

**Sex-specific difference in the effect of altitude on sleep and nocturnal breathing
in young healthy volunteers**

(Supplemental material)

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Table S1 Sleep parameters in men and women at 500 m and 3270 m

	Men				Women			
	500 m	3270 m 1 st night	3270 m 2 nd night	ANOVA, P value	500 m	3270 m 1 st night	3270 m 2 nd night	ANOVA, P value
Objective sleep								
Sleep latency, min	7.8 (4.0, 26.3)	7.3 (3.0, 15.8)	5.8 (3.8, 8.9)	0.500	13.0 (6.8, 21.4)	9.5 (5.3, 15.5)	9.8 (5.1, 18.4)	0.229
TST, min	426.9 (393.9, 468.0)	418.5 (368.8, 458.6)	449.5 (400.3, 457.4)	0.407	427.3 (359.3, 460.7)	441.5 (396.0, 465.9)	451.8 (426.3, 473.0)	0.269
NREM 1, %	14.1 (11.2, 17.0)	19.3 (13.6, 20.3)	12.9 (9.9, 15.8)	0.058	10.7 (8.3, 17.2)	13.1 (8.6, 17.6)	10.4 (7.4, 12.4)	0.444
NREM 2, %	50.3 (48.1, 53.1)	48.9 (41.7, 51.1)	49.2 (44.3, 50.7)	0.301	49.5 (45.1, 58.6)	49.0 (44.5, 54.0)	48.7 (45.0, 53.8)	0.444
NREM 3, %	14.5 (11.3, 15.5)	16.1 (10.3, 19.1)	16.0 (13.5, 17.6)	0.407	13.9 (11.0, 17.5)	15.4 (13.9, 21.7)	16.4 (13.7, 17.9)	0.032
REM, %	22.8 (15.2, 25.4)	20.5 (13.9, 22.6)	23.4 (17.1, 28.0)	0.045	22.6 (16.6, 25.3)	21.8 (16.7, 23.4)	24.2 (20.9, 26.9)	0.068
WASO, min	30.4 (21.8, 56.6)	34.0 (18.5, 81.6)	33.3 (23.8, 50.3)	0.836	22.5 (10.9, 48.1)	40.5 (10.1, 70.6)	26.0 (13.6, 42.1)	0.174
Sleep efficiency, %	87.8 (86.8, 94.6)	90.8 (80.5, 93.8)	91.8 (88.4, 93.4)	0.905	90.5 (86.9, 95.1)	91.1 (82.7, 96.2)	91.2 (88.4, 95.2)	0.174
Arousal index, /h	10.8 (9.1, 13.8)	17.5 (16.1, 20.5) ^a	14.5 (11.7, 17.0) ^b	0.014	10.3 (7.7, 14.8)	13.2 (9.8, 17.3)	11.1 (9.4, 14.2)	0.405
Subjective sleep								
Sleep latency, min	35.0 (10.0, 60.0)	20.0 (12.5, 30.0)	20.0 (12.5, 30.0)	0.127	30.0 (20.0, 30.0)	20.0 (10.0, 30.0)	20.0 (10.0, 30.0)	0.376
TST, min	405.0 (375.0, 427.5)	435.0 (397.5, 482.5)	435.0 (397.5, 483.0)	0.110	420.0 (360.0, 425.0)	430.0 (420.0, 480.0)	430.0 (420.0, 480.5)	0.767
Arousal, events	2.0 (1.0, 3.0)	2.5 (1.0, 4.3)	2.5 (1.0, 4.3)	0.368	3.0 (1.8, 3.3)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	0.142
Heart rate								
NREM heart rate, beats/min	60.7 (56.8, 67.5)	77.1 (72.3, 88.3) ^a	78.6 (73.4, 86.9) ^a	0.007	58.5 (43.8, 63.1)	75.0 (71.6, 82.0) ^a	81.2 (75.4, 86.4) ^a	<0.001
REM heart rate, beats/min	62.0 (58.9, 68.5)	75.0 (71.3, 88.2) ^a	76.0 (72.9, 86.1) ^a	0.008	60.0 (46.2, 66.8)	76.2 (71.9, 82.6) ^a	78.7 (75.9, 83.2) ^a	<0.001

Values represent median (interquartile range). TST, total sleep time; NREM 1-3, non-rapid eye movement sleep stage 1-3; REM, rapid eye movement sleep; WASO, wake time after sleep onset. ^ap < 0.05 comparing with 500 m within the same sex; ^bp < 0.05 comparing with 3270 m 1st night within the same sex.

