The effect of acute intermittent hypoxia on motor learning

NCT Number NCT05341466

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APPROACH:

Methodology: We implemented a placebo controlled, two group study design that characterized how changes in corticospinal excitability are associated with motor adaptation and walking energetics in 26 persons following repetitive exposure to AIH. Each intervention involved 5 consecutive treatment visits. For each treatment visit, participants received an exposure [15, 1.5 min episodes at 9% O_2 (AIH) or 21% O_2 (SHAM) at 1 min intervals]. Split belt adaptation assessments and metabolic cost quantification protocols were implemented at the end of each intervention. Delivery of intermittent gas mixtures was accomplished using air generators [HYP123, Hypoxico] attached to a non-rebreathing face mask. In order to ensure subject safety during interventions, we monitored oxygen saturation (SpO_2), heart rate, respiratory rate and blood pressure [Root 7, Masimo] at 1 second intervals.

Transcranial Magnetic Stimulation: TMS was delivered via a custom-built batwing coil for leg stimulation connected to a DUOMAG unit [Deyemed]. Single pulse TMS with monophasic current waveform was applied to the contralateral motor cortex of the more impaired target TA muscle. Coil position and head position were digitally tracked to ensure similar coil placement in repeated measurements using a Visor 2LT optical system [ANT Neuro]. The hot spot was defined as the region where largest and most consistent MEPs are evoked using a stimulation intensity of 1.2 x resting motor threshold (RMT) intensity. RMT was defined as the stimulator output intensity that elicits MEPs with peak-to-peak amplitudes greater than 50 μV in four out of eight trials in the relaxed muscle. MEPs from the tibialis anterior were obtained during rest and at static contraction of up to 20% MVC. Real-time visual feedback about EMG contraction level was provided. The slope of the recruitment curve reflects gain in MEP amplitude with increasing stimulus intensity, providing an indication of gain modulation. TMS intensity was increased from below motor threshold at stimulator intensity intervals representing 90% to 120% of RMT. 20 randomized stimuli were given per stimulation intensity, and the MEPs were ensemble averaged for analyses. The mean MEP response was plotted against the corresponding stimulation intensity (% of RMT) to produce a stimulus-response recruitment curve. We compared recruitment curve parameters (MEP_{max}, slope) before and after AIH.

Sensorimotor Adaptation: We characterized motor adaptation by quantifying changes in step asymmetry in response to split belt treadmill speed perturbations, before and after repetitive AIH exposure. Step asymmetry was quantified as the ratio of normalized difference in step lengths of each leg. Temporal asymmetry was computed from the time series of joint angles as the lag time at peak cross-correlation of limb angle trajectories. The first 5-10 strides of the 'adaptation' and 'de-adaptation' epochs were used to quantify speed perturbation induced effects. Motor adaptation was evaluated relative to the baseline epoch by comparing step asymmetries during the first and last 10 steps of the 'adaptation' and 'de-adaptation epochs'. A greater difference indicates greater motor adaptation. Improvement of interlimb coordination was estimated based on decreases of asymmetry in both spatial and temporal step parameters. We compared changes in step asymmetry and interlimb coordination between AIH and SHAM interventions.

Net Metabolic Power: We quantified the metabolic costs during treadmill gait before and after AIH during the final 2 minutes of the motor adaptation epochs. We identified spatiotemporal gait parameters that affect the capacity to minimize the metabolic cost in participants with iSCI. We measured the net metabolic power during treadmill walking as the rate of metabolic energy consumption. Participants wore a nose clip and breathed in and out of a mouthpiece to measure the rates of O_2 consumption Vo_2 and CO_2 production Vco_2 (liter/min) using expired gas analysis [ParvoMedics, TrueMax2400]. The measured rates (liter/min) of Vo_2 and Vco_2, which we then converted to metabolic power (J/s) using the Brockway equation as the outcome measure representing the rate of metabolic energy consumption. Metabolic power was normalized to the subject's body weight ($J \cdot s{-}1 \cdot kg{-}1$). To calculate net metabolic power, we subtracted baseline resting metabolic power while quiet standing.

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STATISTICAL ANALYSES:

Hypothesis Testing for Corticospinal Excitability:
We hypothesized that exposure to repetitive, acute intermittent hypoxia enhances CST excitability to the TA (i.e., increase MEP_{max} and recruitment curve slope) after repetitive AIH. TMS testing was completed within this time, as we expected this facilitation to persist for up to 1 hour post-AIH based on prior research in our lab. Data was evaluated for normality using the Kolmogorov-Smirnov test. If data satisfied the normality test, a repeated measures analyses of variance was used to determine if each excitability parameter differed across PRE and POST conditions. Sphericity was assessed using the Mauchly test. If sphericity was violated, we used the Huynh-Feldt corrected p value. Post hoc comparisons were used in the Tukey-Kramer correction for multiple comparisons.

Hypothesis Testing for Motor Adaptation:
Spatiotemporal asymmetry parameters were calculated in each epoch (adaptation, second adaptation) in 3 periods: initial (mean of first 5 strides), early (mean of strides 6-20), and the late (mean of last 30 strides). Differences from BL to adaptation was compared between and within interventions using a mixed model ANOVA at a 0.05 significance level; the between-subjects factor is intervention (AIH vs. SHAM), and the within-subjects factor is time (initial, early change, late), with spatiotemporal parameters (e.g., step length asymmetry, step time asymmetry) as the dependent variables. Analysis of covariance (ANCOVA) was used if PRE measures are significantly different between interventions. If sphericity was violated, we used the Huynh-Feldt corrected p value. Post hoc comparisons used the Tukey-Kramer correction for multiple comparisons.

Hypothesis Testing for Metabolic Cost:
We tested the hypothesis that exposure to repetitive, acute intermittent hypoxia decreased net metabolic power using a mixed model ANOVA at a 0.05 significance level; the between subject's factors is intervention (AIH vs SHAM), and the within subjects' factors is time (initial, early change, plateau), with net metabolic power as dependent variable. A multiple linear regression was implemented to determine the spatiotemporal variables associated with capacity to reduce asymmetry and net metabolic power for the following independent variables: MEP_{max}, recruitment curve slope, step length, step time, stance duration and baseline metabolic power. Variance inflations factors were calculated to avoid multicollinearity with the Akaike information criterion model utilized for model selection.