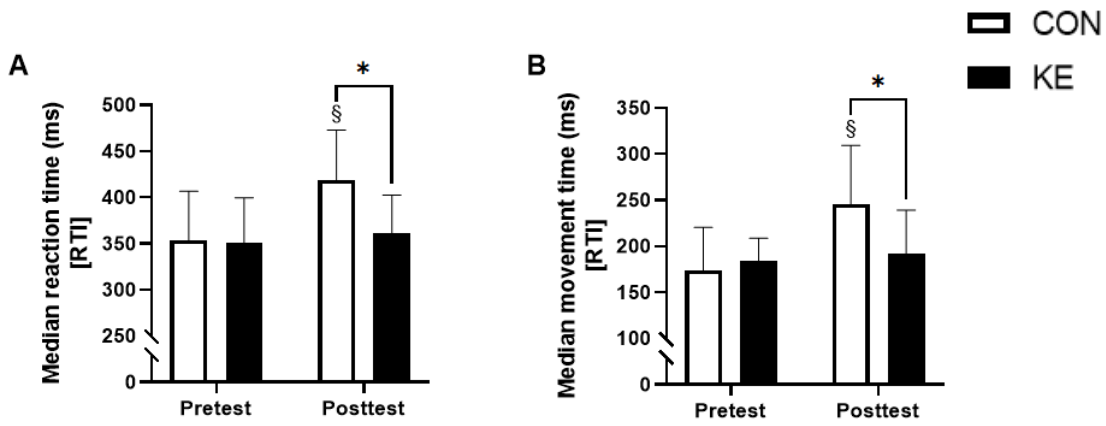
Should you take ketones during exercise?

?

15s | 20 min | 60 min | 3h + 15 min TT

100km ultrarun

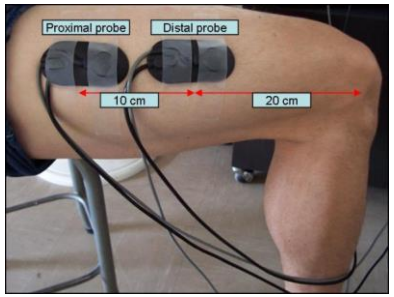
25g KE/h *vs.* placebo

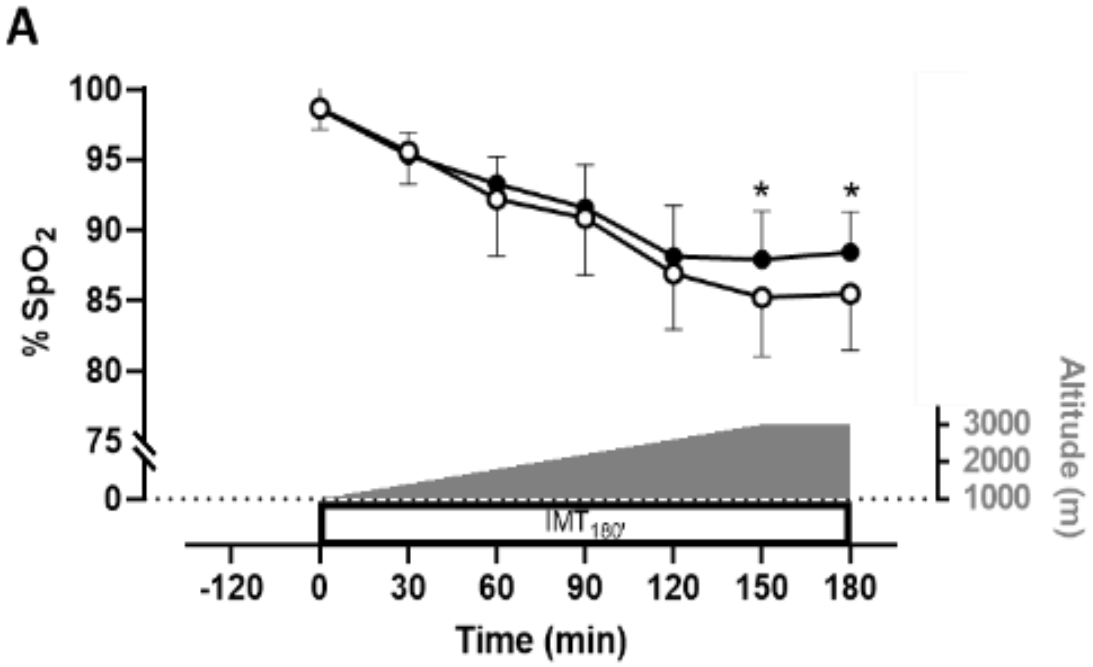


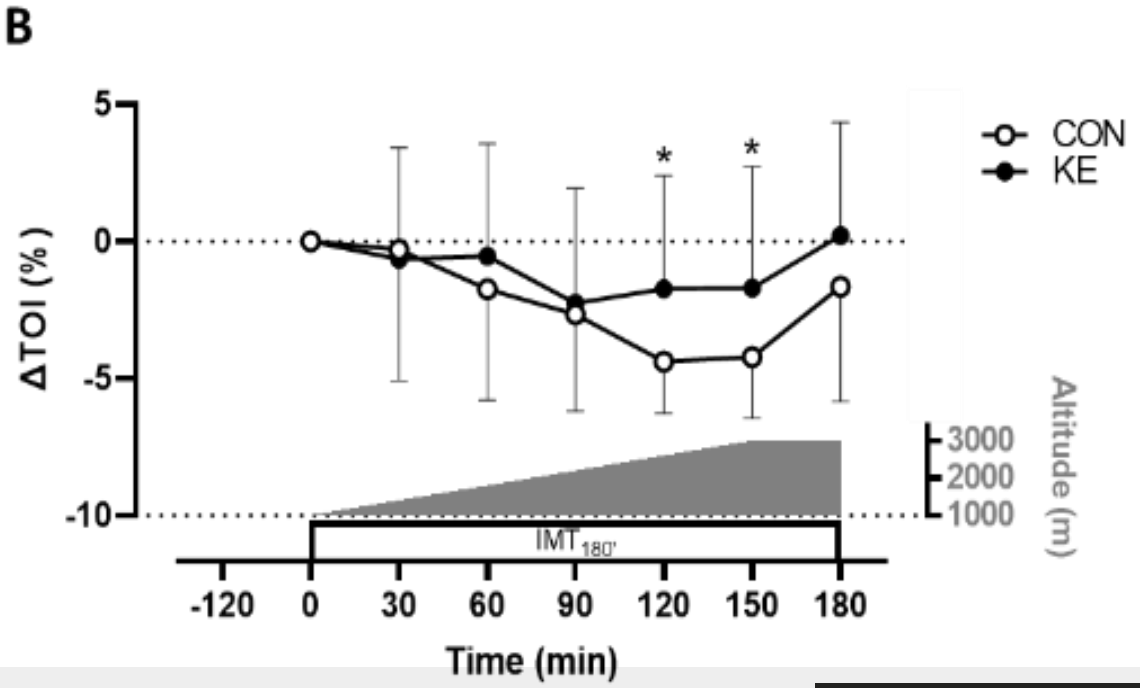
Poffé et al., *J Appl Physiol* (2023)

UHASSELT

KE attenuates oxygen desaturation during hypoxic exercise







Poffé et al., *AJP – Physiol Regul Integr Comp* (2021)

UHASSELT

Beneficial effect on high-altitude sickness?

Acute Mountain Sickness
(AMS)

