Non-invasive assessment of individual hypoxia tolerance in elite athletes: Flow Mediated Skin Fluorescence (FMSF) as an effective diagnostic tool.

Assessment of hypoxia tolerance and determination of the optimal hypoxic training altitude in elite cyclists - a pilot study.

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From Molecules to Mt. Everest - From Science to Practice

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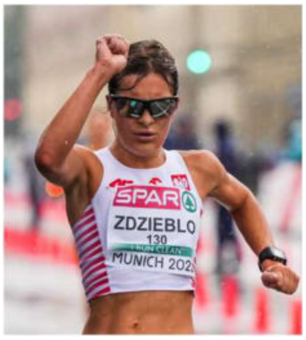

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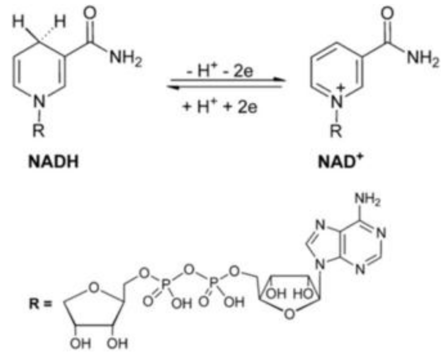
Background

Microcirculation plays a fundamental role in tissue oxygenation. Microcirculatory oscillations known as flowmotion are a recognized feature of blood flow that reflect the functional state of the vascular system.

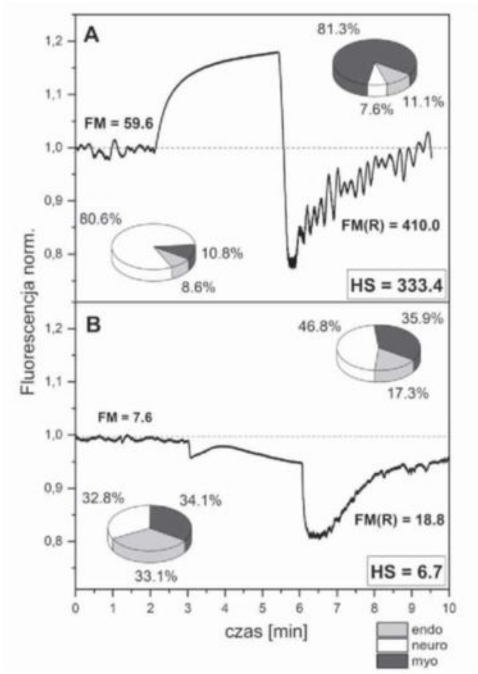
The FMSF (Flow Mediated Skin Fluorescence) technique is based on the measurement of NADH (Nicotinamide Adenine Dinucleotide) fluorescence from skin tissue cells.

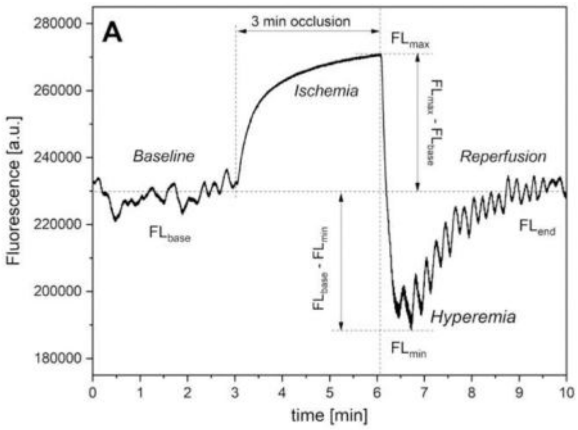
NADH and its oxidized form (NAD^+) play a crucial role in biological systems as redox coenzymes.



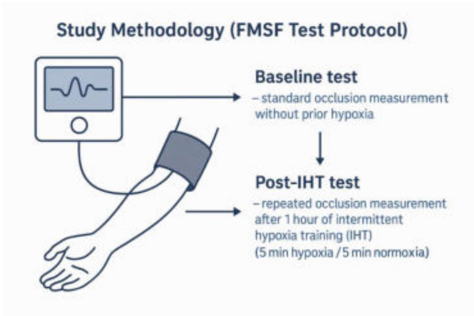
The chemical structures of NADH and NAD^+

The FMSF technique measures changes in the intensity of NADH fluorescence from the skin on the forearm as a function of time.





