Università di Brescia

Dipartimento di Scienze Cliniche e Sperimentali

Dottorato di Ricerca in
«Intelligenza Artificiale in Medicina e Innovazione nella Ricerca clinica e metodologica»

Coordinatore: Prof. Domenico Russo

Assessment of the effects of moderate acute cerebral hypoxia on cognitive functions and neurophysiological indexes

DOTT. MORI FRANCESCO
XL CICLO

Supervisor: Dott. Luca Falciati

Co-Supervisor: Prof. Massimiliano Waldemar Gobbo

Our atmosphere

In high altitude environments, barometric pressure is lower and gasses density is more sparse

High altitude
FiO_2=21%
P=356 millibar

HYPOBARIC
HYPOXIA

Sea level
FiO_2=21%
P=1013.25 millibar

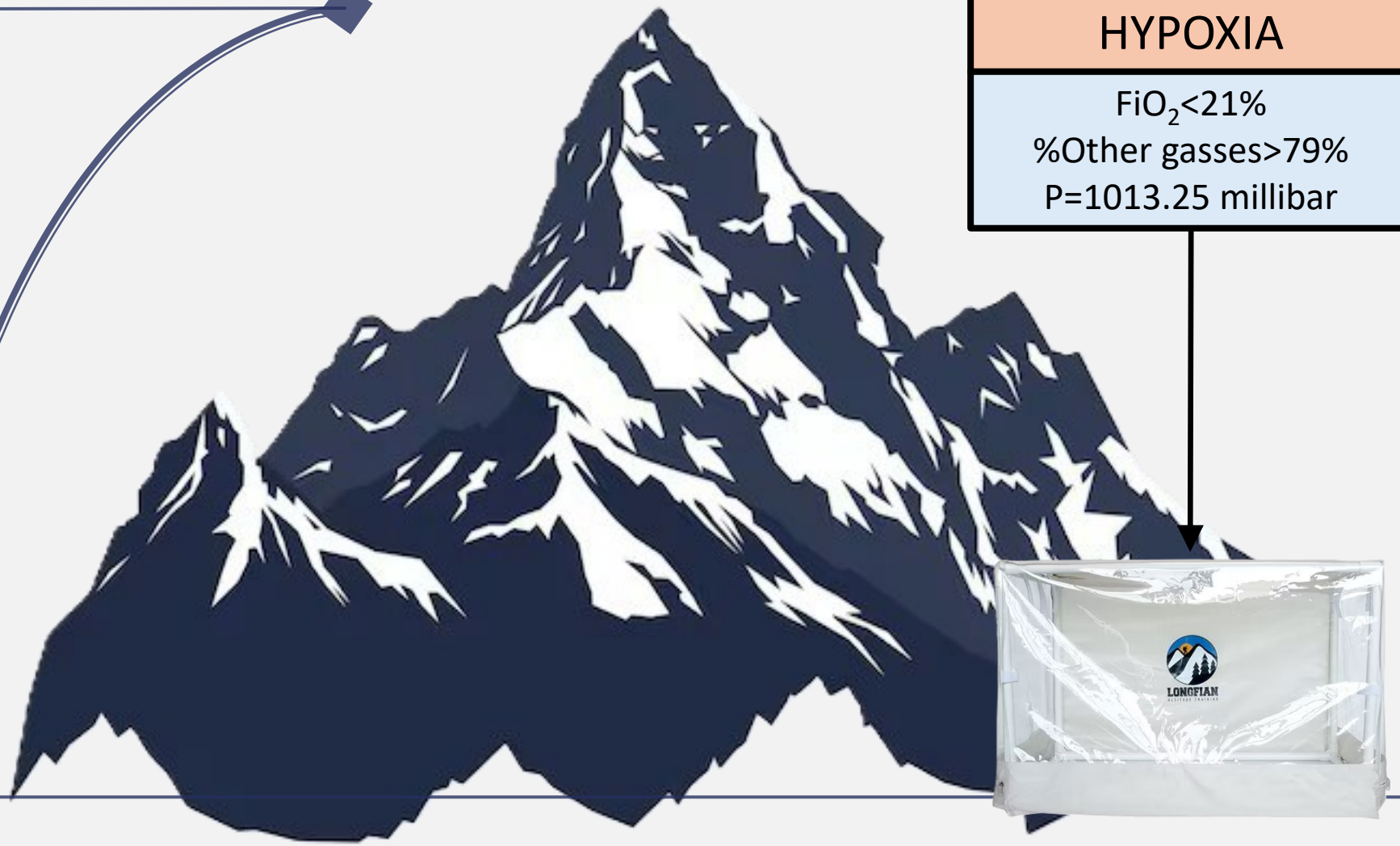
Normobaric hypoxia

In normobaric hypoxia, barometric pressure is the same as sea level but gasses equilibrium is changed