2500m : ~25% of individuals

4000m: ~50% of individuals

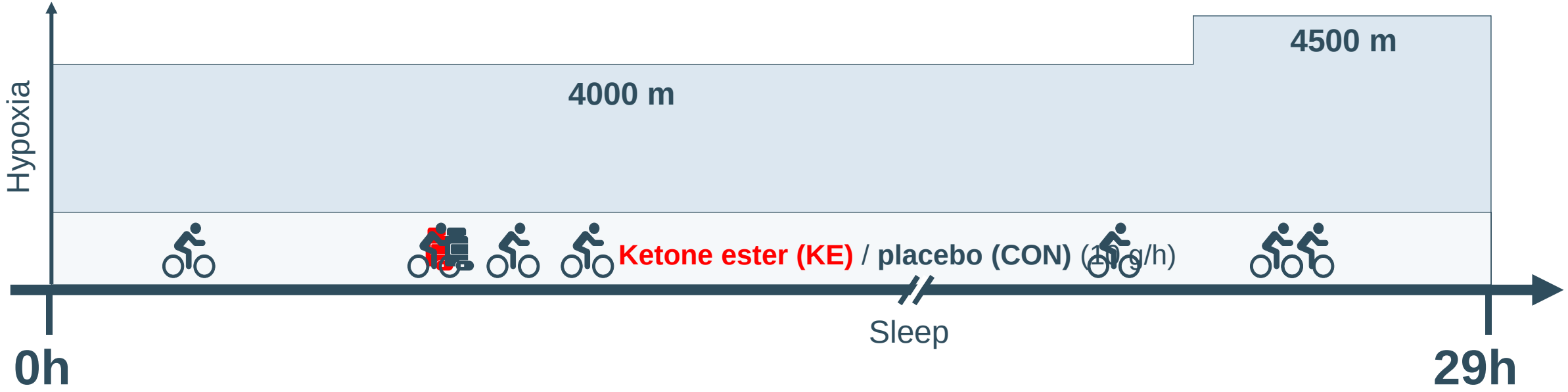
Headache

Nausea

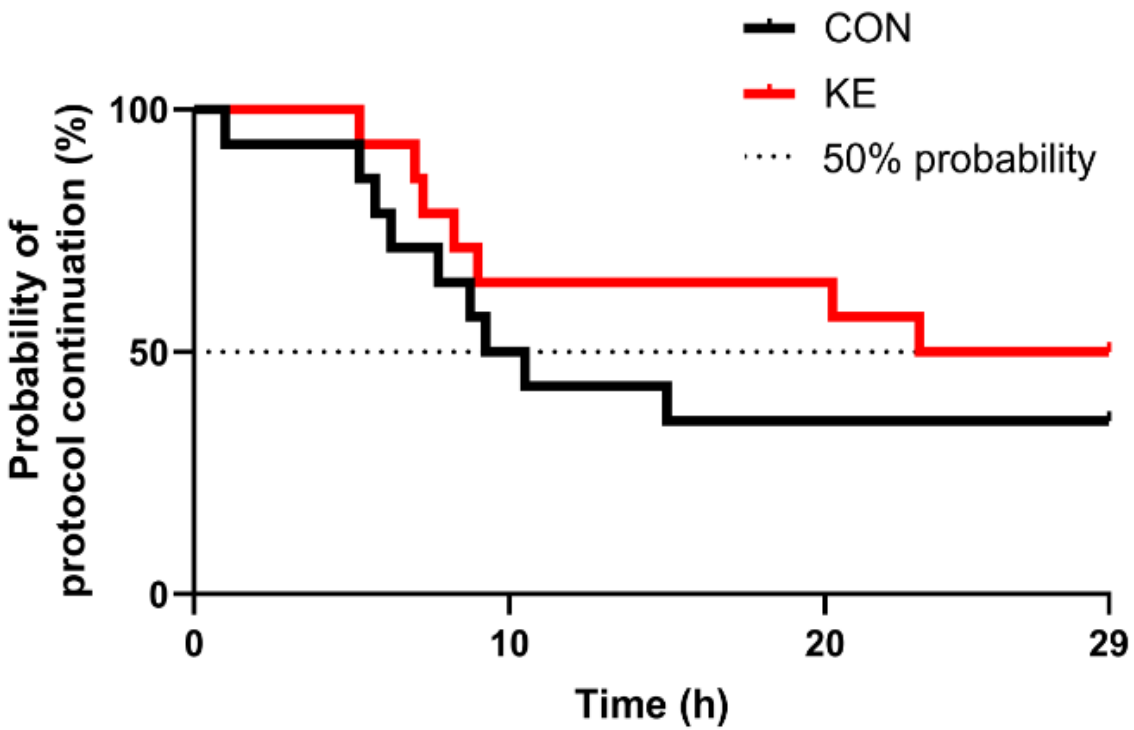
Dizziness

Fatigue

n = 14
18-35 years old, male
Cross-over design

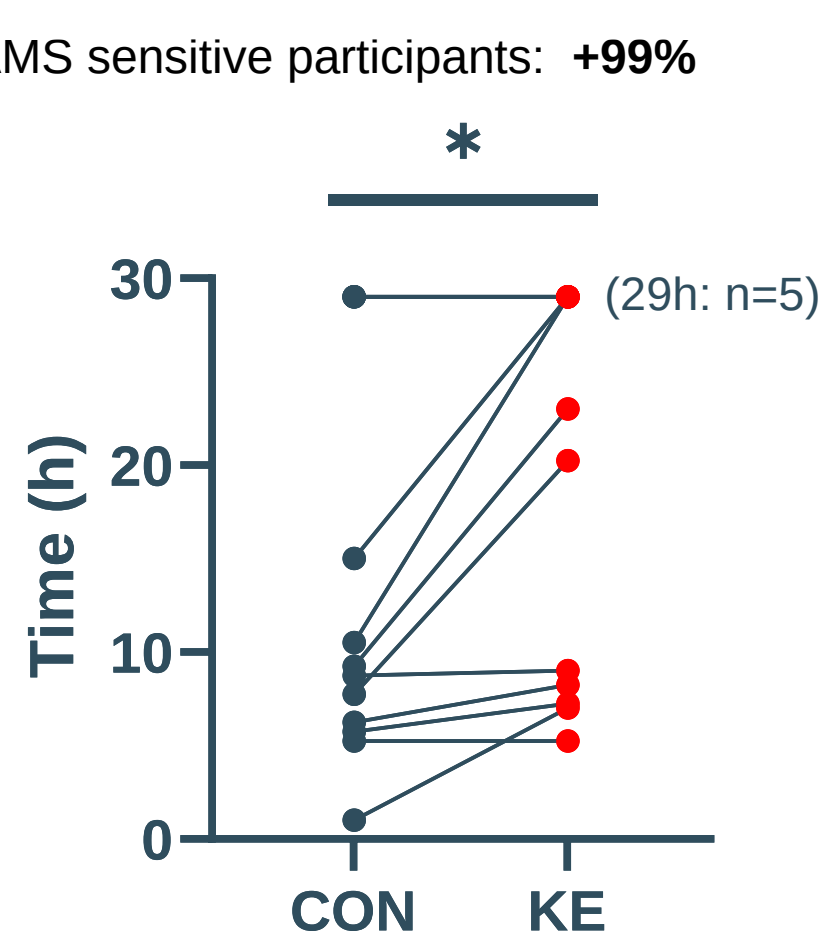


KE increases hypoxic tolerance



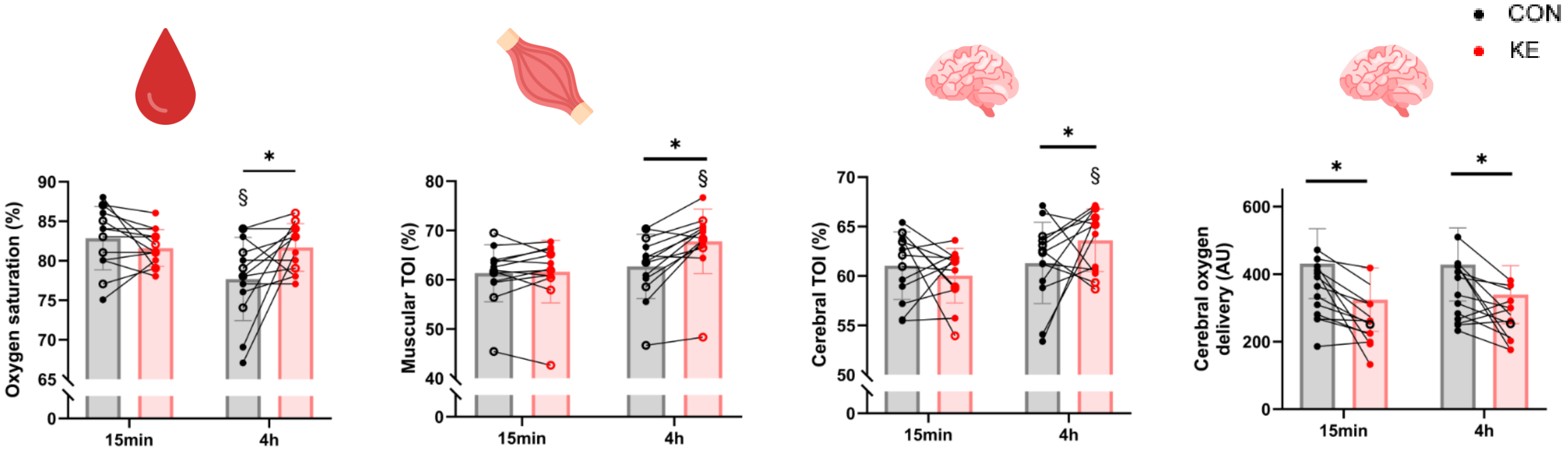
All participants: **+32%**

AMS sensitive participants: **+99%**



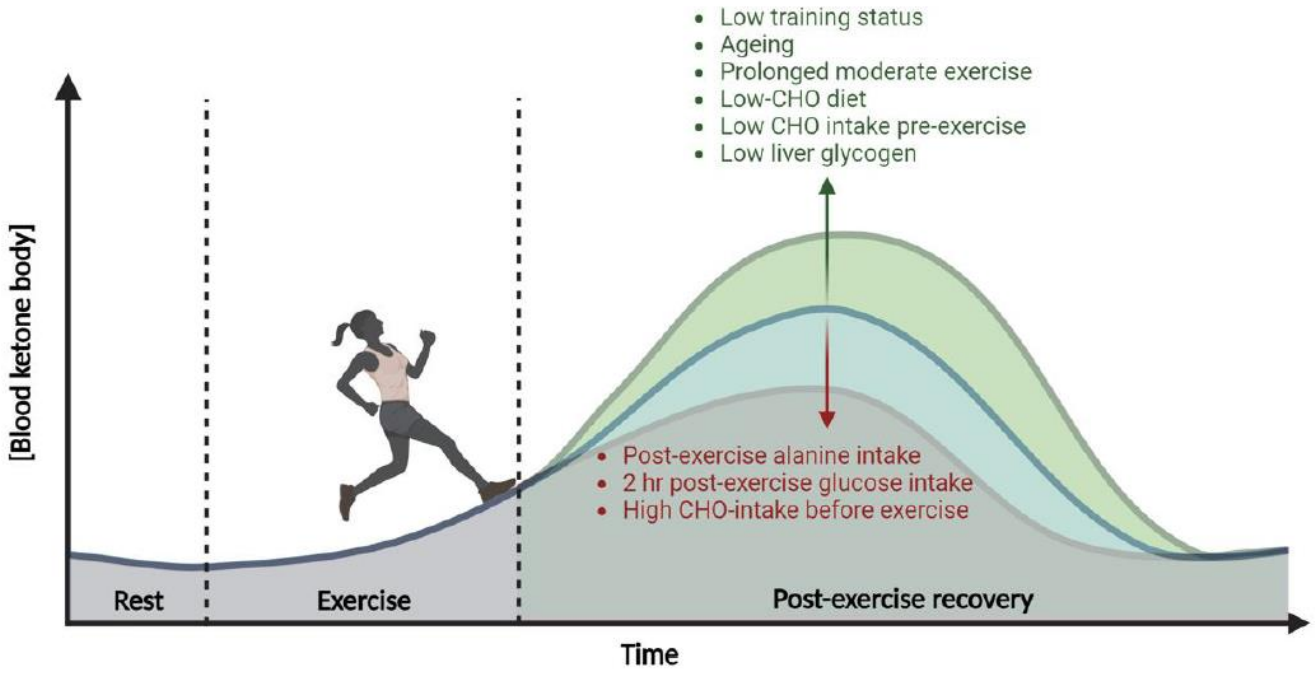
UHASSELT

KE attenuates arterial, cerebral and SkM oxygen desaturation



↑ mitochondrial oxygen efficiency?

How to use ketones to improve performance?