Table S2. Daytime evaluations in women and men at 500 m and 3270 m

	Men				Women			
	500 m	3270 m 1 st day	3270 m 2 nd day	ANOVA, P value	500 m	3270 m 1 st day	3270 m 2 nd day	ANOVA, P value
AMS								

AMS, score		1.0 (0, 2.8)	0 (0, 0.8)		3.0 (0.3, 4.0)	1.0 (0, 3)		
AMS, n (%)		1 (10.0)	1 (10.0)		7 (38.9)	4 (25.0)		
PVT								
Mean RT, ms	355 (348, 389)	362 (336, 391)	342 (338, 369) [*]	0.368	353 (338, 370)	386 (357, 405) ^a	389 (362, 419) ^a	0.001
Lapses, events	6.0 (2.0, 9.0)	5.0 (1.5, 7.0)	3.0 (1.0, 4.5) [*]	0.163	4.5 (1.3, 5.8)	6.0 (3.3, 10.0)	7.0 (4.0, 12.0)	0.125
Fastest 10% RT, ms	277 (253, 302)	271 (256, 306)	273 (250, 281) [*]	0.565	272 (263, 293)	284 (274, 306)	293 (273, 310) ^a	0.028
Slowest 10% RT, ms	520 (477, 704)	544(465, 688)	502 (459, 571)	0.565	501 (462, 537)	541 (500, 582)	502 (459, 571)	0.144
Arterial blood analysis								
pH	7.40 (7.39, 7.43)	7.45 (7.44, 7.47) ^a	7.46 (7.41, 7.48) ^a	0.005	7.41 (7.41, 7.42)	7.45 (7.43, 7.47) ^a	7.47 (7.45, 7.48) ^a	0.001
PaCO ₂ , mmHg	39.2 (35.2, 43.3)	35.5 (33.8, 39.3)	37.0 (33.5, 38.2) [*]	0.206	35.9 (34.4, 41.0)	34.0 (30.0, 38.0)	32.0 (28.5, 32.8) ^{a b}	0.005
PaO ₂ , mmHg	86.6 (81.6, 94.6)	56.0 (49.0, 60.3) ^{a*}	53.0 (49.5, 59.1) ^{a*}	0.001	90.3 (83.1, 95.9)	62.0 (55.0, 64.0) ^a	60.5 (57.5, 64.8) ^a	<0.001
HCO ₃ ⁻ , mmol/L	24.8 (23.9, 26.0) [*]	25.1 (23.8, 26.5)	25.1 (23.8, 27.1) [*]	0.325	22.1 (21.8, 23.5)	24.2 (22.6, 25.1)	23.7 (20.5, 24.5)	0.052
SaO ₂ , %	97.8 (96.1, 98.0)	90.0 (85.5, 92.0) ^a	90.4 (87.5, 91.0) ^{a*}	0.001	97.8 (97.0, 98.0)	92.0 (88.0, 93.0) ^a	92.0 (92.0, 93.8) ^a	<0.001
Venous blood analysis								
Red blood cell, ^10 ¹² /L	5.2 (5.0, 5.4) [*]	5.5 (5.1, 5.7) [*]	5.3 (5.2, 5.7) [*]	0.895	4.5 (4.2, 4.9)	4.6 (4.4, 4.7) ^a	4.8 (4.5, 5.1) ^a	0.012
Hemoglobin, g/L	157.0 (153.0, 162.5) [*]	162.9 (154.6, 167.0) [*]	159.0(155.0, 167.0) [*]	0.955	137.5 (132.5, 140.3)	137.6 (131.7, 142.0)	144.5 (134.8, 148.3)	0.068
Hematocrit, L/ L	0.45 (0.44, 0.47) [*]	0.48 (0.45, 0.50) ^{a*}	0.47 (0.46, 0.51) ^{a*}	0.045	0.39 (0.38, 0.41)	0.42 (0.39, 0.42) ^a	0.43 (0.41, 0.46) ^a	0.001
White blood cell, ^10 ⁹ /L	5.5 (4.9, 6.4)	6.9 (5.8, 8.5)	5.6 (5.0, 8.0)	0.102	5.6 (4.2, 6.4)	6.6 (5.2, 8.4) ^a	6.7 (5.1, 7.7) ^a	<0.001
Platelet, ^10 ⁹ /L	237.0 (206.8, 319.5)	244.0 (213.8, 272.8)	261.0 (238.0, 312.0)	0.396	228.5 (174.5, 254.5)	236.0 (191.8, 261.5) ^a	237.5 (197.3, 306.5) ^a	0.017

