

Effect of Nitrate on Cognitive Function and Neurovascular Coupling at High Altitude

Wesley K. Lefferts, William E. Hughes, Corey N. White, Tom D. Brutsaert, Kevin S. Heffernan
Syracuse University, Syracuse, NY

Cognitive dysfunction at high altitude (HA) may result from suboptimal matching of oxygen supply to neural demand (i.e. neurovascular coupling [NVC]). NVC is modulated by nitric oxide (NO) which initially decreases at HA. **PURPOSE:** Investigate the effect of NO-donor (nitrate) supplementation on NVC and cognitive function at HA. **METHODS:** 20 healthy men (23±3 yrs, BMI 24.3±3.0 kg·m⁻²) participated in this randomized, double-blind, crossover design study on two separate days. Following sea level (SL) cognitive/NVC testing, participants consumed either nitrate (NIT) or a NIT-depleted placebo (PLA). Participants then underwent 120 minutes of HA (11.5±0.2% O₂) and all cognitive/NVC testing was repeated. NVC was assessed by measuring the change in mean middle cerebral artery (MCA) blood flow velocity during a cognitive challenge (incongruent Stroop task) using transcranial Doppler. Additional cognitive testing targeted the memory and executive function domains using memory recognition, maze, and choice reaction tasks. Brachial artery flow-mediated dilation (FMD) and salivary nitrite were assessed as systemic proxies of NO-metabolism. **RESULTS:** Salivary nitrite significantly increased following supplementation at HA for NIT compared to PLA (p<0.05). FMD and memory performance significantly decreased and executive function, reaction time and MCA reactivity were unchanged at HA in both conditions (p>0.05). **CONCLUSION:** NIT significantly increased salivary nitrite levels at HA compared to PLA. However, NIT was unable to prevent reductions in FMD or decreased memory at HA nor was NIT able to augment NVC at HA compared to SL. This research was supported by a Foundation Research Grant from the American College of Sports Medicine

Table 1. NO-metabolism, cognitive function, and NVC at SL and HA between conditions (mean ± SD)

	Placebo (PLA)		Nitrate (NIT)	
	SL	HA	SL	HA
SaO ₂ (%)	98 ± 2	75 ± 6*	98 ± 2	75 ± 7*
FMD (%)	6.22 ± 3.62	4.87 ± 3.22*	8.13 ± 3.14	5.52 ± 3.14*
Salivary nitrite (AU)	0.1 ± 0.2	0.2 ± 0.3	0.1 ± 0.2	2.7 ± 1.0†*
<i>NVC</i>				
ΔMCA Mean velocity (cm·s ⁻¹)	+ 5 ± 6	+ 5 ± 9	+ 7 ± 7	+ 6 ± 7
<i>Cognitive measures</i>				
Verbal memory index ^a	75 ± 9	70 ± 10*	75 ± 5	71 ± 10*
Maze accuracy	30 ± 14	28 ± 11	29 ± 12	31 ± 10
Choice reaction time (ms)	343.35 ± 73.64	346.52 ± 31.85	328.72 ± 34.56	350.52 ± 26.52

SL, sea level; HA, high altitude; SaO₂, arterial oxygen saturation; FMD, flow mediated dilation; MCA, middle cerebral artery.

^acalculated as (immediate memory recognition + delayed memory recognition)

*p<0.05 vs SL; †p<0.05 vs PLA