After exercise
to improve
training adaptation and recovery

Poffé & Robberechts, *AJP* (2024)

UHASSELT

Ketone ester as a recovery drink during a ‘Tour de France’

		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Week 1	AM	70 min **IMT** 100/55%	Rest	30 min **HIIT**	70 min **IMT** 100/55%	30 min **HIIT**	70 min **IMT** 100/55%	***Test Wk1***
	PM	Rest	Rest	60 min **ET** 70%	60 min **ET** 70%	60 min **ET** 70%	60 min **ET** 70%	60 min **ET** 77.5%
Week 2	AM	70 min **IMT** 100/65%	Rest	30 min **HIIT**	70 min **IMT** 105/65%	30 min **HIIT**	70 min **IMT** 110/80%	***Test Wk2***
	PM	Rest	Rest	90 min **ET** 77.5%	60 min **ET** 85%	90 min **ET** 80%	60 min **ET** 90%	90 min **ET** 85%
Week 3	AM	120 min **HIIT & ET** 85%	Rest	70 min **IMT** 110/80%	120 min **ET-TT$_{30min}$** 85% - 30’ all-out	70 min **IMT** 110/80%	70 min **IMT** 110/85%	***Posttest Test Wk3***
	PM	Rest	Rest	90 min **ET** 90%	Rest	120 min **ET** 95%	150 min **HIIT & ET** 92.5%	Rest

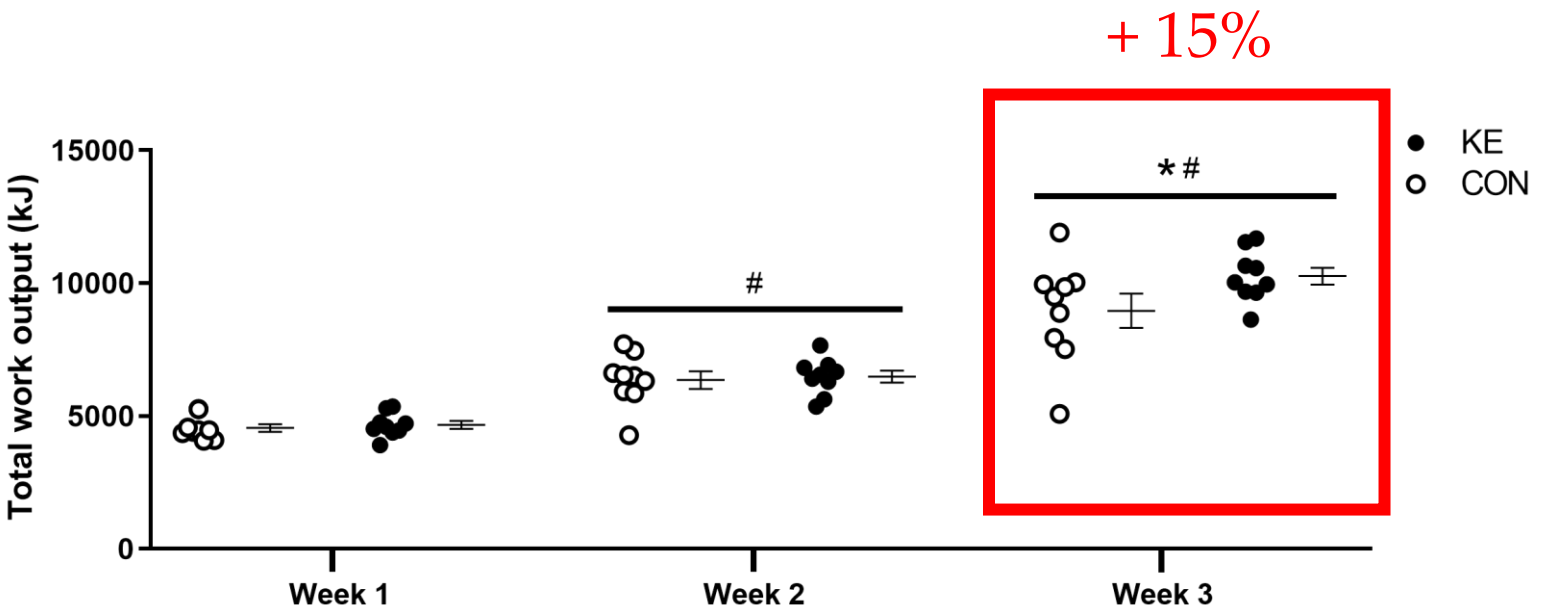
+ 25g KE/PL doses

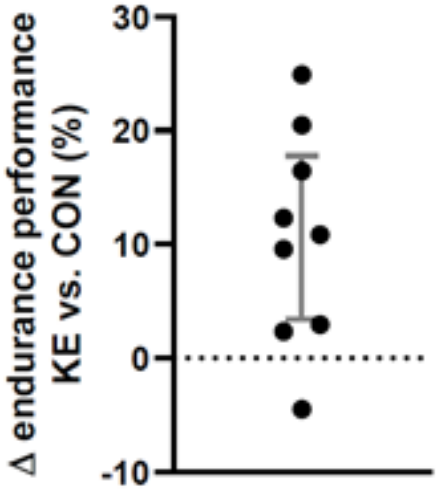
2-3 * daily

Poffé et al., *J Physiol* (2019)

UHASSELT

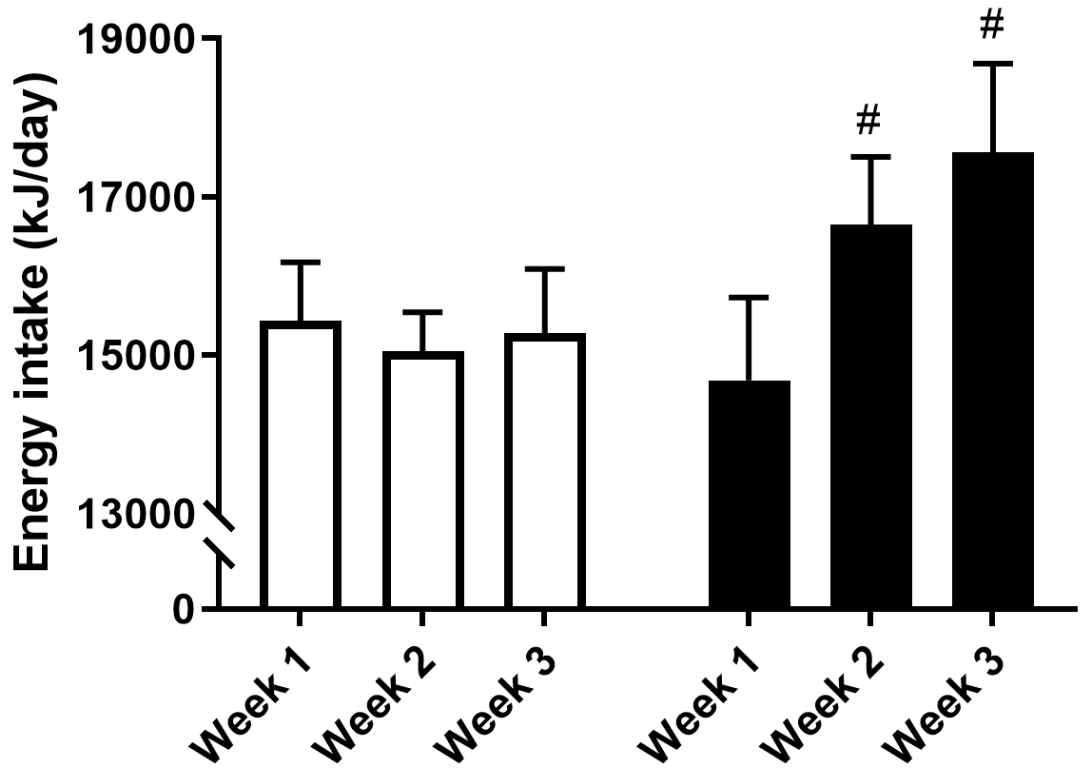
KE increased sustained training workload

