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Altitude-related variations in heart rate variability among native Japanese Alpine residents: A cross-sectional study

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Abstract

Background & objectives: Living at high altitudes causes chronic exposure to hypoxia, which triggers various physiological and autonomic adaptations. While previous studies in Himalayan populations have demonstrated enhanced parasympathetic activity among high-altitude natives, the autonomic adaptations in Japanese Alpine populations remain poorly characterized. This study assessed the impact of altitude on cardiac autonomic activity through heart rate variability (HRV) analysis in healthy Japanese residents of the Japan Alps.

Methods: A cross-sectional study was conducted among the Japanese population residing at high, intermediate and low altitudes of Nagano and Yamanashi prefectures. Two areas from each altitude category were selected. Based on the population of the selected areas, the sample size was distributed using probability proportional to size sampling. Systematic random sampling was then used to select participants. For each participant, a 5-min ECG was recorded using lead II of a Power Lab system. HRV analysis was performed to derive time and frequency-domain indices from spectral analysis of successive R-R intervals.

Results: We found significantly lower values of time domain HRV indices including standard deviation of all normal-to-normal intervals (SDNN) and root mean square of successive differences between normal heartbeats (RMSSD) among the people residing at higher altitudes in the Japanese Alps. Conversely, the LF/HF ratio was significantly elevated in high-altitude residents, indicating sympathetic predominance.

Interpretation & conclusions: Residents living at high altitudes in the Japanese Alps exhibit reduced overall HRV and enhanced sympathetic cardiac activity compared to those residing at lower and intermediate elevations, reflecting a distinct adaptive response to chronic hypobaric hypoxia that differs from Himalayan high-altitude populations. These findings suggest that genetic background and altitude duration may influence autonomic adaptation patterns.

Key words: Autonomic nervous system - heart rate variability - high altitude - hypobaric hypoxia - Japanese Alps - sympathetic predominance

Introduction

High altitude (HA) is defined as an altitude greater than 2500 meters above sea level (mASL) or approximately 8200 feet[1]. It is estimated that about 83 million people worldwide reside at elevations above 2500 mASL, primarily in South America, Central Asia, and Eastern Africa[2]. The partial pressure of oxygen decreases as altitude increases causing hypobaric hypoxia that drives acclimatization in sojourners and physiological adaptations in natives.

Living at high altitudes causes chronic exposure to hypoxia, which triggers various physiological and autonomic adaptations, and many high-altitude residents show successful acclimatization. However, long-term exposure leads to time-dependent alterations in autonomic nervous system (ANS) function, even in healthy individuals[3].

The ANS plays a vital role in regulating cardiovascular function and is influenced by both external factors (e.g., environment, stress) and internal factors (e.g., hormones). The parasympathetic and sympathetic discharge on the sinus node controls the heart rate. Increased parasympathetic stimulation causes a decrease in heart rate (HR), whereas increased sympathetic stimulation leads to an increase in heart rate[4].

One of the most reliable non-invasive markers of ANS function is heart rate (HR) variability, which reflects the cardiac sympathetic-vagal balance[5,6]. It represents the variation in the time intervals between successive cardiac cycles. This variation of a healthy heart is complex and constantly changes in response to physiological and psychological challenges to maintain homeostasis. HR variability, measured from electrocardiogram (ECG) recordings, is an affordable, non-invasive, practical and reproducible measure and remains a gold standard technique for assessing autonomic regulation of the heart[7].

Previous studies in Himalayan populations, such as those conducted in Sikkim and Nepal, have reported enhanced parasympathetic activity and higher HRV indices among high-altitude natives compared to lowlanders[8,9]. However, these findings may not be generalizable to other high-altitude populations due to genetic differences, duration of altitude residence, and environmental factors. The Japan Alps, comprising the Hida Mountains, Kiso Mountains, and Akaishi Mountains, represent a unique high-altitude environment where indigenous populations have resided for generations, yet autonomic function in these populations remains understudied[10].