During the FMSF test, blood flow in the forearm is temporarily blocked with a pressure cuff and then released.



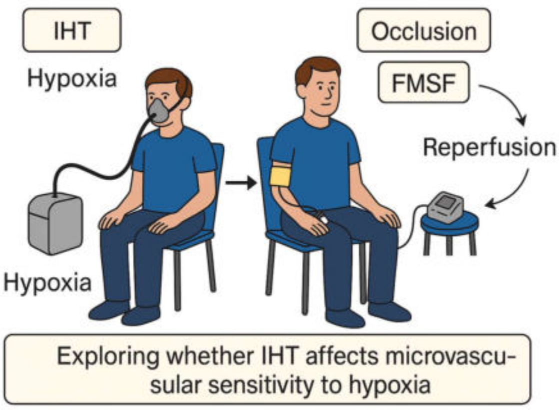
When the blood flow is stopped, oxygen supply decreases, and NADH fluorescence increases.
After releasing the cuff, blood flow returns, oxygen supply rises, and fluorescence decreases.

By analyzing these changes, the device provides information about:
- **Microcirculatory function** (blood vessel response)
- **Metabolic regulation** (cellular energy response)

This method is **non-invasive**, **safe**, and allows **quantitative assessment** of skin metabolism and vascular health.

Hypothesis

We hypothesized that **systemic hypoxic preconditioning** through IHT may **modulate local microvascular reactivity** measured by FMSF technique, and that the magnitude and direction of these changes could **reflect individual sensitivity or tolerance to hypoxia**.



Participants

Competitive athletes (pilot cohort, n=10). All procedures were completed within a short, standardized window.

Day A

FMSF test

+

Acute hypoxic exposure for microvascular response (IHT)

+

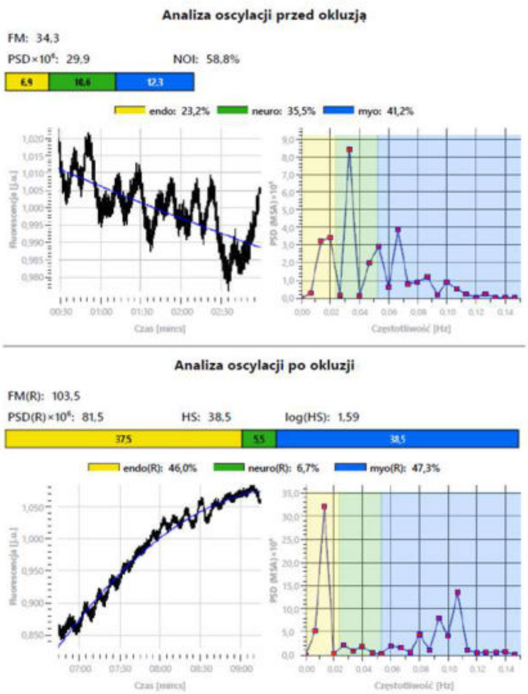
FMSF test

Test Protocol

The test is performed in a seated position. Patient preparation: no food intake within 2 hours prior to the test, no physical activity on the day of the test, and no intensive training for two days before the test.

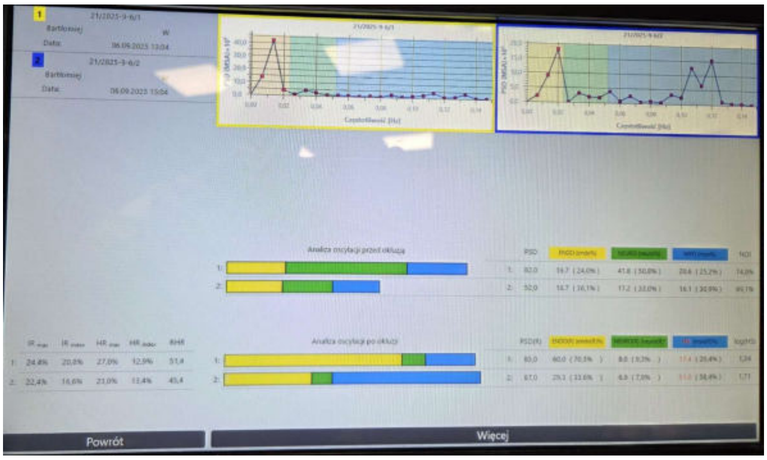
Test phases:
Resting phase (baseline): 3 minutes.
Occlusion phase: arm compression with a pressure cuff for 3 minutes.
Reperfusion phase: release of cuff pressure and recording of fluorescence changes for 5 minutes.