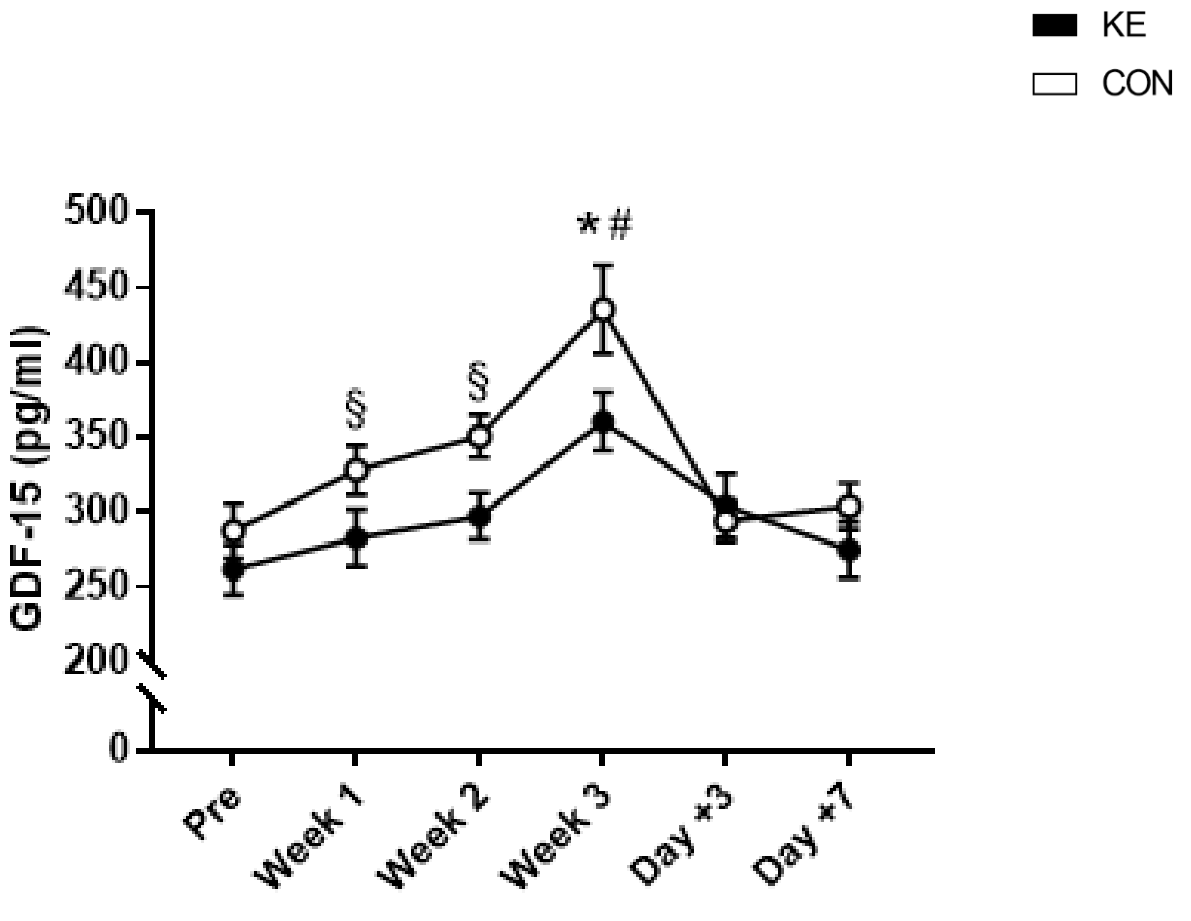




- Training workload
- 30 min TT
- 120 min training + 30 min TT

KE stimulated spontaneous energy intake

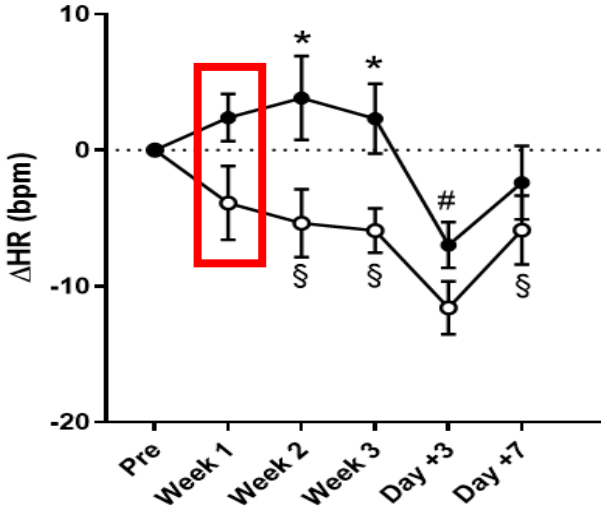




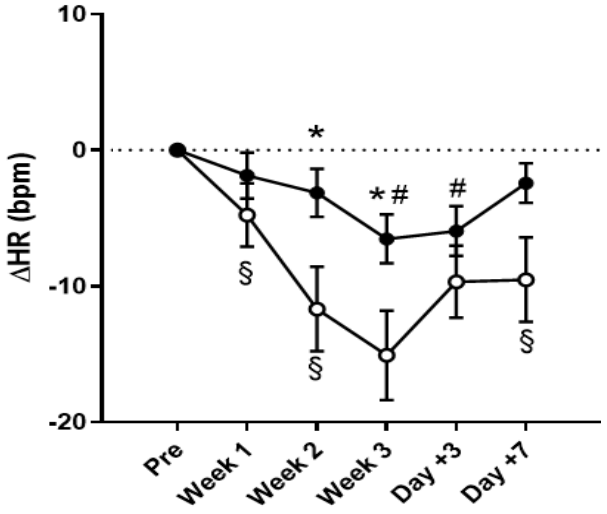
KE suppressed heart rate drop

● KE
○ CON

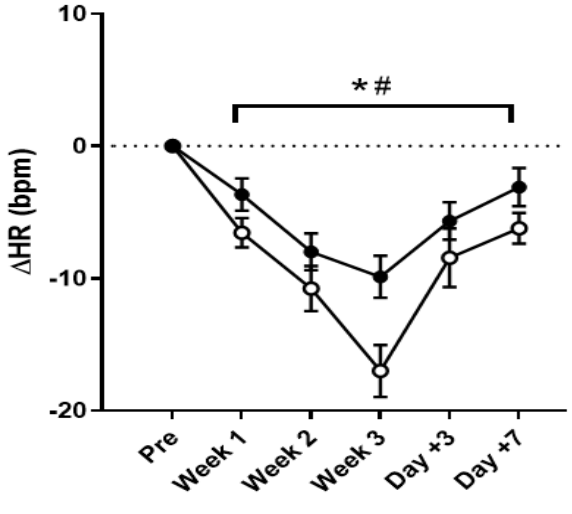
Resting HR



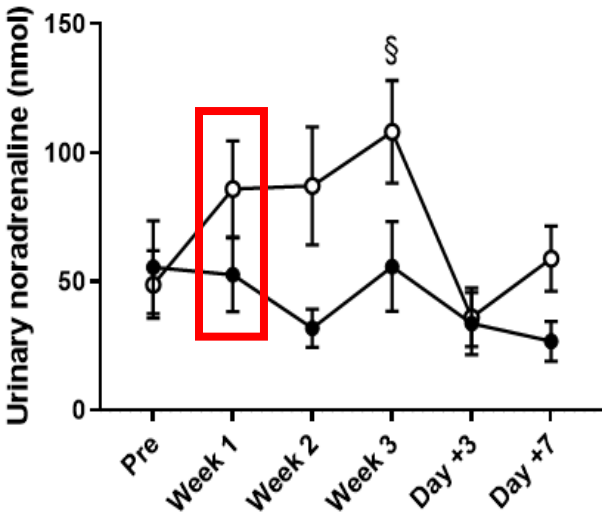
Submax HR



Peak HR

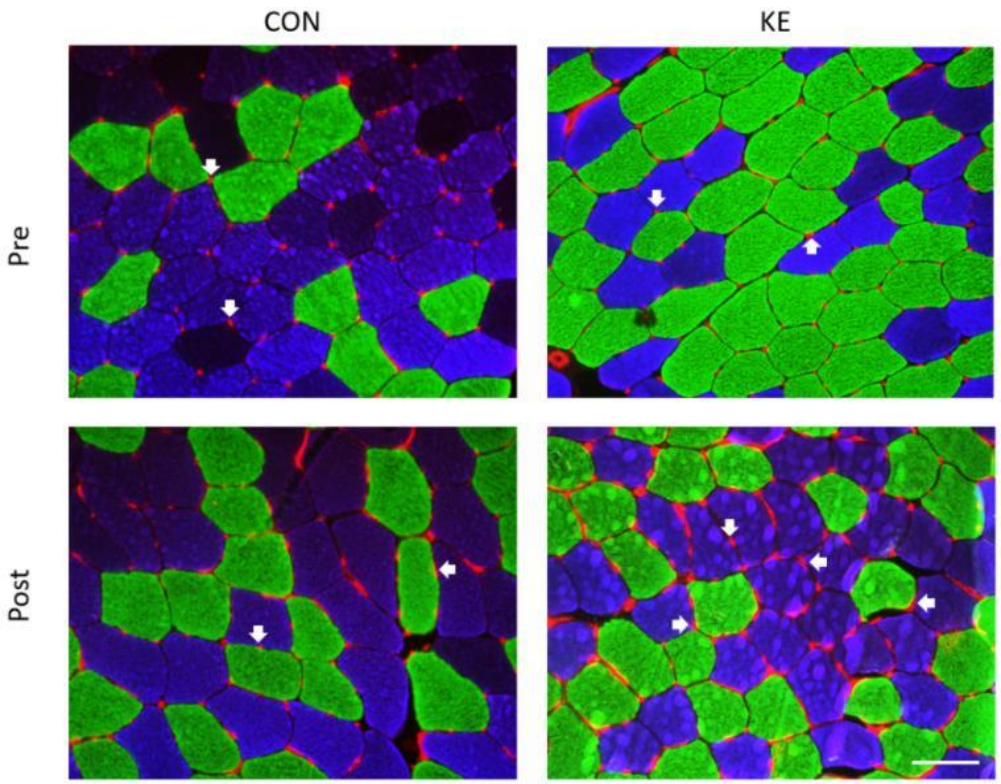


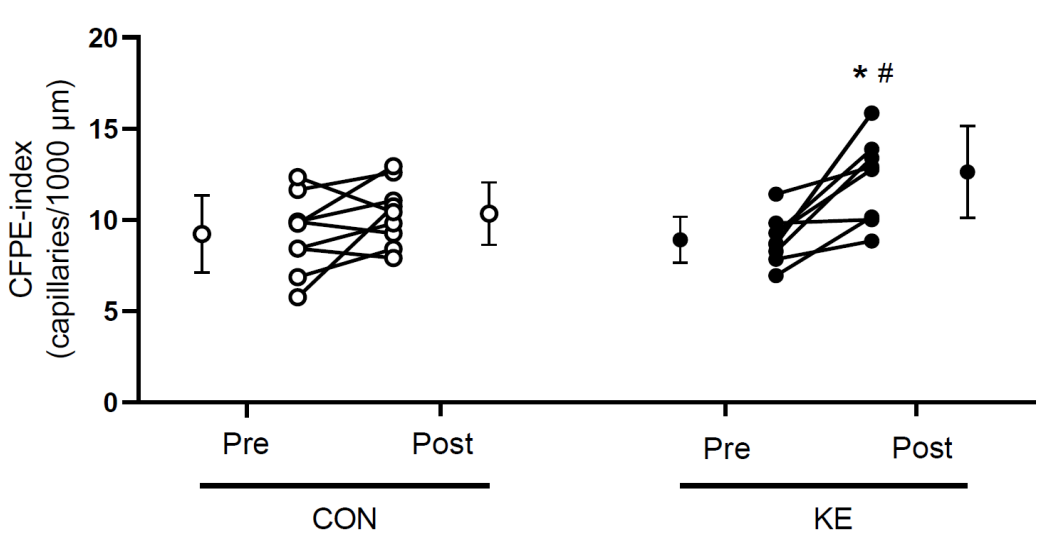
Nocturnal noradrenalin excretion

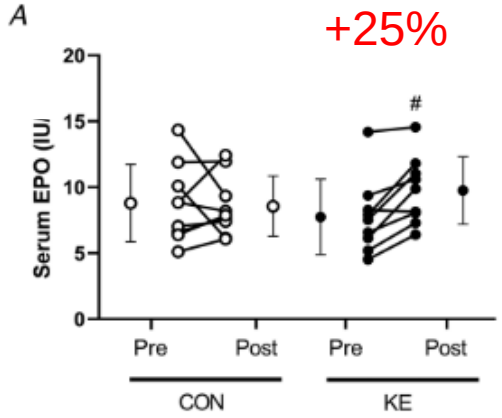


UHASSELT

KE increased skeletal muscle capillarization







+25%

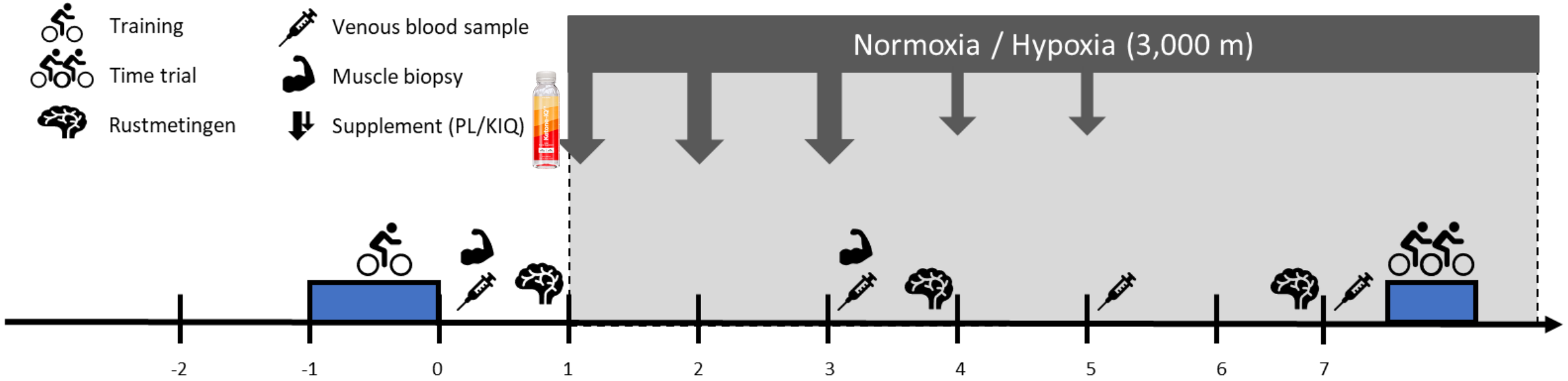
- Muscle angiogenesis
- Muscle oxidative capacity
- Erythropoiesis