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Given the unique genetic background of Japanese populations and the distinct topographical features of the Japan Alps, this study was conducted to evaluate the impact of altitude on autonomic function by analysing HR variability in healthy adult population residing at different altitudes in Nagano and Yamanashi prefectures.

Materials & Methods

This cross-sectional study was undertaken by the department of Physiology, Shinshu University School of Medicine, Matsumoto, Nagano, Japan from November 2023 to October 2024 after obtaining the ethical clearance from the Institutional Ethics Committee. Written permissions were also secured from the municipal authorities and local community leaders of the selected study regions. Written informed consent was obtained from all participants prior to inclusion in the study. The confidentiality of all data was strictly maintained, and participant anonymity was ensured throughout the research process.

Study design and setting: This cross-sectional study was conducted among healthy, permanent residents of Nagano and Yamanashi prefectures residing at varying altitudes. To investigate the influence of altitude on heart rate variability, participants were categorised into three altitude groups: low altitude (<1500 meters above sea level), intermediate altitude (1500–2500 mASL), and high altitude (>2500 mASL), based on the classification by Barry and Pollard (2003)[11]. To ensure geographic representation within each altitude category, two locations were randomly selected using the lottery method. This stratified approach helped ensure that the sample represented the broader population across different altitudinal zones of the Japanese Alps.

Inclusion and exclusion criteria: Participants included healthy adult males and females who were born and brought up at their respective altitudes (thereby excluding migrants and re-entrants) and were willing to provide written informed consent. Individuals were excluded if they were chronic smokers (occasional smokers abstained for at least two hours before ECG recording), were on long-term medication for chronic illnesses such as cardiovascular or respiratory diseases, hypertension, or diabetes mellitus, were pregnant or within three months postpartum, had any acute illness at the time of data collection, or declined participation.

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Sample size calculation and sampling strategy: This analysis is part of a larger project assessing both pulmonary function tests (PFT) and heart rate variability in native Japanese Alpine residents at different altitudes. As no prior HRV data were available for this specific population, the standard deviation of a PFT parameter from a previous altitude study[12], was used for sample size estimation to ensure adequate power. A relative error of 5 per cent, 95 per cent confidence interval (CI) and a potential attrition rate of 10 per cent was considered. The final estimated sample size was 420.

Two areas each from high altitude [Kamikochi (2450 m ASL) & Norikura (3026 m ASL)], intermediate altitude [Shinhotaka (2000 m ASL) & Fujimi (1650 m ASL)], and low altitude [Matsumoto City (610 m ASL) & Kofu City (273 m ASL)] were selected by lottery. Population enumeration of each area was followed by participant allocation using probability proportional to size (PPS), reflecting the larger resident population at intermediate altitude compared to high and low altitudes. Consequently, the intermediate altitude group (n=195) had a larger sample than the high (n=105) and low (n=120) altitude groups. The electoral list served as the sampling frame; the first participant was chosen randomly, and the remainder systematically, to ensure unbiased selection.

HR Variability recording: To ensure the reliability of HR variability measurements, participants were instructed to abstain from consuming stimulant substances such as coffee, alcohol, tobacco, and cigarettes for at least two hours prior to ECG recording. A history of a good night's sleep was confirmed before the session. Participants were asked to take complete rest for at least 10 min before HR recording. During the recording, participants were advised to stay calm, relaxed, and avoid speaking. Recordings were carried out in a quiet room to minimize external disturbances, with proper skin preparation and removal of metallic jewellery, watches, and electronic devices.

ECG recordings were conducted for five min in a seated position using PowerLab equipment (AD Instruments), following the guidelines established by the 1996 'Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology'[13]. Data were collected between 9 AM and 2 PM in community centers, clinics, and municipal offices across the selected regions.

