IAA HIS 2019
Dubai, UAE

HUMAN METABOLIC DOWNREGULATION FOR SPACE-STRESS TOLERANCE: (PRELIMINARY) EXPERIMENTAL PROOF-OF-CONCEPT

Jungle Innovations

Keywords: Weightlessness, G-Force, Metabolic Rate, Torpor, Human

ABSTRACT

Human tolerance of chronic gravitational unloading, such as space-weightlessness, is reduced, in part, because larger animals are subjected to a much greater mass-related counter-gravity metabolic cost (CGMC), more specifically, enzyme-driven *mass* activity, that which powers & sustains life. Removing this component from the metabolic bottom-line leads to desynchrony between various interdependent metabolic reactions, as indicated by the basic, *fundamental*, metabolic life-equation which governs all biochemical reactions.[1-6] On Earth, the $CGMC_{1\text{-}G\oplus}$ contributes ~35% & ~10% to the minimum existential or basal metabolic rate (BMR) of a 100-kg human & 10-g mouse, respectively, due to the absolutely greater enzyme mass that comes with size; the non-linear discrepancy despite a 10,000-fold size difference is due to the lower pound-for-pound or mass-specific metabolic rate (MR_S) of larger animals, here reduced to $1/12^{th}$. Furthermore, because elapsed (metabolic) time is just the inverse of MR per unit mass, a time-dose effect manifests so that the metabolic *clocks* become progressively more desynchronized & pathologies inevitably manifests.[7-8] However, it is known that animals in a metabolic state of torpor, i.e., sub-BMR, can be rendered effectively *immune* to chronic unloading, even very large ones, e.g., hibernating bears tolerate up to 8 months of near-complete inactivity. Torpid states can so profoundly slow metabolic activity &, thus, biological times that animals appear as if metabolically *down-sized & suspended in time,* de-animated. Indeed, in this state many key pathways are temporarily decoupled, say, *broken, &/*or remodeled for greater protection, others are upregulated by the off-nominal exposure.[9] This is not altogether surprising since the best way to protect an intricate *metabolic machine* is to temporarily Lego-like disassemble it. Indeed, since torpor is expressed in an extremely varied range of mammals & known to confer unmatched enhanced tolerance against a myriad of other major metabolic stressors, e.g., extreme acceleration/deceleration, thirst, starvation, isolation, confinement, inactivity, infection, intoxication (e.g., hypercapnia/oxia), hypoxia, hypo/hyperthermia, ionizing-radiation, darkness, decompression-illness, even time itself, if humans could express this state they might similarly manifest broad-spectrum biomedical protection, i.e., *game-changer*. Interestingly, because the CGMC contribution expands in torpor vis-à-vis the thermoregulatory burden, weightlessness should result in the most profound torpor &, thus, the most profound biological slowing & protection, it would transform weightlessness into a novel space-life-support resource that maximizes conservation of resource, including time, & well beyond what could be achieved on Earth, i.e., fortuitous given the extreme & austere environment; back-of-the-envelope calculations predict a biological time dilation factor of about 12, equivalent to what would be realized on reaching ~99.5% the speed-of-light, as previously suggested.[10] Now, the lowly physiological vitals of hibernating bears stand on par with that of similar sized breath-hold diving seals, an environment in which the CGMC is near-collapsed by buoyancy, leading some to suggest that *"the bear may 'dive' into hibernation"*, so that this strategy might be the long-suspected pathway that opens-up the possibility of

bear-like sustaining this state.[10-15] Revealed here, seal/bear-like down-powered metabolic capabilities of some human breath-hold divers, including, a telltale constellation of classic physiological hallmarks that typify this state: spontaneous, ultra-fast & profound temperature-dependent & -independent sub-BMR, e.g., core-body (brain) cooling.[16] Efforts are presently geared towards determining the absolute depth & sustainability of this state.[16]

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