Poffé et al., *J Physiol* (2023)

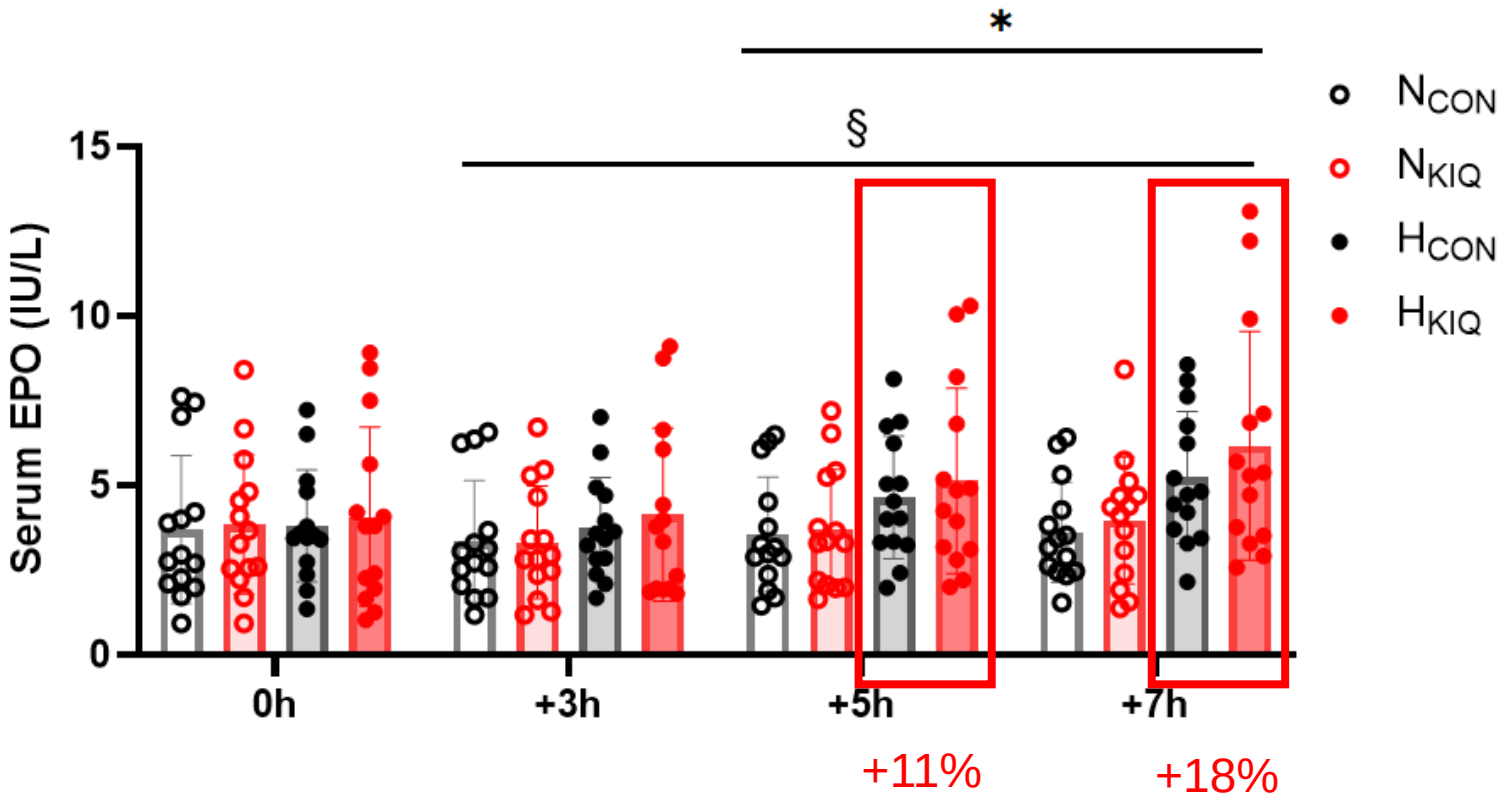
UHASSELT

EPO effect additive to altitude?

n = 15
13 male ↔ 2 female
Cross-over design
N_{CON} – N_{KIQ} – H_{CON} - H_{KIQ}



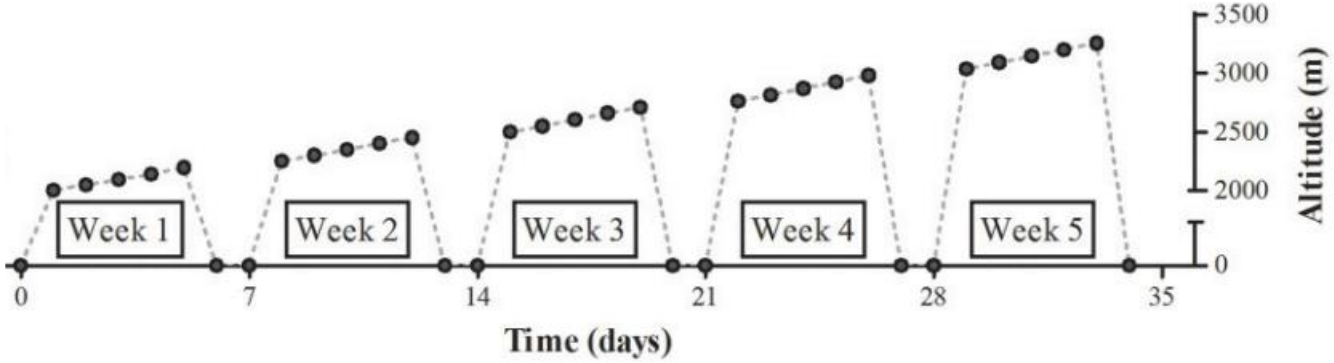
KIQ improved EPO response to altitude

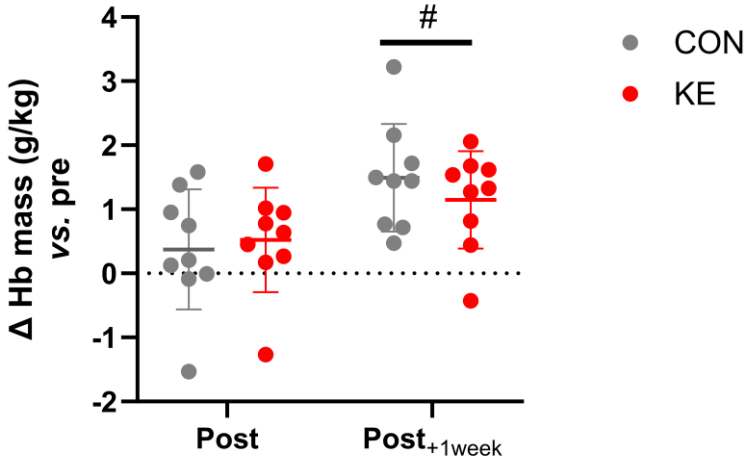


KE does not improve hemoglobin mass

N=18 healthy male & female volunteers

5 days/week at sea-level (~9h/week)