High altitude
FiO_2=21%
P=356 millibar

NORMOBARIC HYPOXIA

FiO_2<21%
%Other gasses>79%
P=1013.25 millibar



Sea level
FiO_2=21%
P=1013.25 millibar

Physiological cascade

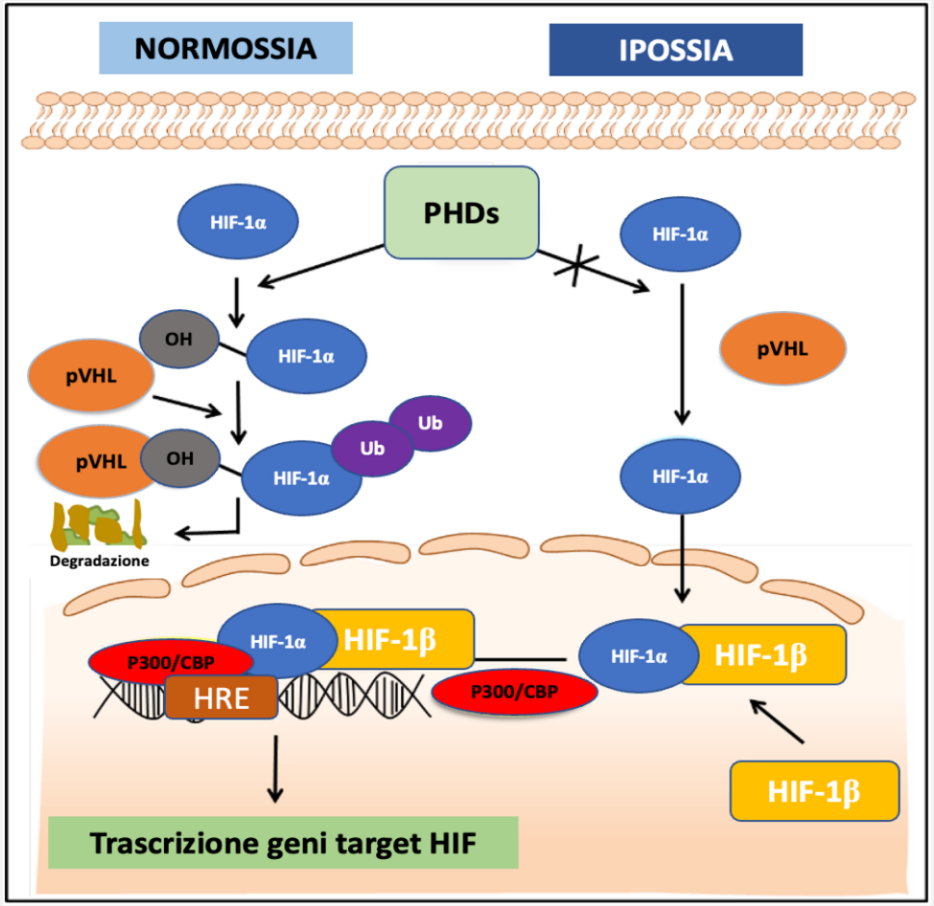
The 2019 Nobel Prize in Medicine: William G. Kaelin Jr., Sir Peter J. Ratcliffe, and Gregg L. Semenza

Hypoxia induced physiological cascade

Hypoxia Inducible Factor (HIF)

Vascular Endothelial Growth Factor (VEGF) and angiogenesis

Erythropoietin and erythropoiesis



The effects of normobaric hypoxia have been extensively studied in the context of muscle function: resistance training under hypoxic conditions can improve muscle performance.

In contrast, the neurophysiological and cognitive effects associated with exposure to it have been relatively unexplored.