After completing first FMSF test, the subject undergos an IHT session in a seated position, consisting of cyclic breathing of hypoxic air (FiO_2 9%) through a mask for 5 minutes, alternated with 5 minutes of ambient air breathing (FiO_2 21%). The second FMSF test is performed just after the IHT session.



Fluctuation components depending on frequency range:

•**ENDO – endothelial component (0.0095–0.021 Hz).** Related to the endothelial activity, the ability of vessels to regulate blood flow depending on nitric oxide (NO).
•**NEURO – neurogenic component (0.021–0.052 Hz).** Related to the regulation of vascular tone by the autonomic nervous system.
•**MYO – myogenic component (0.052–0.15 Hz).** Related to the activity of vascular smooth muscle.

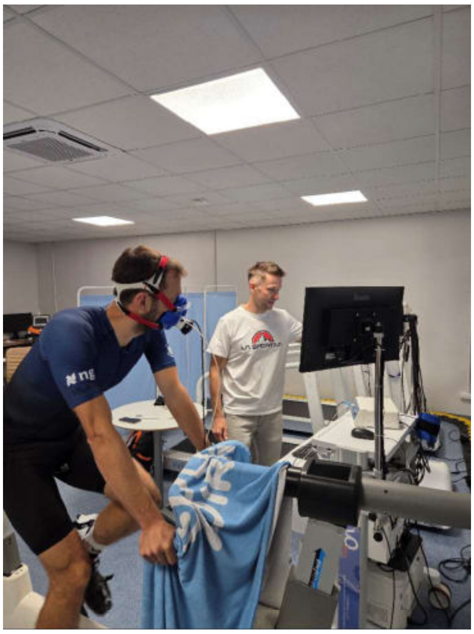


Day B

Normoxic ramp test (VT1 identification)

Incremental ramp test in normoxia.

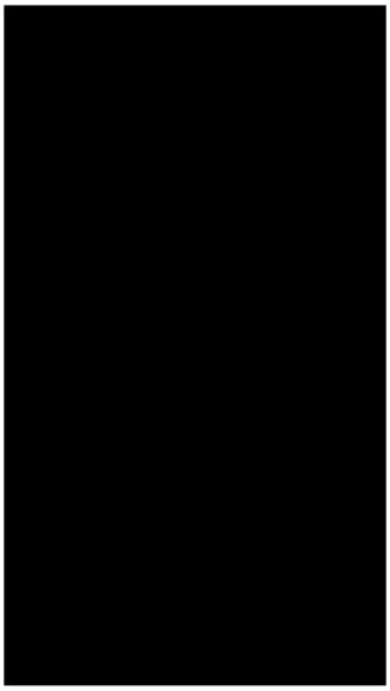
Determination of the ventilatory threshold VT1 using standard ventilatory pattern criteria, and recording of the threshold load [W] at VT1.