The ECG data were analysed offline using LabChart software, utilizing the HR Variability module, which extracts inter-beat (RR interval) variations. Parameters analysed included time-domain indices such as the standard deviation of normal-to-normal RR intervals

(SDNN), the root mean square of successive RR interval differences (RMSSD), and the percentage of consecutive RR intervals differing by more than 50 millisec (pNN50). Frequency-domain measures included total power (TP), high-frequency (HF) power in the range of 0.15–0.45 Hz, low-frequency (LF) power in the range of 0.04–0.15 Hz, and the LF/HF ratio, representing the balance between sympathetic and parasympathetic activity.

Statistical analysis: Statistical Package for the Social Sciences (SPSS) version 27.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Demographic variables were summarized by descriptive statistics. To examine the association of altitude on HR Variability parameters, one-way analysis of variance (ANOVA) was employed, followed by Bonferroni post hoc tests for multiple comparisons. P value of less than 0.05 (two-tailed) was considered statistically significant.

Results

A total of 420 healthy participants were included, comprising 208 males (49.5%) and 212 females (50.5%). The mean age of the participants was 38.4±14.2 yr (Table I).

The results indicated statistically significant differences in time-domain parameters like SDNN and RMSSD across the three altitude groups (Table II). Pairwise comparisons between altitude groups showed that, in the time-domain analysis, SDNN and RMSSD values were significantly lower in high-altitude residents than in both intermediate and low-altitude residents. No meaningful differences were observed between the low and intermediate-altitude groups. In the frequency-domain analysis, the LF/HF ratio was significantly higher in high-altitude residents compared with those at intermediate and low altitudes, indicating enhanced sympathetic activity. Total power was lower in high-altitude residents compared with those at low altitudes. Values in the intermediate group were similar to those in both the low and high-altitude groups.

Discussion

This study examined HR variability among healthy, permanent residents of the Japanese Alps living at low (<1500 m), intermediate (1500–2500 m), and high altitudes (>2500 m), aiming to explore the chronic effects of altitude on cardiac autonomic regulation. We found significantly lower mean values of time-domain HR variability indices like SDNN and RMSSD in the high-altitude group, with significantly elevated LF/HF ratio in frequency-domain analysis. Other indices such as pNN50, LF, and HF showed trends toward reduced

values at high altitude but did not reach statistical significance. These findings suggest that long-term residence at high altitude in the Japanese Alps is associated with reduced overall HRV and greater sympathetic modulation.

These findings contrast with those reported in Himalayan populations. Sharshenova et al.[14] reported elevated SDNN, HF power, and TP in children living at moderate altitudes in Kyrgyzstan, and Malhotra et al.[15] observed greater parasympathetic activity among high-altitude natives compared to acclimatized lowlanders in the Himalayas. Bhattarai et al.[8] observed higher SDNN at rest and faster post-exercise recovery to resting phase in highlanders, indicating more efficient autonomic regulation. Passino et al[16] noted a predominance of high-frequency (HF) components in highlanders, while Boushel et al[17] attributed the lower resting heart rate in acclimatized highlanders to enhanced parasympathetic neural tone.

In contrast, our study in the Japanese Alpine population demonstrates a pattern of reduced HRV and sympathetic predominance among high-altitude residents. This discrepancy may be attributed to several factors. First, genetic differences between East Asian and South Asian populations may influence autonomic adaptation mechanisms. Second, the duration of altitude residence differs; while Himalayan populations have inhabited high altitudes for millennia, Japanese Alpine communities have shorter evolutionary histories at these elevations. Third, environmental factors such as temperature extremes and dietary patterns may contribute to distinct physiological adaptations.

Studies investigating acute high-altitude exposure have documented patterns similar to our findings in chronic residents. Oliveria et al[18], in a systematic review, showed that acute hypoxia typically reduces HR variability by causing vagal withdrawal and sympathetic activation. Yuanyuan et al[19] and Saito et al[20] similarly observed decreased HRV indices and blunted autonomic responses during acute exposure in simulated hypoxic environments. Our findings suggest that Japanese high-altitude natives may not achieve the same degree of parasympathetic adaptation observed in Himalayan populations, instead maintaining a pattern of autonomic regulation more closely resembling acute exposure responses.