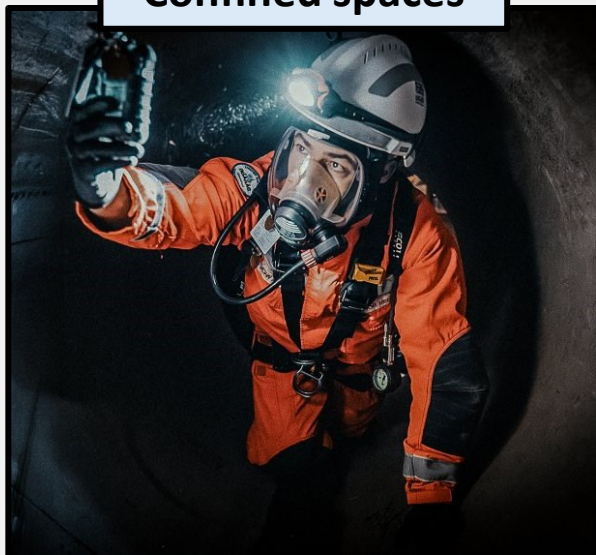
Fields of interests

Exercise physiology

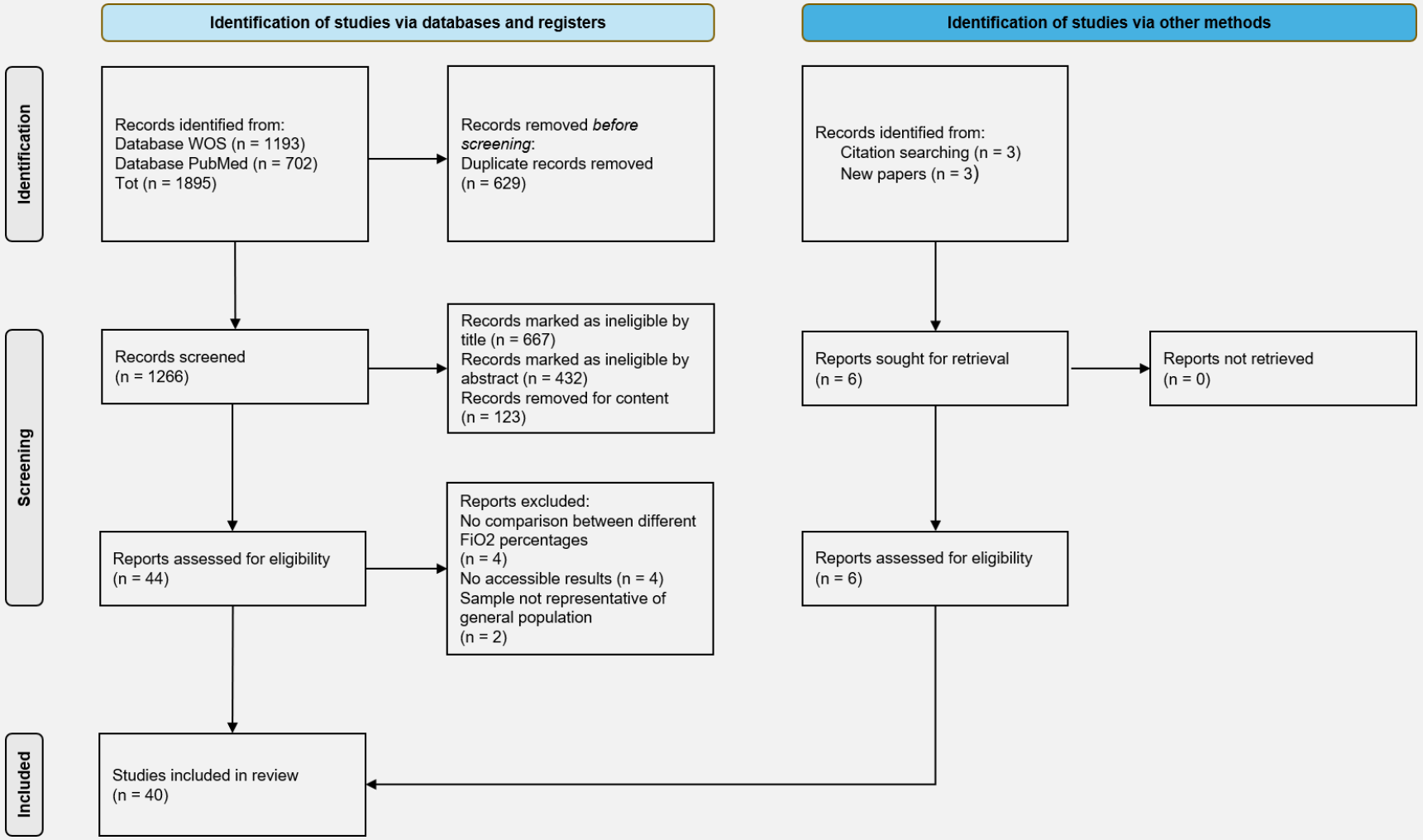
Medicine

Space research