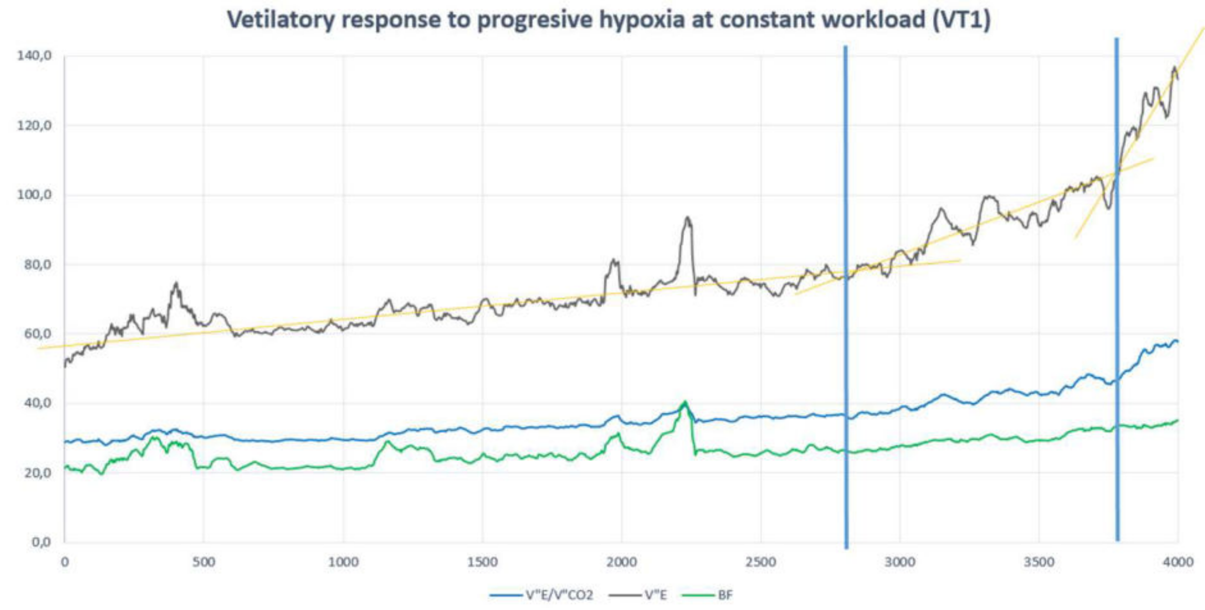


Day C

Progressive hypoxia test at constant load

- The participants performed a cycle ergometer test at a constant load determined on Day B.
  In the hypoxic chamber, the fraction of inspired O_2 was gradually reduced ("continuous increase of simulated altitude").
- Breath-by-breath respiratory parameters were recorded: VE, BF, VT, VE/VCO_2.
- We recorded the Hypoxic Ventilatory Response (HVR) as a change in the breathing pattern (↑VE and ↑BF, usually well reflected by VE/VCO_2), observed at the same constant load while the inspired O_2 fraction continues to decrease.