The elevated LF/HF ratio observed in our high-altitude group indicates sympathetic predominance, which may represent a different adaptive strategy to chronic hypoxia. While enhanced parasympathetic activity may promote cardiovascular efficiency in

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Himalayan populations, sustained sympathetic activation in Japanese Alpine residents may reflect a stress-response adaptation to hypobaric hypoxia. This pattern is consistent with observations by Bhaumik et al[21] and Roche et al[22], who showed reduced parasympathetic activity and increased sympathetic drive in individuals exposed to high altitude.

Interestingly, studies tracking individuals over days have found an initial drop in HRV and parasympathetic activity followed by partial recovery by day 5, indicating early stages of adaptation[21]. However, our cross-sectional data suggest that complete restoration of parasympathetic dominance may not occur in all populations, even with generational altitude exposure. Longitudinal studies tracking Japanese Alpine residents over extended periods would be necessary to confirm whether our findings represent a stable adaptation or an intermediate stage of acclimatization.

The reduced HRV observed in our study may have clinical implications. While the Lake Louise Score (LLS) remains the standard clinical measure for diagnosing acute mountain sickness, it is subjective. Recent evidence, including a meta-analysis by Tsai et al[23], indicates that HR variability indices such as pNN50 may predict altitude illness risk. The reduced SDNN and RMSSD in our high-altitude residents may indicate increased susceptibility to autonomic dysfunction under additional physiological stress.

Our study has several strengths. It is among the first to assess HRV across multiple altitude categories in a Japanese population, providing valuable comparative data to Himalayan studies. The inclusion of three altitude levels allowed a gradient analysis of autonomic patterns across elevations. However, certain limitations must be acknowledged. The sample size at high altitude was modest due to demographic constraints of the Japanese Alps. We did not measure biochemical markers such as catecholamines or cortisol, which could have provided direct physiological corroboration of autonomic findings. Additionally, genetic analysis was not performed to explore potential polymorphisms affecting autonomic function. Lastly, the design being cross-sectional, it excludes causal inference. Longitudinal studies could better establish whether altitude itself drives these differences or whether selection factors influence residence patterns.

In conclusion, this study demonstrates that lifelong residence at high altitude among Japanese Alpine individuals is associated with reduced HR variability and sympathetic predominance, indicating a distinct pattern of autonomic adaptation to chronic hypobaric

hypoxia that differs from previously studied Himalayan populations. These findings highlight the importance of genetic background and population history in shaping physiological adaptations to high-altitude environments.

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Conflicts of Interest: None declared.

Use of Artificial Intelligence (AI)-Assisted Technology for manuscript preparation: The authors confirm that there was no use of AI-assisted technology for assisting in the writing of the manuscript and no images were manipulated using AI.

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Tables and Legends

Table 1. Descriptive demographic Parameters of Japanese Alpine population residing at three different altitudes

Demographic parameters	High altitude, n=105 (Mean±SD)	Intermediate altitude, n=195 (Mean±SD)	Low altitude, n=120 (Mean±SD)	Total, n=420 (Mean±SD)
Gender n (%)				
Male	48 (45.7)	98 (50.3)	62 (51.7)	208 (49.5)
Female	57 (54.3)	97 (49.7)	58 (48.3)	212 (50.5)
Age (in yr)	39.2±14.8	36.8±13.6	39.6±14.1	38.4±14.2
Height (in cm)	162.4±8.2	163.1±9.1	161.8±8.9	162.5±8.8
Weight (in kg)	64.2±11.8	63.5±12.1	65.3±11.4	64.2±11.8
BMI (kg/m^2)	24.3±3.6	23.9±3.4	25.0±3.8	24.3±3.6

Table 2. Comparison of HR variability parameters of Japanese Alpine population residing at high, intermediate and low altitudes