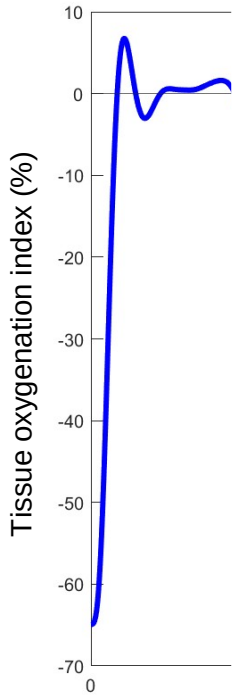
2 to 3x/day: 25g KE/PL

UHASSELT

Near Infrared Spectroscopy

Vascular occlusion protocol

Baseline



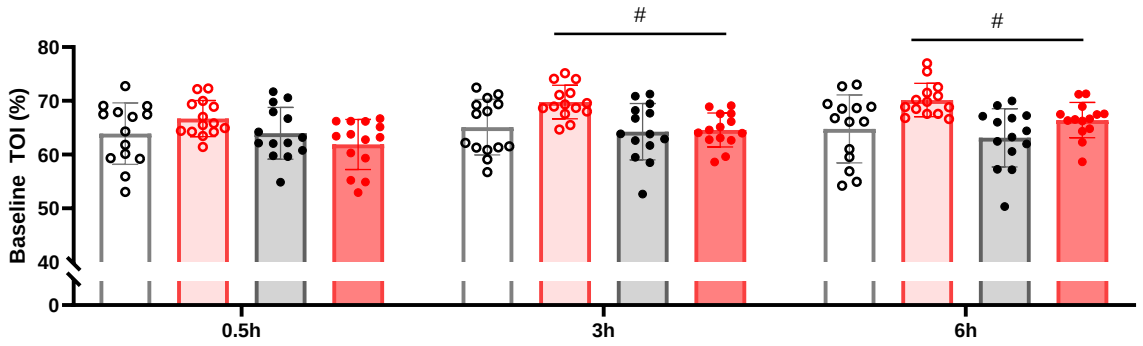
UHASSELT

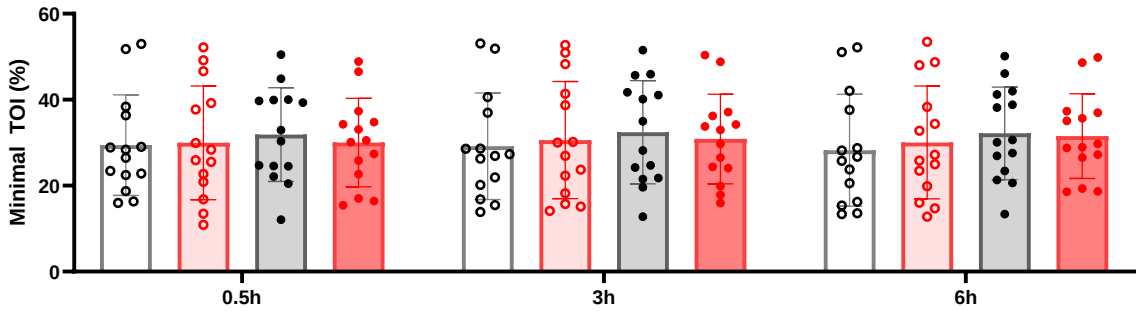
Occlusion

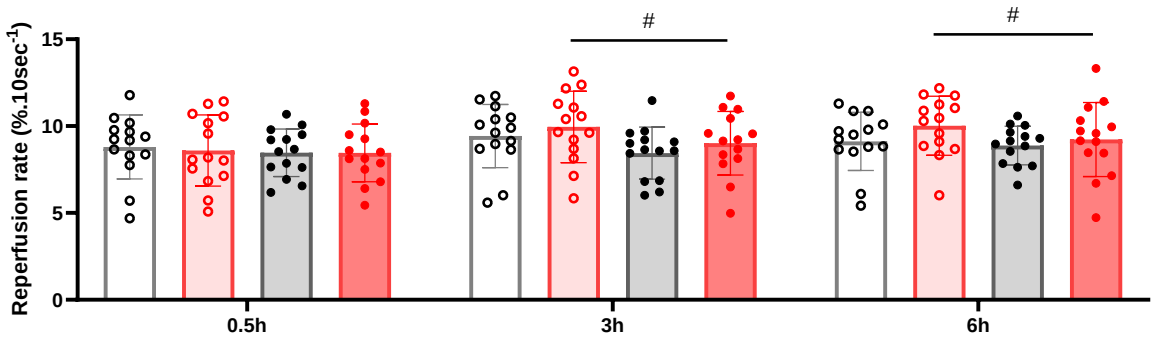
Reperfusion

Increased oxygen extraction capacity

Increased microvascular responsiveness







N_{CON}

N_{KIQ}

H_{CON}

H_{KIQ}

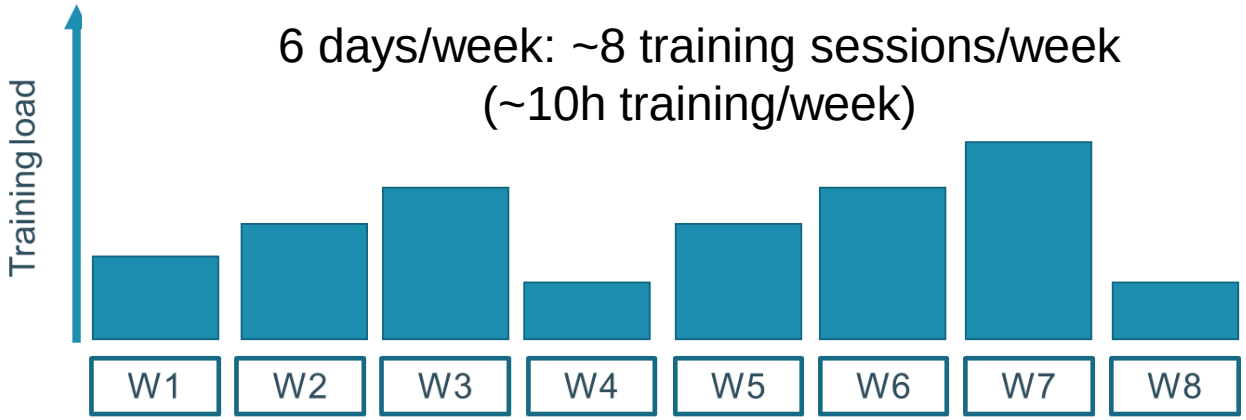
 # p < 0.05 for KIQ vs. CON

UHASSELT

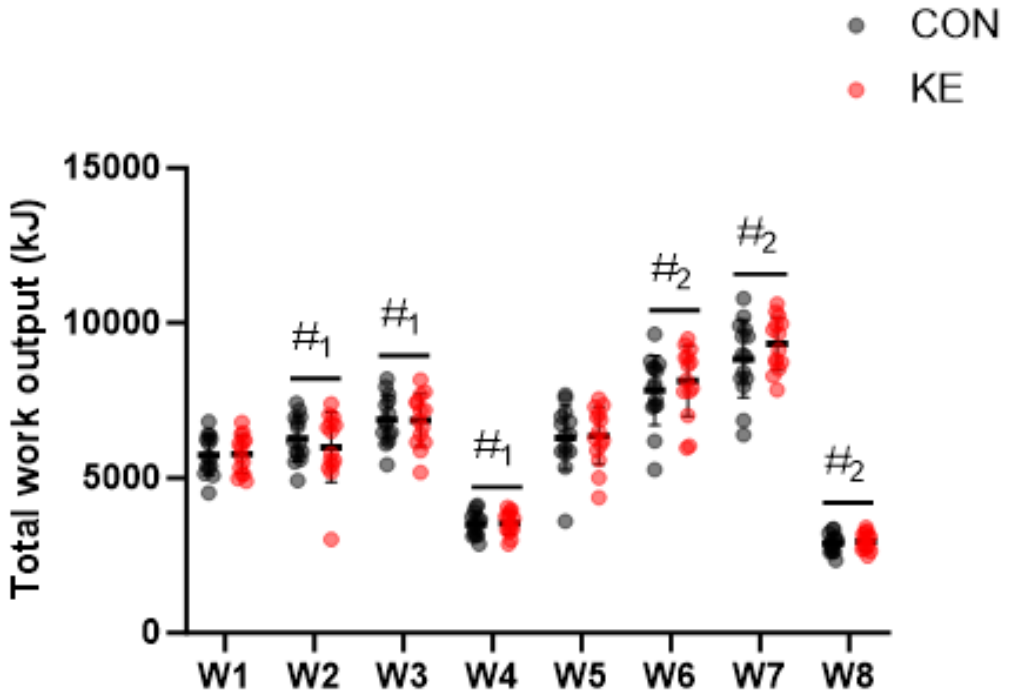
KE during ‘normal training’

N=28 well-trained cyclists & triathletes

6 days/week: ~8 training sessions/week
(~10h training/week)



2 to 3x/day: 25g KE/PL

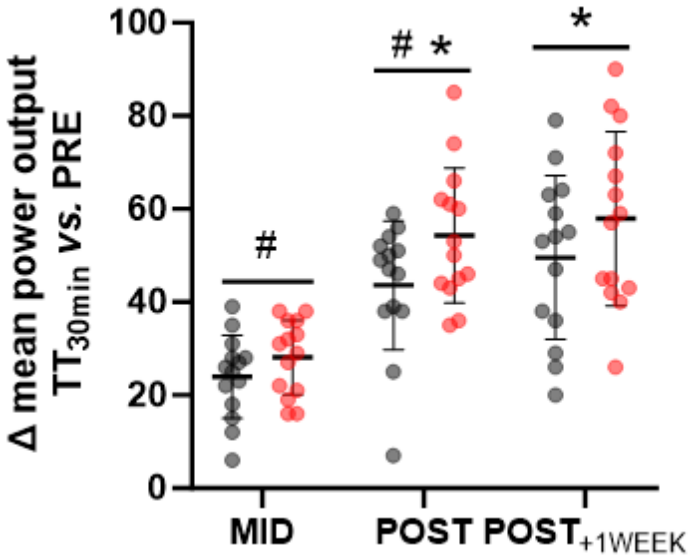


+ no differences in energy/macronutrient intake

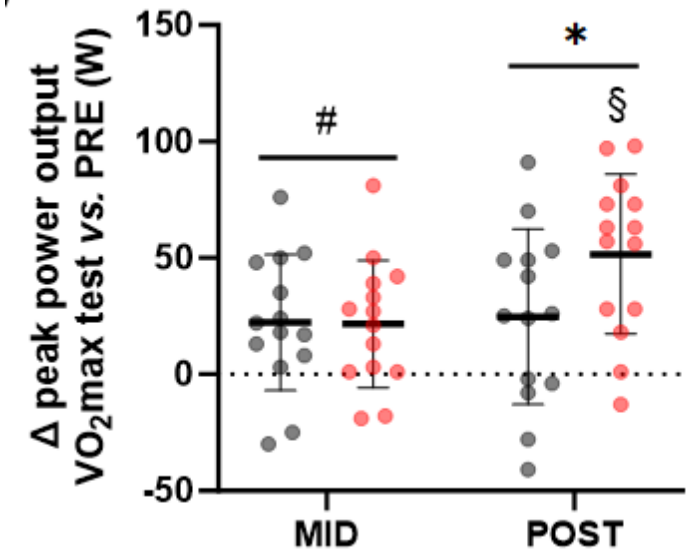
KE increases endurance performance & VO_2max