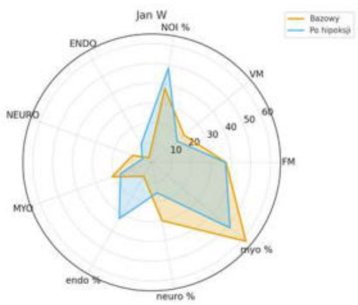


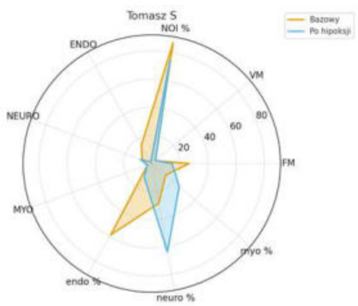


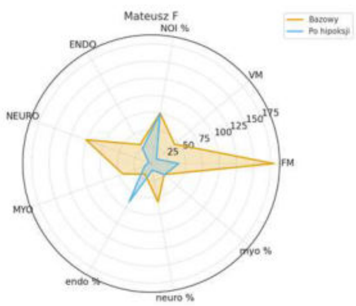
RESULTS

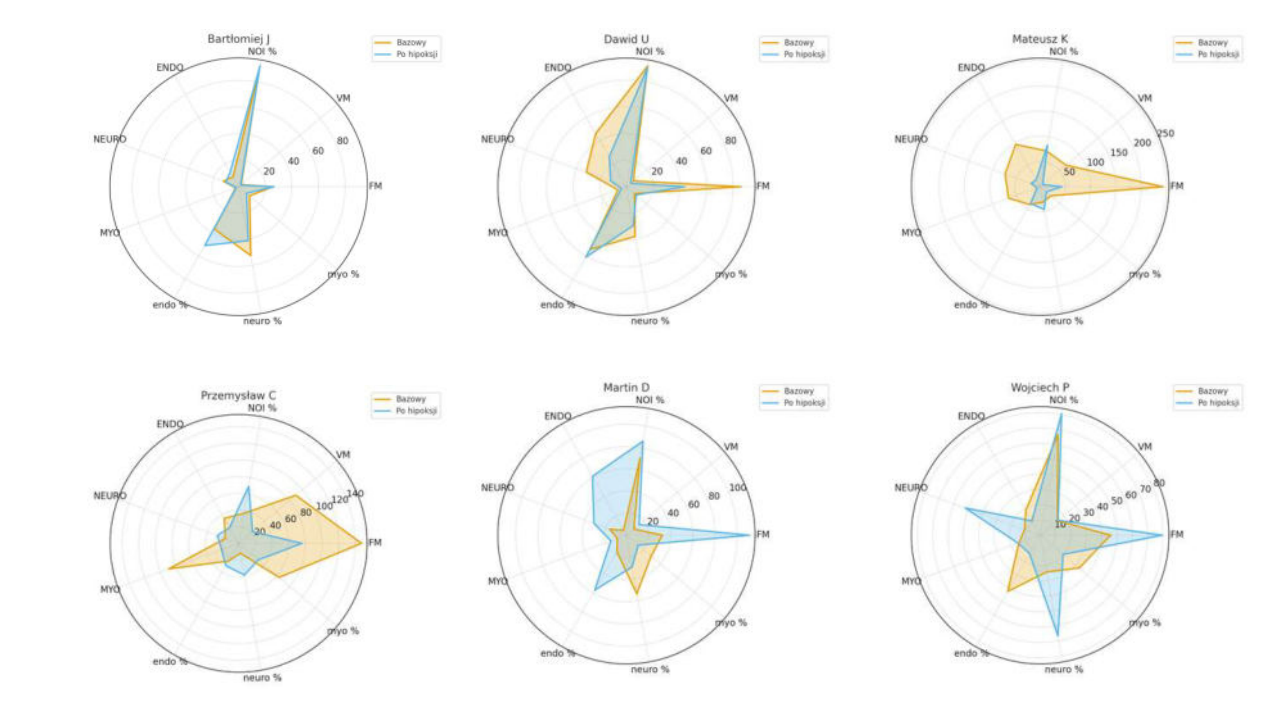
FMSF + IHT + FMSF

Orange shows the baseline profile before IHT sesion
Blue shows the baseline profile after hypoxia.
Axes are the main FMSF parameters (FM, VM, ENDO, NEURO, MYO) and thier spectral contributions (NOI%, endo%, neuro%, myo%).

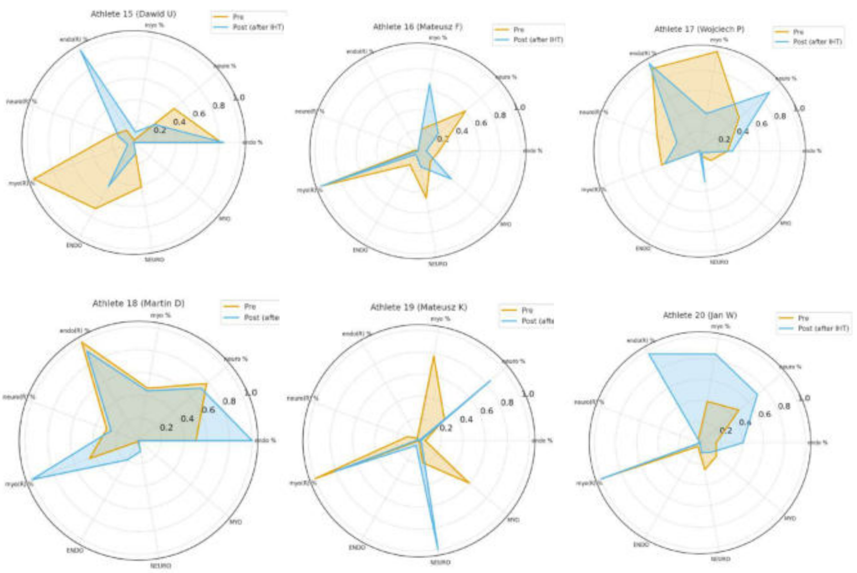








1. Individual radar plots show high variability in vascular responses among athletes, indicating that each participant reacts differently to hypoxic preconditioning.
2. After IHT session, all components showed diverse individual trends.
3. These results suggest that the vascular response to occlusion after systemic hypoxia is highly individualized, reflecting personal sensitivity and adaptation capacity to hypoxic stress.
4. FMSF analysis allows for visual assessment of personal microcirculatory patterns, helping to identify athletes with stronger or weaker endothelial, neurogenic and myogenic reactivity after hypoxic exposure.