Confined spaces



Systematic review



1895 Total papers

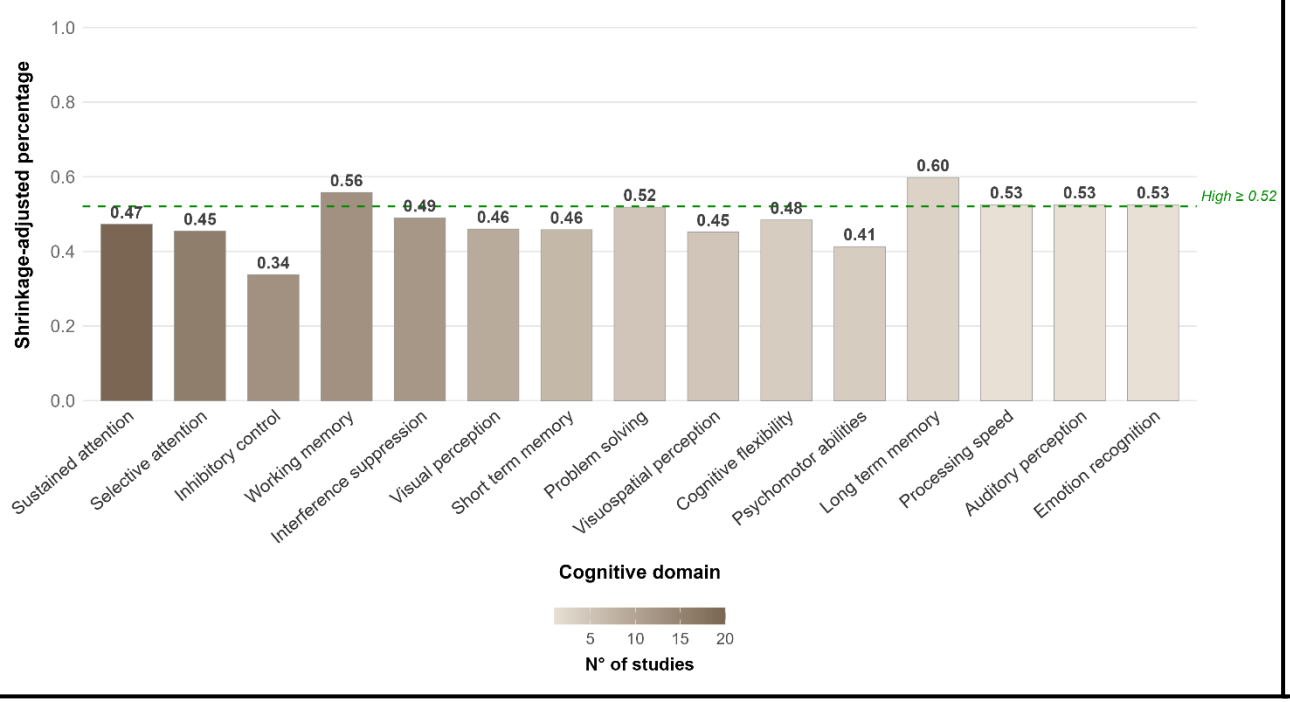
Parallel screening of title, abstract and full-text

