ME-CFS-CC26-004 - Mechanism-based Reversibility Evaluation and Stratified Endophenotyping of Treatment-response in ME/CFS

Zusammenfassung

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is defined by post-exertional malaise and exertional intolerance, yet lacks objective biomarkers to stratify patients or guide therapy. Converging evidence frames it as a disorder of imbalanced tissue energy supply and demand. In our first WWTF round, a controlled hypoxic challenge unmasked a dynamic metabolic-vascular failure: an absent adaptive rise in brain lactate and markedly stronger negative coupling between neuronal integrity (tNAA) and perfusion in patients than controls, with parallel impairment of skeletal-muscle phosphocreatine recovery and oxidative capacity.

ME-RESET aims to localise this failure and test its reversibility. We hypothesise that the activity-dependent deficit is dissociable into an oxygen-supply/perfusion-limited component versus an intrinsic mitochondrial oxygen-utilisation defect, shared systemically or tissue-selective, and that it is partially reversible by targeted elevation of tissue oxygen. In a randomized delayed-start design, 50 patients (25:25), Bell 30–70, undergo three controlled-hypoxic-challenge (CHC) sessions, each pairing multi-organ MRI/MRS - brain under systemic hypoxia (85% SpO2) and calf under arterial occlusion - with circulating read-outs (lactate/pyruvate ratio, HIF-axis transcripts, VEGF/EPO, ISR mitokines GDF-15/FGF-21, cf-mtDNA, 8-OHdG). Hyperbaric oxygen therapy (10 sessions, 2.2 ATA) serves as an interventional probe of reversibility. The primary endpoint is the within-subject pre/post-HBOT change in objective metabolic-vascular signatures; FUNCAP-27 is the co-primary clinical anchor. Linear mixed models and cross-validated machine learning will define mechanistic endophenotypes and predict response.

ME-RESET will deliver stratification biomarkers and proof-of-concept for oxygen-modulation of metabolic inflexibility, with translational relevance to post-acute infection syndromes and mitochondrial-driven neurodegeneration.

Wissenschaftliche Disziplinen:
Radiology (70%) | Neurology (15%) | Internal medicine (15%)

Schlagworte:
ME/CFSMetabolic Dysfunction Hyperbaric Oxygen TherapyOxygen MetabolismMultimodal MRI

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https://www.wwtf.at/funding/programmes/ei/ME-CFS-CC26-004/