HRV parameters	High altitude, n=105 (Mean±SD)	Intermediate altitude, n=195 (Mean±SD)	Low altitude, n=120 (Mean±SD)	Total, n=420 (Mean±SD)	P value
NN Interval	712.4±78.6	738.5±89.4	745.2±91.3	732.8±87.5	0.02
SDNN	38.2±16.4	52.4±19.8	55.6±20.2	49.6±19.6	<0.001
RMSSD	32.4±18.6	48.3±22.4	51.2±23.6	44.8±22.3	<0.001
pNN50	8.4±9.2	14.6±12.8	16.2±13.4	13.4±12.2	0.08
Total power	2845.3±1684.2	3654.8±1987.6	3842.5±2156.3	3486.2±1964.8	0.03
LFP	28.4±10.6	31.2±12.4	32.6±11.8	30.8±11.6	0.12
HFP	26.8±14.2	34.6±16.8	36.4±17.2	33.2±16.4	0.09
LF:HF	1.86±1.42	1.24±0.98	1.18±0.92	1.38±1.14	0.002

NN, normal-to-normal; SDNN, standard deviation of all NN intervals; RMSSD, root mean square of successive differences between NN intervals; pNN50, percentage of successive NN intervals differing by more than 50 milliseconds; LFP, low-frequency power (0.04–0.15 Hz); HFP, high-frequency power (0.15–0.45 Hz); LF:HF ratio, ratio of low-frequency power to high-frequency power

