



Therapeutic hypoxia and cognitive dysfunction after myocardial infarction

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Cognitive impairment following Myocardial Infarction (MI)

Up to 30% of patients after myocardial infarction exhibit measurable cognitive deficits, primarily affecting executive functions.

Symptom onset can occur within just a few weeks following the acute event.

Pathological hypoxia as a risk factor etiologies: myocardial infarction, stroke, heart failure.

Mechanisms: cerebral ischemia, neuroinflammation, blood–brain barrier (BBB) disruption, white matter degeneration.

The Heart–Brain Axis Cardiovascular dysfunctions contribute to secondary neurological deficits.

The underlying pathophysiology supports the existence of a close interrelationship between cardiac health and brain function.

Why is physical activity important in hypoxic conditions after a heart attack?

- Myocardial infarction -> cardiomyocyte necrosis -> release of DAMPs (damage-associated molecular patterns) -> activation of the immune system cells -> massive production of pro-inflammatory cytokines and antibodies.
- Phase post myocardial infarction:
 - Inflammatory phase (first few days): dominated by IL-1B, IL-6, TNF-alpha;
 - Repair and remodeling phase: decrease in IL-1B, IL-6, increase in IL-10, TGF-B.
- Moderate, controlled exercise post myocardial infarction has anti-inflammatory and immunomodulatory effects: reduces levels of pro-inflammatory cytokines (IL-6, TNF-alpha); increases IL-10 and other anti-inflammatory cytokines; improves vessel sensitivity, reduces oxidative stress; influences heart remodeling in a more favorable direction (less fibrosis, better contractile function).
- This is known as the "anti-inflammatory effect of exercise."

The commission's approval for research

- This study was approved by the Bioethics Committee No. 7/2017 of 18 May 2017.
- This study was registered in the international Australian New Zealand Clinical Trials Registry, number ACTRN12619001350112, on 1 October 2019.
- Nr1-IX/2023 z dn 21.09.2023 (Komisja Bioetyczna ds. Badań Naukowych).

Research objectives

- Describe mechanisms linking myocardial ischemia, hypoxia and cognitive impairment
- Evaluate neurocognitive diagnostic tools (Stroop test)
- Present preliminary clinical observations on therapeutic hypoxia

Methods

- Narrative review + pilot intervention with normobaric hypoxia (2500–3000 m simulated altitude)
- 20 supervised ergometer training sessions
- Assessment: cognitive function, cytokine profiles, endothelial function

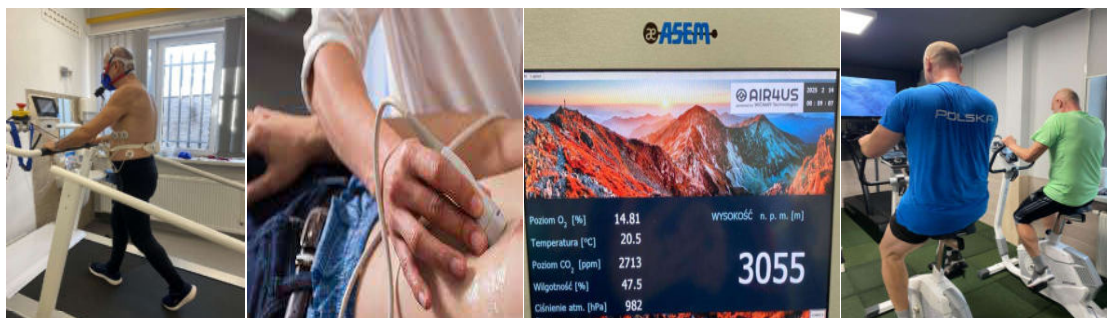
Hypoxia in Post-Myocardial Infarction and Cardiovascular Disease Patients

- **In individuals with cardiovascular disease, hypoxia may:**
 - Exacerbate cerebral and myocardial ischemia
 - Increase the susceptibility to cardiac arrhythmias
 - Decrease exercise tolerance
- **Potential consequences include:**
 - Deterioration of cognitive functions, particularly memory and attention
 - An elevated risk of executive dysfunction
- **Clinical implications:**
 - The necessity for cautious planning of exercise interventions under hypoxic conditions
 - Continuous monitoring of oxygen saturation and systemic physiological responses

Exercise training in hypoxic environments

Moderate physical exercise under hypoxic conditions:

- Does not impair cognitive function
- May even enhance cognitive performance



Exercise training in hypoxic environments

Proposed mechanisms:

- Central nervous system (CNS) stimulation
- Increased catecholamine release
- Improved cerebral blood flow



Comparison of pathological vs. therapeutic hypoxia

Feature	Pathological Hypoxia	Therapeutic Hypoxia
Source	Stroke, heart failure, MI	Controlled hypoxic training (2500–3000 m simulated altitude)
Character	Chronic, often uncontrolled	Acute, supervised and dosed
Cytokine profile	↑ IL-6, ↑ TNF-α (proinflammatory)	↓ IL-6 and TNF-α, ↑ IL-10 (anti-inflammatory)
Effect on BBB	Damage to endothelial integrity, permeability ↑	Stabilization of BBB, repair – enhanced tight junctions
Cognitive impact	Decline in executive function, memory loss	Improvement in attention, working memory, processing speed

The Stroop Test – What is it about?

- **Assessment of executive functions:**

- Inhibition of automatic responses
- Interference control
- Attention shifting

- **Key effect:**

- Prolongation of reaction time under incongruent conditions (so-called interference cost)

- **Outcome measures:**

- Reaction time
- Number of errors
- Difference in reaction times between congruent and incongruent conditions

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Cognitive interference testing in individuals with cardiovascular conditions

- **The Stroop test enables the assessment of:**

- Executive function performance, which may be impaired following myocardial infarction
- The impact of hypoxia or rehabilitation on brain function

- **Findings from studies indicate that post-infarction patients often exhibit:**

- Prolonged reaction times
- A higher number of errors in the Stroop test

- **It may serve as:**

- A monitoring tool for evaluating the effects of rehabilitation training under normoxic and hypoxic conditions
- An indicator of improvement or deterioration in cognitive functioning

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Cognitive performance in hypoxic conditions

- **Hypoxia typically impairs:**

- Working memory
- Attention
- Processing speed
- Executive functions

- **The severity of impairment depends on:**

- The level of hypoxia
- Duration of exposure
- Exercise intensity

- **Possible phenomenon:** central fatigue (decreased brain efficiency)

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Applied significance

- **The Stroop test detects subtle impairments in executive functions**

- **The results are particularly relevant for:**

- pilots, mountaineers, individuals exposed to hypoxic conditions
- athletes training under hypoxia
- people with neurodegenerative diseases
- patients after myocardial infarction and cardiac diseases

- **Moderate physical exercise may protect the brain from the adverse effects of hypoxia.**

Conclusions

- Pathological hypoxia damages cognitive function; therapeutic hypoxia may protect the brain
- Promising pilot results justify further interdisciplinary research
- Potential shift toward integrated cardioneurological rehabilitation

Review

Hypoxia and Cognitive Functions in Patients Suffering from Cardiac Diseases: A Narrative Review

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