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EVALUATION OF THE EFFECTS OF 60-DAYS HEAD-DOWN BED REST AND NUTRITIONAL COUNTERMEASURE ON CARDIAC CIRCADIAN RHYTHMS

Abstract

Aims. Prolonged weightlessness exposure associated to space flight generates cardiac deconditioning, with potential implications on ECG circadian rhythms. Head-down (-6 degrees) bed-rest (HDBR), as model of chronic circulatory unloading, simulates sustained microgravity exposure. We aimed at evaluating the impact of 60-days HDBR on beat-by-beat RR and ventricular repolarization (QTend) duration circadianity and the effectiveness of nutritional countermeasure (CM).

Methods. 20 males (34±7 years), enrolled at MEDES (Toulouse, France) after study ethical approval and signed informed consent, were randomly allocated into a CM group (N=10), undergoing daily nutritional vitamin and antioxidant cocktail supplementation during HDBR, or control group (CTRL, N=10). Day (7AM-11PM) and night (11PM-7AM) cycle was imposed. For each subject, 12-leads 24-hours Holter ECG (1000 Hz, H12+, Mortara Instrument Inc.) was acquired 9 days before HDBR (BCD-9), the 5th (HDT5), 21st (HDT21) and 58th (HDT58) day of HDBR, the first (R+0) and 8th (R+7) day after HDBR. For each extracted 24h RR and QTend beat-to-beat series, circadianity was evaluated by Cosinor analysis, resulting in MESOR (Midline Statistic of Rhythm), oscillation amplitude (OA, measuring half variation within a night-day cycle), and acrophase (temporal value at the maximal amplitude of the fitting sinusoid). Statistical analysis was applied to test the effects of 60-days HDBR versus BCD-9 (Wilcoxon, $p<0.05$), and to compare CTRL and CM (Mann-Withney, $p<0.05$).

Results. Compared to BCD-9, at HDT5, RR (CTRL:+17.4%, CM:+16.6%) and QTend (CTRL:+3.5%, CM:+1.7%) MESOR showed the maximum increment, with RR MESOR then recovering along HDBR (CTRL:+11.4% at HDT21, CM:-2.2% at HDT58). Conversely, compared to BCD-9, at R+0 an abrupt decrease was visible both in RR (CTRL:-21.4%, CM:-27%) and QTend (CTRL:-9%, CM:-10.9%), with a trend to baseline values at R+7. During HDBR, OA decreased in both RR (CM:-43.4% at HDT21, higher than CTRL:-28.5%), and QTend (CM up to 48.7% at HDT58). Post-BR, OA restored to baseline, except for QTend in CTRL at R+0 (+33.2%). Acrophase was shifted backward during HDBR (CTRL:-3.2% and

CM:-5.3% at HDT5), and postponed at R+0 compared to BCD-9 (CTRL: RR 4:19AM[4:06;4:42] versus 4:00AM[3:30;4:12]; QTend 4:36AM[4:12;4:54] versus 4:12AM[3:42;4:30]). Circadianity uncoupling between RR and QTend, as difference between acrophases, was found in CTRL at HDT5 (-4'56"[-13'54";1'53"]) compared to BCD-9 (15'57"[8'36";23']), and in CM at HDT58 (-1'[-12';20'36"] versus 0'54"[-5';30'36"]).

Conclusions. 60-days HDBR affects ECG circadian rhythms notwithstanding the nutritional countermeasure, by reducing amplitude and altering acrophase, differently in RR and QTend. The observed changes appeared reversible and within physiologic limits.