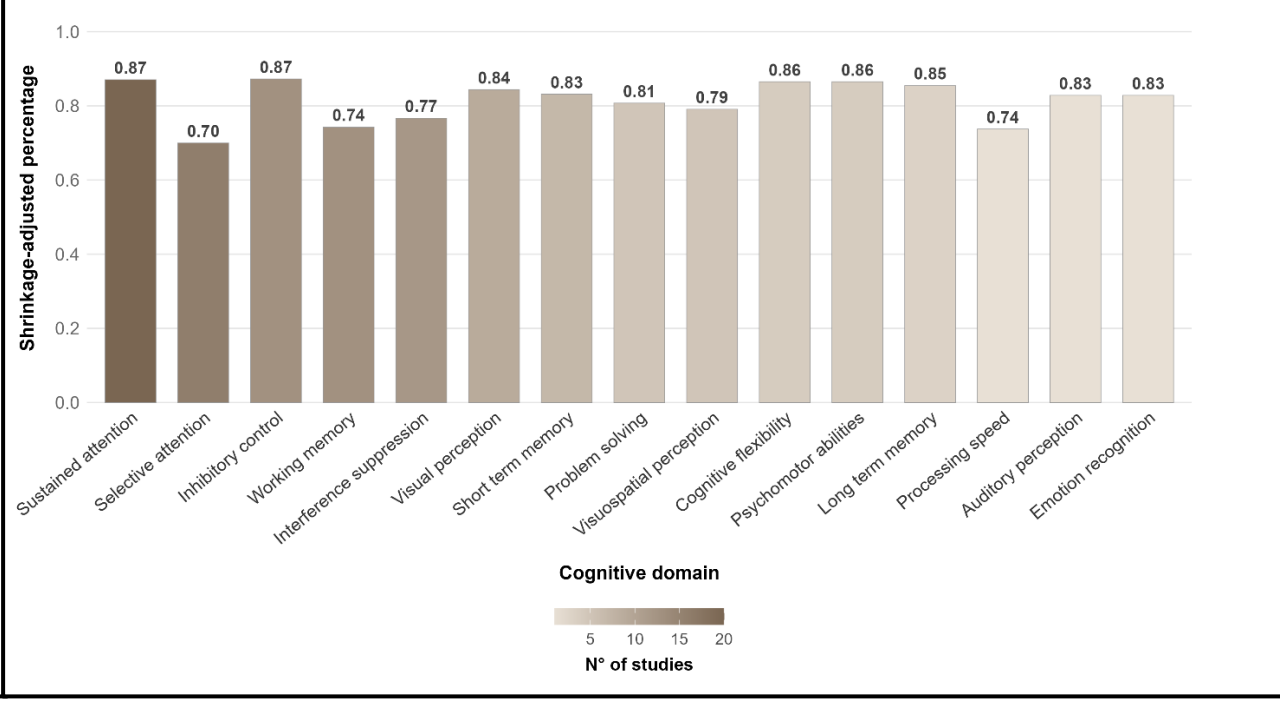
40 included studies

Most impacted domains appears to be Working Memory, Problem Solving and Long term Memory	In acute normobaric hypoxia, cognitive symptoms are present but only transitory

Findings

COGNITIVE DOMAIN	N	COGNITIVE ASSESSMENT			NEUROPHYSIOLOGICAL ASSESSMENT	
		% STUDIES REPORTING SIGNIFICANCE	SHRINKAGE-ADJUSTED PERCENTAGE		% STUDIES REPORTING SIGNIFICANCE	SHRINKAGE-ADJUSTED PERCENTAGE
Sustained attention	20	0.47	0.4726	Average	0.90	0.8704
Selective attention	16	0.44	0.4545†	Low	0.63	0.6996
Inhibitory control	13	0.23	0.3377	Low	0.92	0.8726
Working memory	13	0.62	0.5581	High	0.69	0.7426
Interference suppression	12	0.50	0.4899	Average	0.73	0.7668
Visual perception	9	0.44	0.4599	Average	0.88	0.8437*
Short term memory	7	0.43	0.4581†	Low	0.86	0.8312
Problem solving	5	0.60	0.5185*	Average	0.80	0.8074
Visuospatial perception	5	0.40	0.4518†	Low	0.75	0.7907
Cognitive flexibility	4	0.50	0.4841	Average	1.00	0.8650
Psychomotor abilities	4	0.25	0.4127	Low	1.00	0.8650
Long term memory	3	1.00	0.5982	High	1.00	0.8547
Processing speed	1	1.00	0.5252	High	0.00	0.7373
Auditory perception	1	1.00	0.5252	High	1.00	0.8282





Oxygen percentages

HYPOXIA	N	SIGNIFICANT RESULTS %	AFFECTED COGNITIVE DOMAINS %
MILD 21%<FiO2≤16%	7	14%	13%
MODERATE 16%<FiO2≤12%	25	44%	60%
SEVERE <12%	20	85%	80%

Working memory

- **DLPFC:** persistent neural activity, high metabolic demand
- Balance between excitation **(NMDA)** and inhibition **(GABA)**
- ↓O2 → E/I imbalance → alteration

Problem solving

- Strictly related to basic executive functions, directly derive from their integration
- **Executive Control Network** (DLPFC, parietal cortex, caudate nuclei): requires sustained activity and high metabolic activity
- ↓$CMRO_2$ shifts resources toward survival-critical circuits

Long term memory

- **Hippocampus:** low capillary density, sparse network of anastomoses, terminal vessels
- **PFC (DLPFC/VLPFC)** supports memory encoding
- Reduction of **hippocampus–PFC connectivity and DMN** (posterior cingulate cortex /cuneus)

Objectives

Non-invasively identify neurophysiological and cognitive markers associated with acute exposure to normobaric hypoxia.