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Figures and Legends

Figure 1. Map of study locations in the Japanese Alps

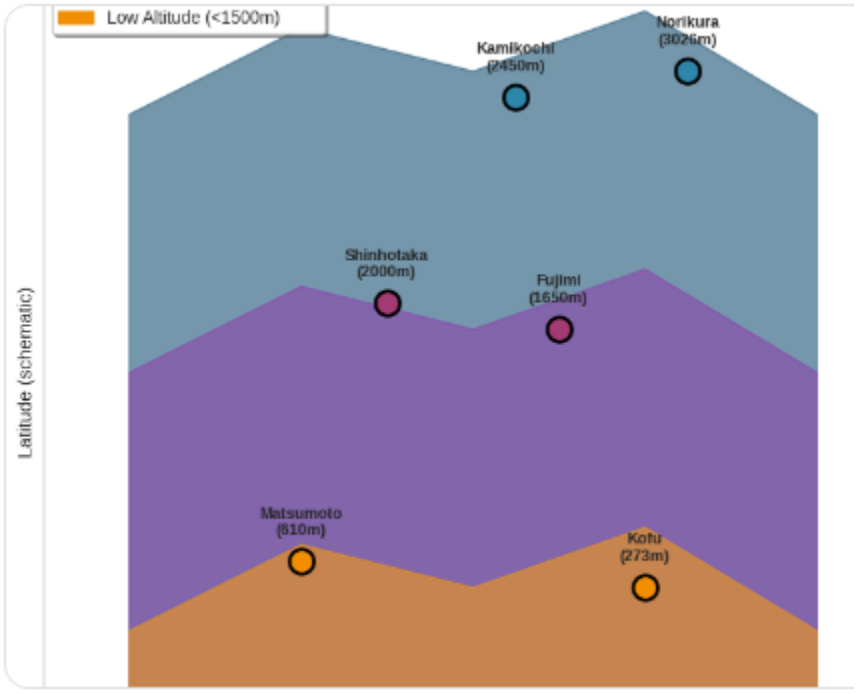

Figure 2. Comparison of time-domain HRV indices across altitude groups

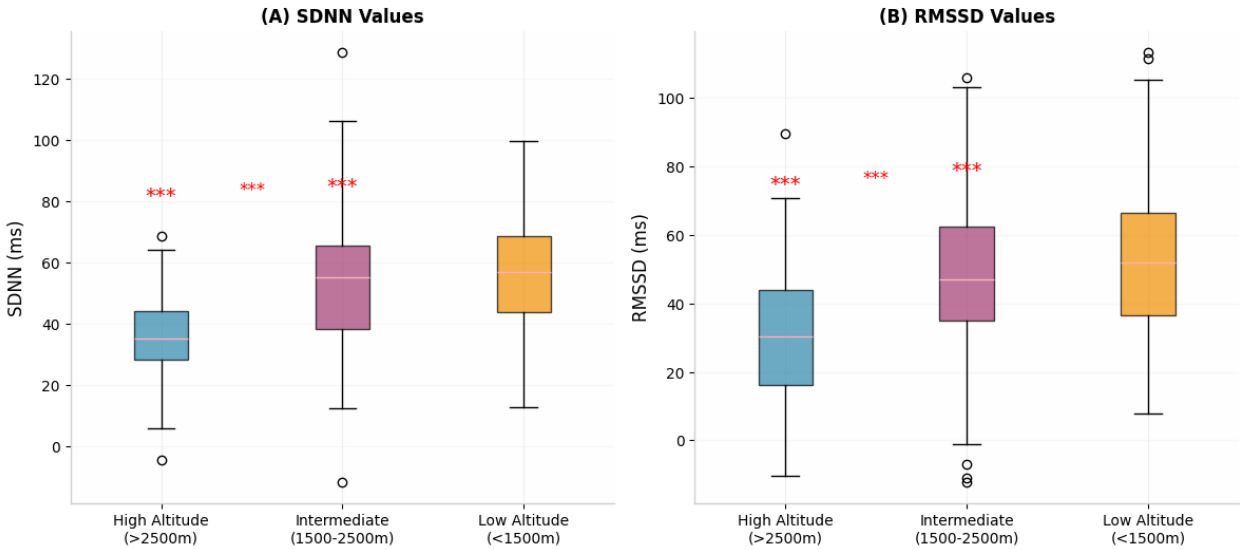

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Figure 3. Comparison of frequency-domain HRV indices across altitude groups

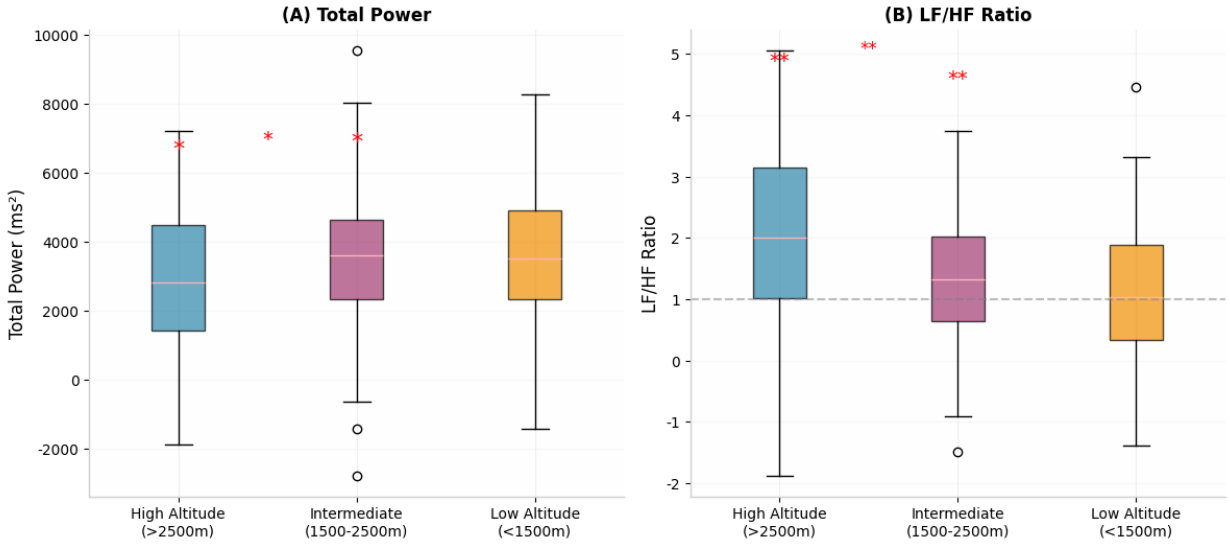

Figure 4. Correlation between altitude and HRV parameters

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