Values represent median (interquartile range). AMS, acute mountain sickness; PVT, psychomotor vigilance test; RT, reaction time. PaCO₂, partial pressure of carbon dioxide in artery; PaO₂, partial pressure of oxygen in artery; HCO₃⁻, Bicarbonate Radical; SaO₂, oxygen saturation in artery. ^ap < 0.05 comparing with 500m within the same sex; ^bp < 0.05 comparing with 3270 m 1st night within the same sex; ^{*}p < 0.05 men vs. women at identical altitude and day.

Table S3 Univariate and multivariate generalized least square regression analysis models investigating predictors for AMS score and PVT

AMS severity, defined by the Lake Louise questionnaire				
Independent variables	Univariate analysis		Multivariate analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Age, years	-0.02 (-0.34, 0.31)	0.923		
BMI, kg/m ²	-0.09 (-0.29, 0.10)	0.352		
Sex (women vs. men)	1.21 (-0.02, 2.45)	0.054	1.16 (-0.07, 2.38)	0.060
AHI, /h	0.01(-0.05, 0.04)	0.860		
Central AHI, /h	-0.01 (-0.09, 0.09)	0.917		
Mean oxygen saturation, %	-0.03 (-0.16, -0.10)	0.606		
Total sleep time, min	-0.01 (-0.02, 0.01)	0.293		
Sleep efficiency, %	-0.05 (-0.12, 0.02)	0.183	-0.03 (-0.10, 0.04)	0.442
Arousal index, /h	-0.03 (-0.16, 0.10)	0.640		
Days at high altitude (2 nd vs.1 st)	-1.00 (-2.21, 0.21)	0.101	-0.89(-2.10, 0.32)	0.145
PVT reaction time, 1/ms				
Independent variables	Univariate analysis		Multivariate analysis	
	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Age, years	0.007 (-0.017, 0.030)	0.575		
BMI, kg/m ²	-0.002 (-0.019, 0.015)	0.803		
Sex (men vs. women)	-0.076 (-0.201, 0.049)	0.198	-0.078 (-0.200, 0.043)	0.204
Total sleep time, min	-0.001 (-0.002, 0.001)	0.208		
NREM 3, %	-0.006 (-0.019, 0.007)	0.340		
Sleep efficiency, %	-0.001 (-0.011, 0.009)	0.877		
Wake time after sleep time, min	0.001 (-0.002, 0.002)	0.967		
Mean oxygen saturation, %	0.008 (0.001, 0.016)	0.029		
AHI, /h	-0.003 (-0.007, 0.002)	0.259		
Altitude (3270 m vs. 500 m)	0.143 (0.267, 0.019)	0.024	0.144(0.021, 0.268)	0.023
Days at high altitude (2 nd vs.1 st)	-0.052 (-0.182, 0.077)	0.422		

AMS, acute mountain sickness; PVT, psychomotor vigilance test; BMI, body mass index; NREM 3, non-rapid eye movement sleep stage 3; AHI, apnea hypopnea index.