CON
KE

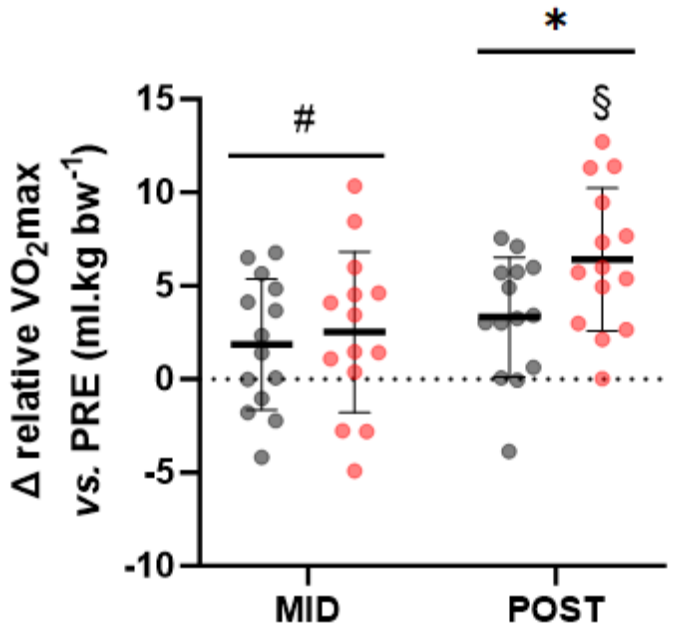
30 min TT



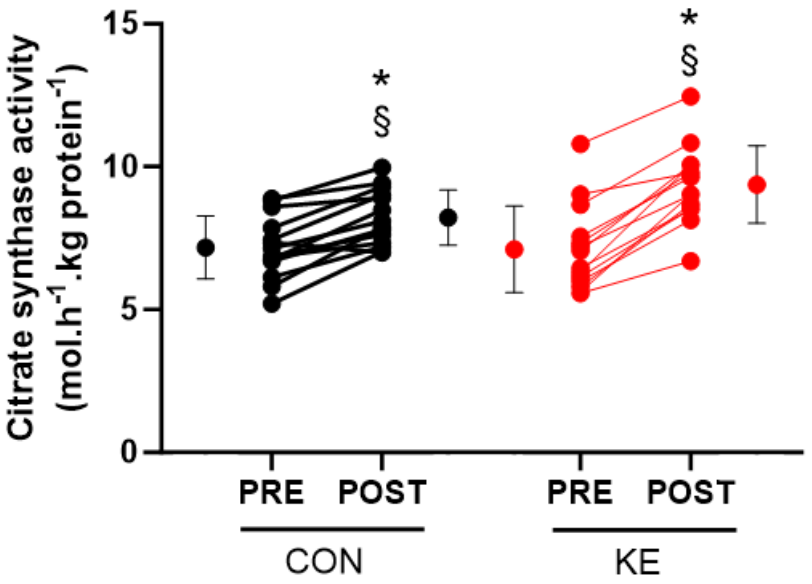
Peak power VO_2max test

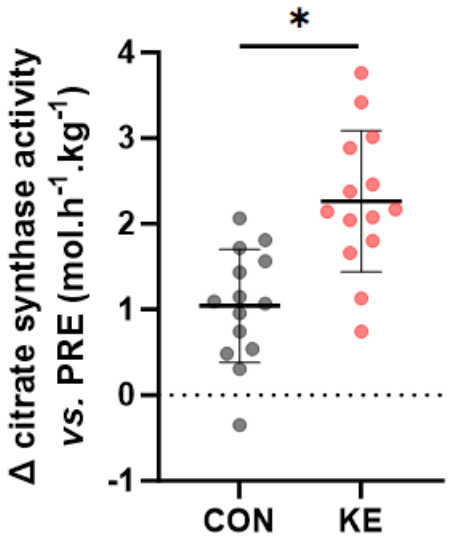


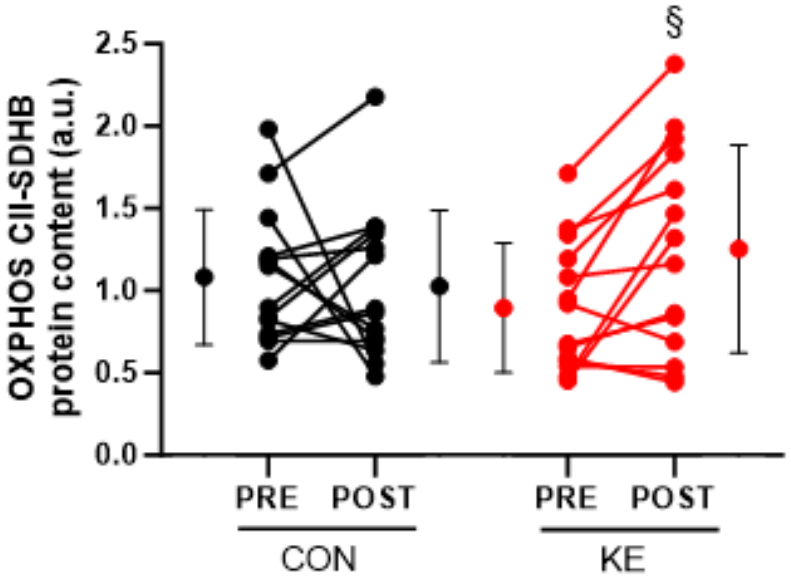
VO_2max



KE increases mitochondrial content/oxidative potential







UHASSELT

Clinical potential?




n = 24

Unilateral immobilization

Unilateral retraining (3x/week)
4-6x12 reps @65% of 1RM

Week 1	Week 2	Week 3	Week 4	Week 5	Week 6

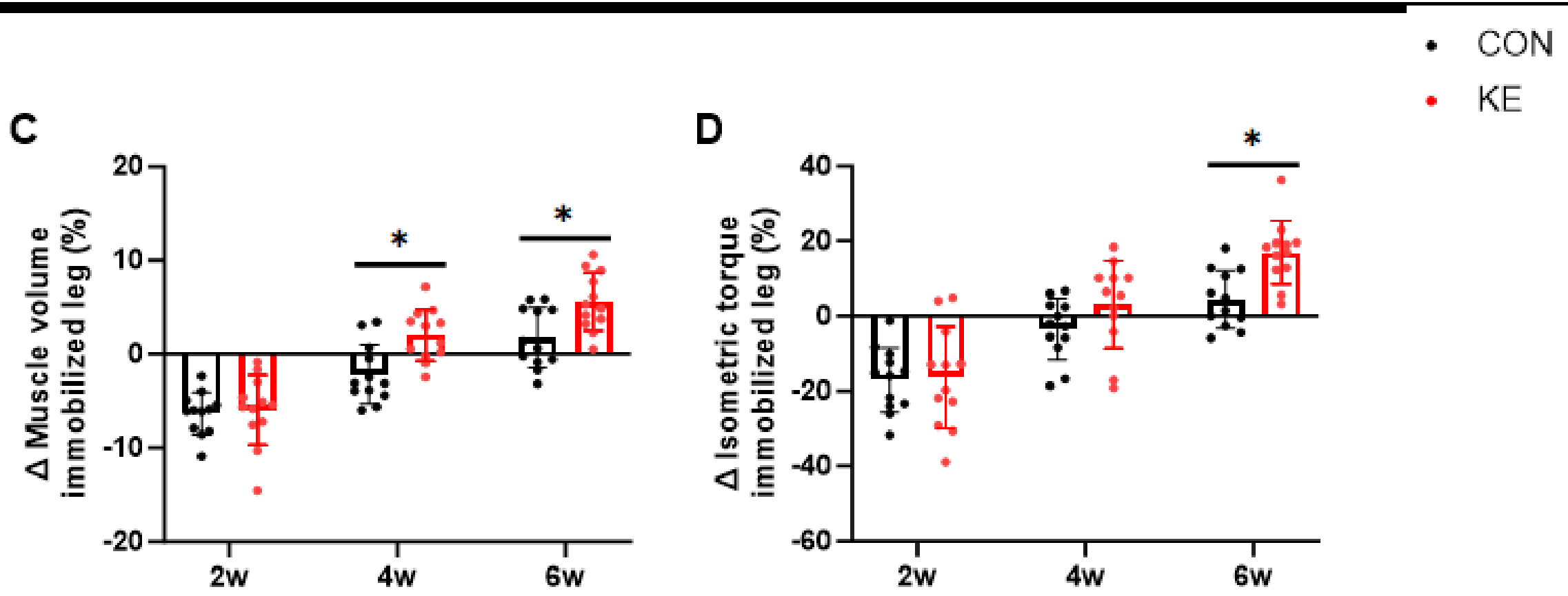
n = 12
KE

3x 20g ketone monoester/day

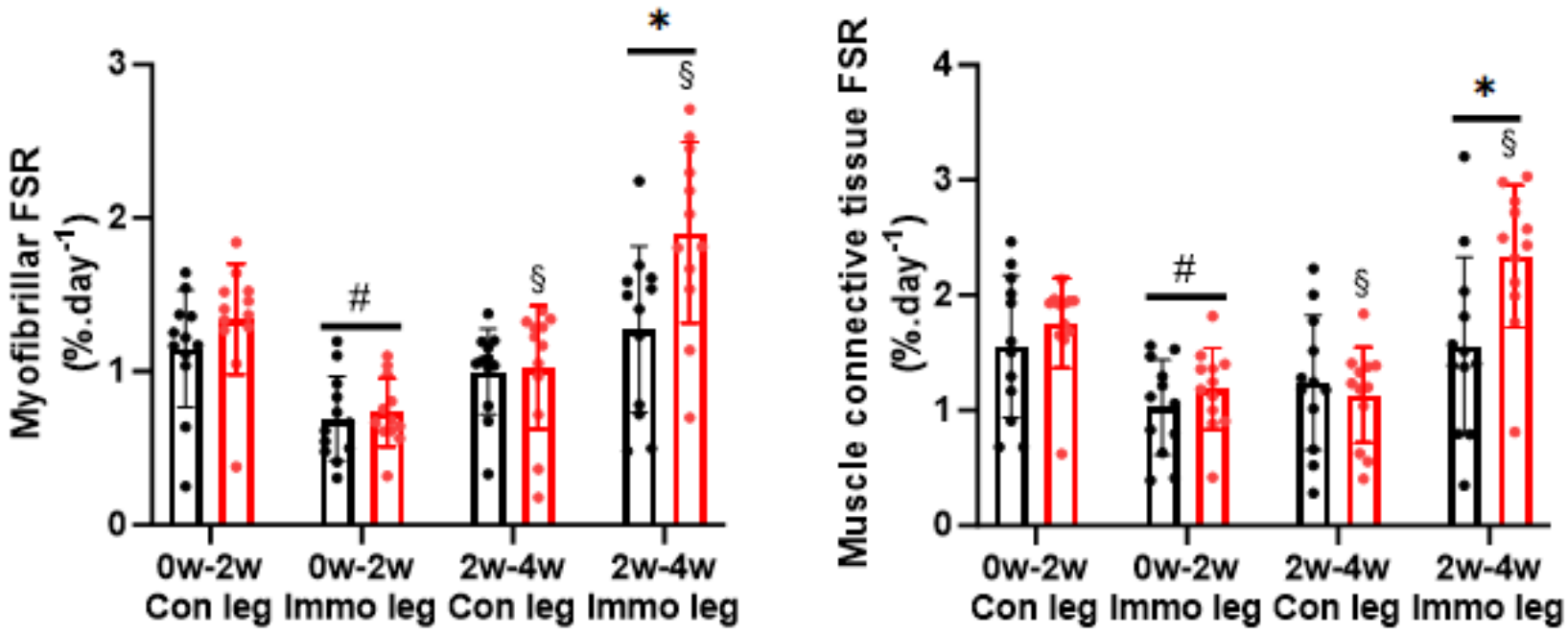
n = 12
CON

3x isocaloric placebo/day (MCT)

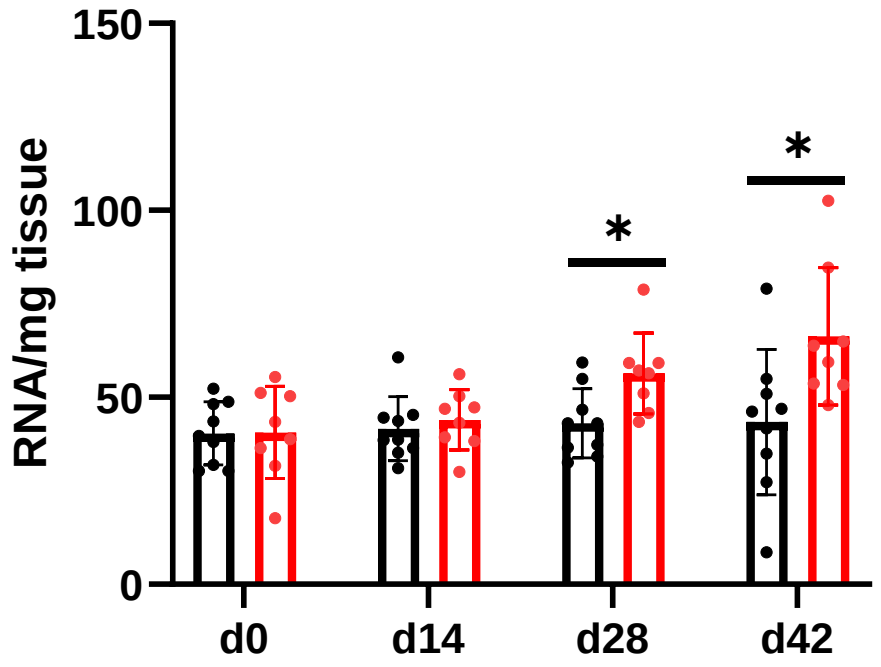
KE ↑ muscle volume & torque during rehabilitation