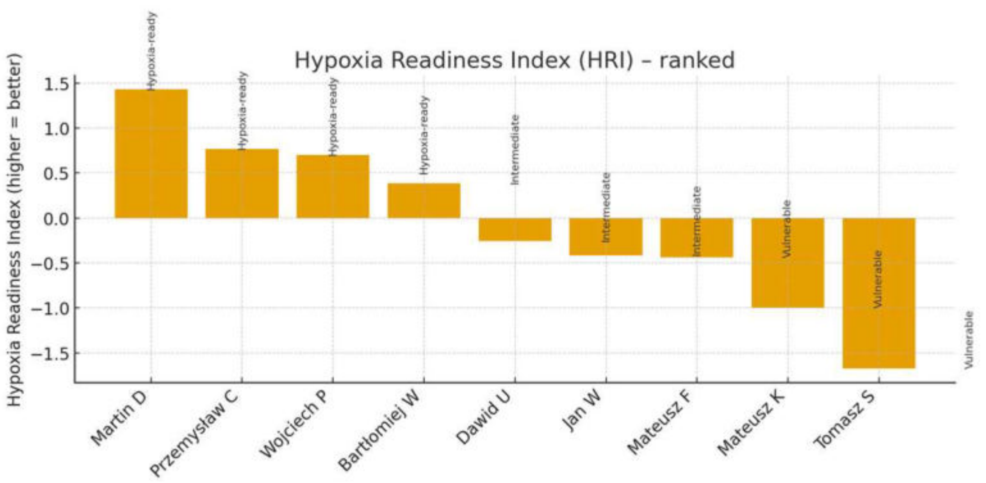
Primary Outcome: Hypoxia Readiness Index (HRI)

Goal: combine ventilatory economy under hypoxia and acute microvascular changes into a single, interpretable score to decide who is **ready** for hypoxic training blocks.

Inputs to HRI

- All inputs are converted to **z-scores within the cohort**. Directions are chosen so that "more is better."
- **ΔVE/VCO_2 (hypoxia – VT1 normoxia)** → **lower is better** (better ventilatory economy) → use **−z(ΔVE/VCO_2)**
- **ΔNOI% (FMSF post – baseline)** → **higher is better** → **z(ΔNOI%)**
- **ΔFM (post – baseline)** → **higher is better** → **z(ΔFM)**
- **ΔENDO (post – baseline)** → **higher is better** → **z(ΔENDO)**
- **Δmyo% (post – baseline)** → small positive weight → **z(Δmyo%)**
- **HTI*** → supportive, small weight → **z HTI*)**

$$\mathbf{HRI} = 0.7 \cdot \left[-z(\Delta VE/VCO_2)\right] + 0.5 \cdot z(\Delta NOI\%) + 0.5 \cdot z(\Delta FM) + 0.3 \cdot z(\Delta ENDO) + 0.2 \cdot z(\Delta myo\%) + 0.2 \cdot z(HTI^{*})$$



Each bar is one athlete; **higher = better predicted readiness** for hypoxic training. Class labels above bars (**Hypoxia-ready / Intermediate / Vulnerable**). HRI is a composition of **ventilatory economy** (lower ΔVE/VCO_2), **microvascular improvements** (ΔNOI%, ΔFM, ΔENDO, Δmyo%).

Conclusions

- Our pilot study suggests that athletes with lower $\Delta VE/VCO_2$ and favorable FMSF deltas may be better candidates for hypoxic training.
- IHT sesion applied at rest can modulate local microvascular reactivity measured after occlusion using the FMSF technique.
- Following IHT exposure, post-occlusion FMSF recordings revealed a notable increase in endothelial (endo%) activity, accompanied by a decrease in neurogenic (neuro%) and a slight reduction in myogenic (myo%) components. This indicates a shift toward endothelial-dominated regulation of skin microcirculation during reperfusion.
- IHT session may enhance endothelial responsiveness, potentially reflecting an early vascular adaptation aimed at improving oxygen delivery and perfusion efficiency under hypoxic stress.
- Observed individual differences in post-hypoxia responses highlight the potential of FMSF testing as a non-invasive method to assess personal sensitivity or tolerance to hypoxia, which may be valuable for athlete monitoring and personalized training optimization.
- Our future study will validate Hypoxia Readiness Index (HRI) against training outcomes.

Hypoxia improves mood

Thank YOU ☺