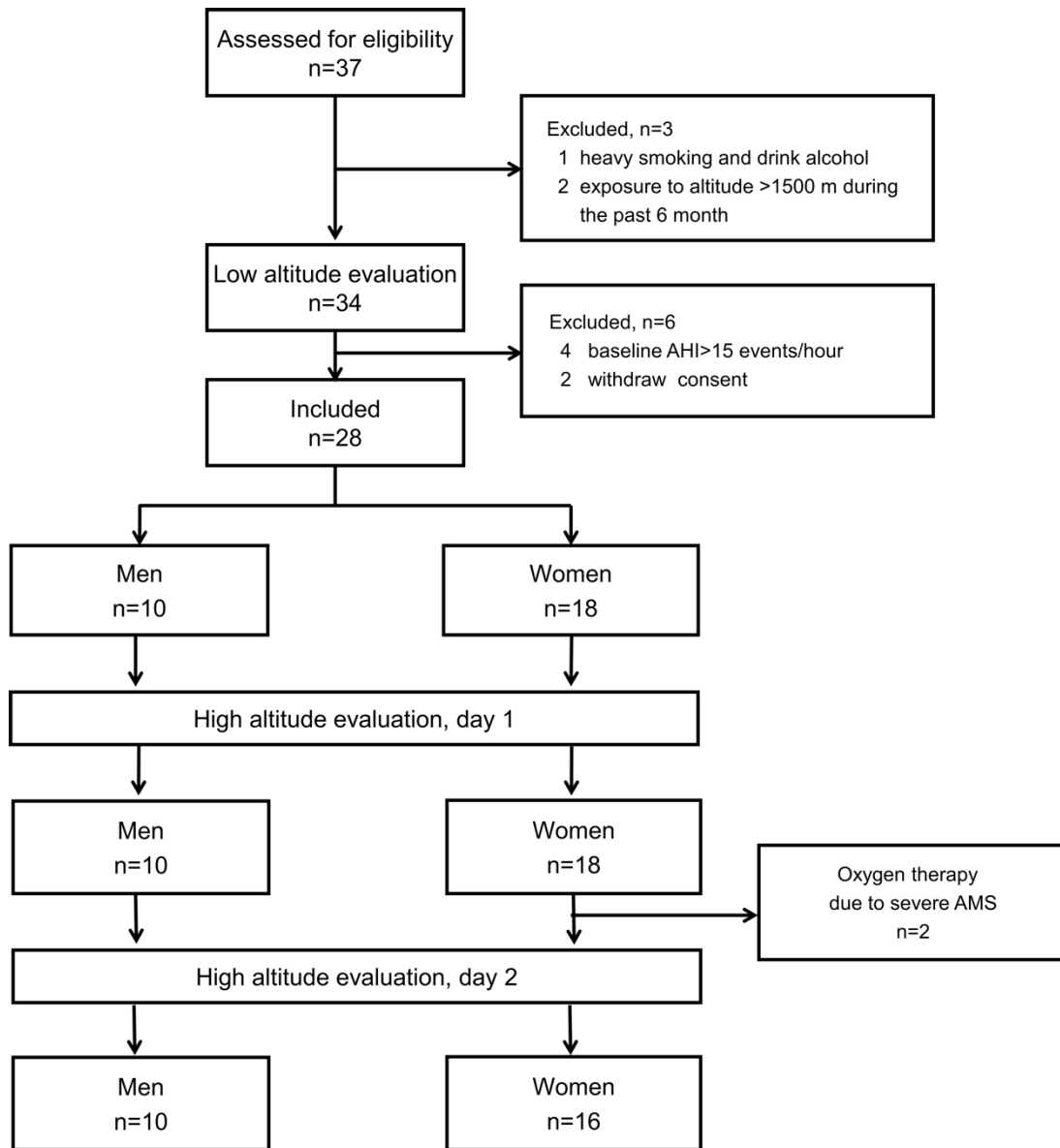


Figure S1. Flowchart.

Low altitude evaluations were performed at 500 m; high altitude evaluations at 3270 m.