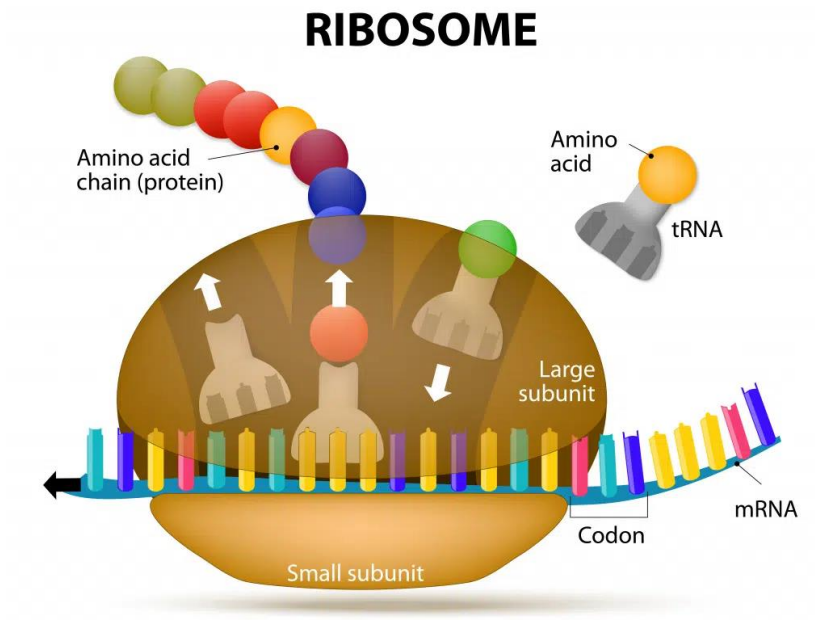


KE ↑ muscle protein synthesis

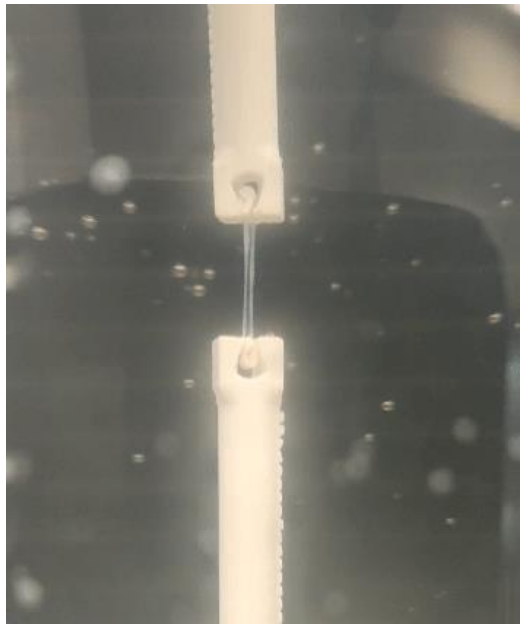


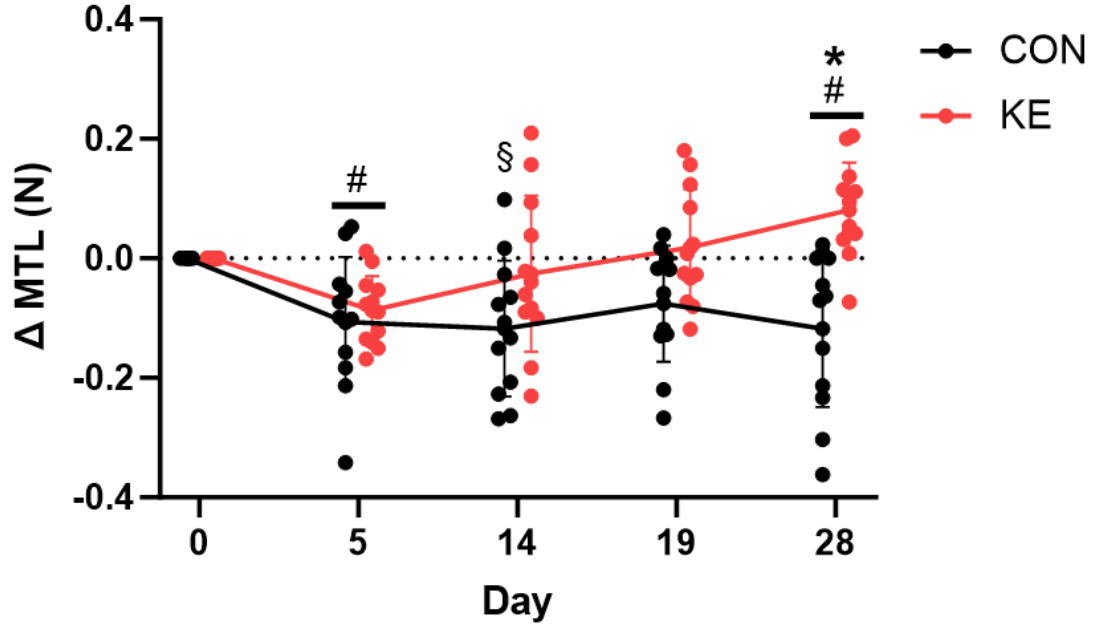
KE ↑ muscle translational capacity





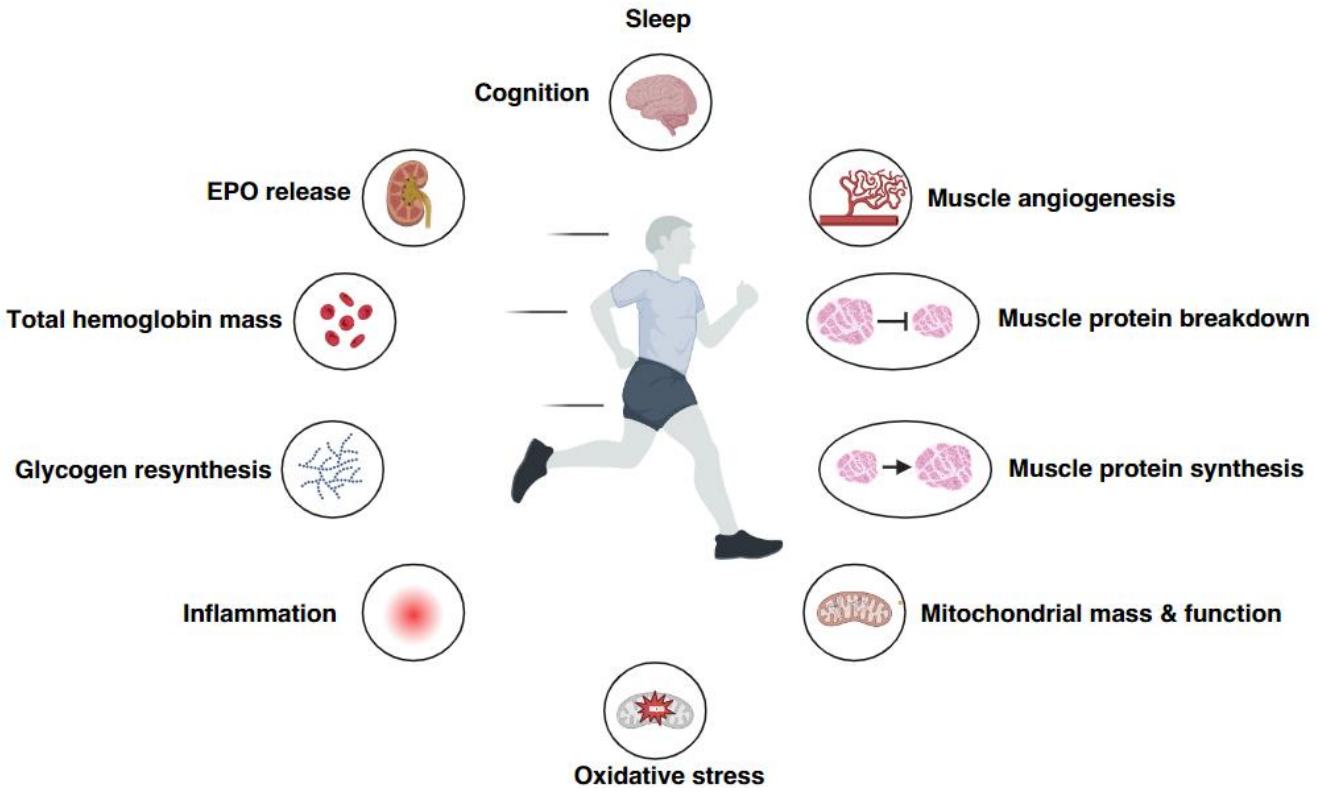
KE ↑ engineered ligament function





Conclusion

No acute effect on exercise performance



Clinical potential!

UHASSELT

KU LEUVEN

fwo Research Foundation Flanders
Opening new horizons

Research group

Dr. Ruben Robberechts
Drs. Myrthe Stalmans
Drs. Wout Lauriks
Drs. Louise Engelbrecht
Drs. Domen Tominec
Dr. Domiziana Costamagna

Martijn Kusters
Christophe Dausin
Monique Ramaekers

Prof. Peter Hespel
Prof. Katrien Koppo

Collaborators

Prof. Tadej Debevec
Prof. Luc van Loon
Prof. Genevieve Albouy
Prof. Elmarie Terblanche
Prof. Pieter Vermeersch

Prof. Keith Baar
Prof. Grégoire Millet
Prof. Guido Claessen
Prof. Stijn Bogaerts
Prof. Sebastiaan Dalle

Dr. Latt Mansor
Dr. Ruud Van Thienen
Dr. Lander Vanysacker

Dr. Tim Podlogar
Dr. Jan Vanderroost

Drs. Ben Narang

Drs. Youri Bekhuis

Contact: chiel.poffe@uhasselt.be