Contribute to basic neurophysiological research, exploring the mechanisms of adaptation to hypoxia and analyzing how certain brain networks may be prioritized over others.

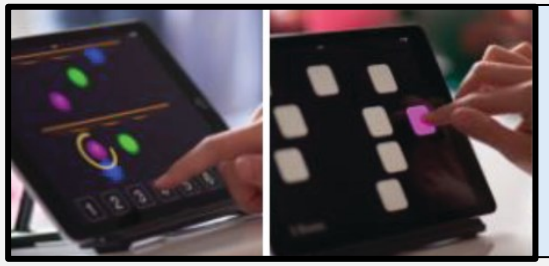
Isolcell
CONTROLLED ATMOSPHERE SINCE 1958

Thanks to the collaboration with Isolcell S.p.A., we can use a normobaric hypoxia tent inside our own lab

Normobaric hypoxia tent

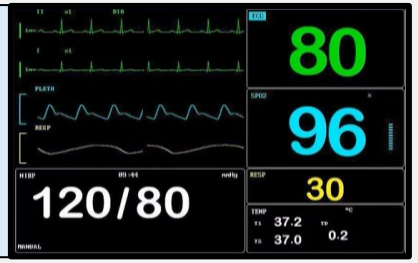
Methods

EEG



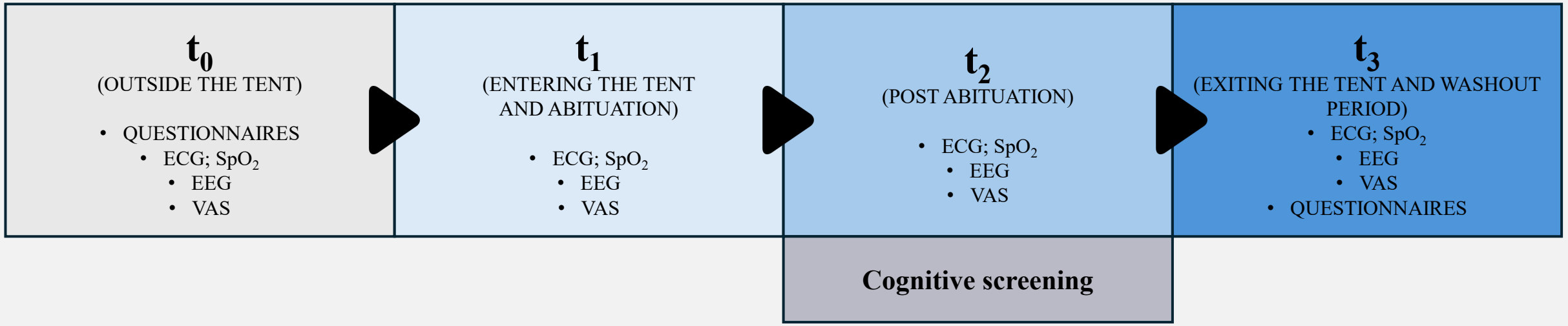
Cognitive tests Battery

Cardiac telemetry and Pulse oximeter



Experimental design

- Within subjects design
- 3 different conditions
- Continuous monitoring of vital signs



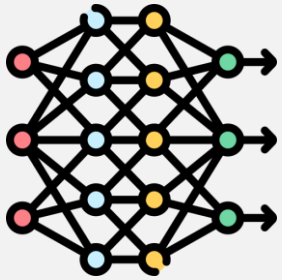
Analysis

Each variable will be analysed considering time, condition and the interaction of both

To highlight specific patterns of cognitive alterations in a standardized way

To analyze changes in functional connectivity between different cortical regions

Correlation analyses between cognitive and neural measures searching for a brain signature response to hypoxia



If the characteristics allows it, a machine learning model will be developed integrating neurophysiological measurements at rest and performance on behavioral tasks

Università di Brescia

Thank you for the attention