AHI, apnea hypopnea index; AMS, acute mountain sickness

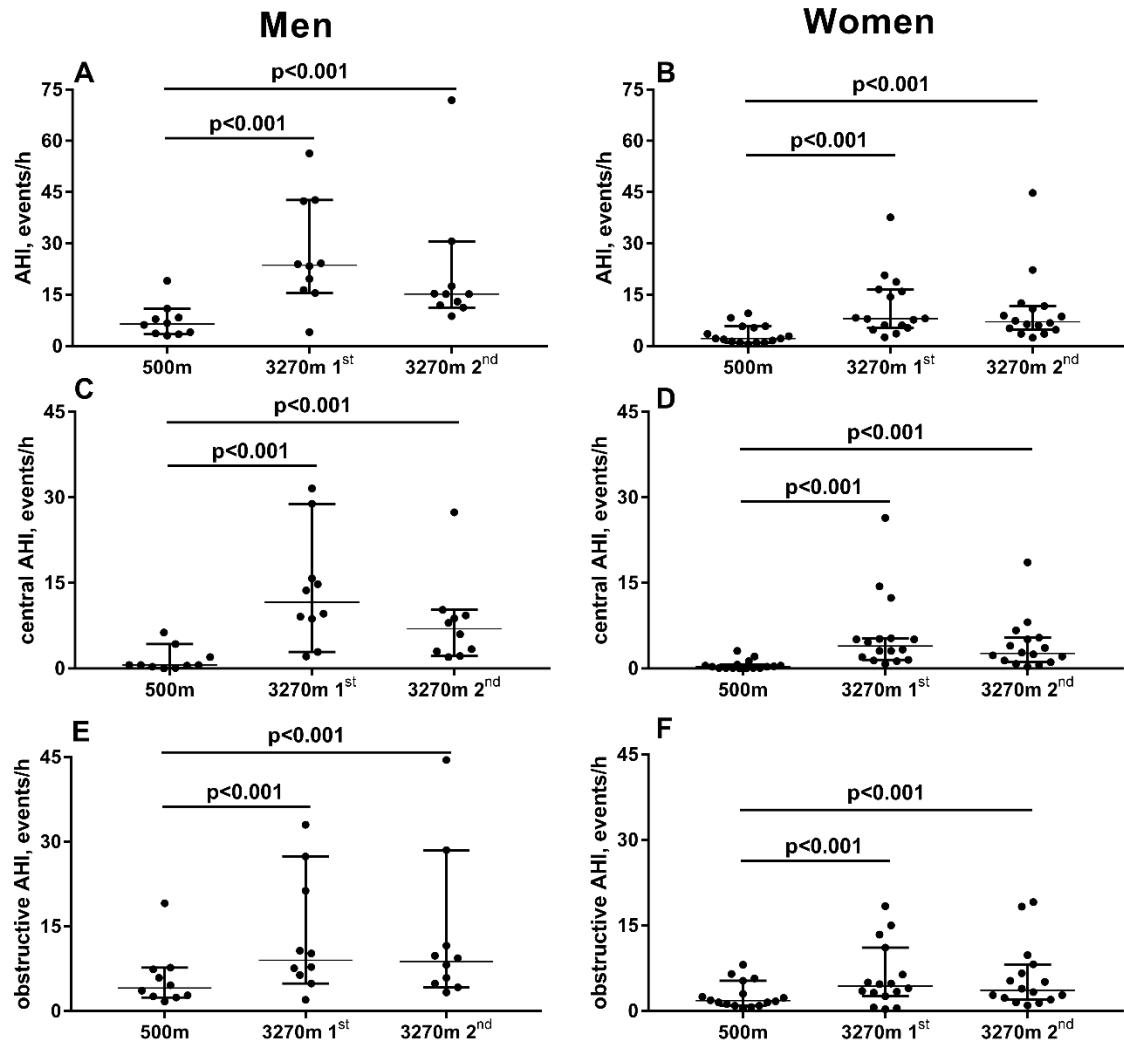


Figure S2 Individual values in total AHI (Panel A and B), central AHI (Panel C and D) and obstructive AHI (Panel E and F) at 500 m and 3270 m during the first and second night in men and women.

AHI, apnea hypopnea index.