



OPEN The effects of pyrroloquinoline quinone and nicotinamide mononucleotide supplementation on interoception following acute exhaustive exercise: a randomised, double-blind, placebo-controlled study

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Interoception, the process by which the nervous system perceives and interprets internal bodily signals, is essential for athletes to effectively modulate motor decisions but may be impaired after exhaustive exercise. This study investigated the effects of pyrroloquinoline quinone (PQQ), nicotinamide mononucleotide (NMN), and their combination on interoception following acute exhaustive exercise. Sixty participants were randomly assigned in a double-blind, placebo-controlled trial to receive either placebo (320 mg cornflour), PQQ (20 mg PQQ + 300 mg cornflour), NMN (300 mg NMN + 20 mg cornflour), or a combined supplement (20 mg PQQ + 300 mg NMN). Supplements were ingested 60 min before completing an acute exhaustive exercise protocol using the Bruce treadmill test. Interoception was measured using the Body Perception Questionnaire (BPQ) and the Multidimensional Assessment of Interoceptive Awareness (MAIA) at baseline and post-exercise. Group differences were examined using chi-square and one-way ANOVA, while mixed-design ANOVA was applied to evaluate interoception and exercise capacity indicators. Significant improvements over time were observed in BPQ scores (89.45 vs. 95.08, $p = 0.006$), Self-regulation (2.79 vs. 3.02, $p = 0.015$), Body Listening (2.36 vs. 2.76, $p < 0.001$), and Trusting (2.97 vs. 3.21, $p = 0.031$). Body listening was the only domain that demonstrated a significant group $\times$ time interaction ($p = 0.016$), with the PQQ group showing significant improvement ($p < 0.001$). These findings suggest that PQQ supplementation may enhance specific aspects of interoception following acute exhaustive exercise.

Keywords Interoception, Nutrition, Exercise, Pyrroloquinoline quinone, Nicotinamide mononucleotide

Interoception, defined as the nervous system's capacity to sense, interpret, and integrate signals originating from within the body¹, is crucial for adaptive responses to physiological changes. During exercise, various internal changes such as increased heart and respiratory rates, muscle pain, and emotional fluctuations are transmitted to the central nervous system. The body then perceives and interprets these signals as subjective sensations, including fatigue, pain, and muscle soreness². This process, referred to as "exercise interoception", is enhanced by exercise via stimulated visceral signals, increased peripheral sensitivity, and improved neural plasticity^{3,4}. Interoceptive feedback plays a critical role during exercise, enabling the individual to assess their physical functional status and fatigue levels, facilitating necessary adjustments to maintain performance⁵. Enhancing interoception positively influences exercise performance based on the interaction between exercise and interoception³. Notably, during

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high-intensity exercise, athletes increasingly depend on interoceptive cues to regulate performance, yet excessive oxidative and inflammatory stress can compromise the accuracy of these signals, highlighting the vulnerability of interoception under extreme exertion.

Nutritional supplementation represents an effective strategy for improving physical function and exercise performance. Evidence suggests that fasting or nutritional supplements can influence cardiac interoception by modulating autonomic nervous system activity and neuro-related mechanisms^{6,7}, indicating a potential relationship between nutritional interventions and interoception. Moreover, previous studies have shown that nutritional supplementation can affect psychophysiological responses during exercise⁸, implying that nutrition may influence bodily awareness and the adaptive control of physiological states during exercise. However, there is limited research on how nutrition specifically affects exercise interoception, and effective nutritional strategies for enhancing exercise interoception remain poorly defined.

Pyroloquinoline quinone (PQQ) is a vitamin-like coenzyme that the human body cannot synthesize⁹. It exhibits diverse physiological effects, including neuroprotective properties exerted through several mechanisms. PQQ demonstrates strong antioxidant properties¹⁰, effectively preventing oxidative stress-induced neuronal death by activating the nuclear factor erythroid 2-related factor 2/antioxidant response element (Nrf2/ARE) pathway, which strengthens antioxidant defenses^{11,12}. Moreover, PQQ promotes neuronal growth and repair by upregulating the expression of nerve growth factor (NGF) and its receptors¹³, and supports mitochondrial function by activating the AMP-activated protein kinase/peroxisome proliferator-activated receptor gamma coactivator 1- α (AMPK/PGC-1 α) and sirtuin 1 (SIRT1) pathways, thereby enhancing energy metabolism and reducing oxidative stress. In addition, PQQ modulates nuclear factor-kappa B (NF- κ B) signaling to suppress neuroinflammation and preserve synaptic integrity¹², while also improving neurotransmitter secretion in the brain, increasing catecholamines and mitigating synaptic dysfunction, thereby enhancing peripheral sympathetic nerve signals^{14,15}. Human studies have validated that PQQ enhances multiple cognitive abilities while concurrently increasing prefrontal cortex activity^{16,17}, and also contributing to the regulation of emotions by reducing fatigue, anxiety and depression¹⁸. These effects of PQQ support the neural mechanisms of interoceptive improvement, providing a potential basis for interoception regulation under physiological stress.

Nicotinamide mononucleotide (NMN) is a precursor to nicotinamide adenine dinucleotide (NAD⁺), and its supplementation increases NAD⁺ concentrations¹⁹. NAD⁺ replenishment enhances the activity of SIRT1, an NAD⁺-dependent deacetylase that contributes to mitochondrial biogenesis, supports neuronal survival, and inhibits inflammatory signalling mediated by NF- κ B^{20–22}. Through these mechanisms, NMN alleviates oxidative stress and neurodegeneration^{23,24}, prevents neuronal damage, supports remyelination, and improves cognitive performance^{25,26}.

Both PQQ and NMN appear to act on the AMPK/SIRT1/PGC-1 α signalling network, though through distinct mechanisms. PQQ tends to activate this pathway directly, initiating antioxidant and neuroprotective responses, whereas NMN increases NAD⁺ availability to sustain SIRT1-dependent activity. Given their complementary modes of action, concurrent supplementation with PQQ and NMN may represent a promising strategy to support neuronal energy metabolism and maintain interoceptive stability under physiological stress.

Regarding exercise performance, long-term PQQ supplementation may benefit aerobic endurance and promote recovery from exercise-induced fatigue²⁷. NMN supplementation has been shown to improve the ventilatory threshold and extend exercise duration in endurance exercise²⁸. However, whether their combined supplementation can influence interoceptive processing and physiological regulation during exhaustive exercise remains unclear.

Given the insufficient evidence regarding the impact of nutrition on exercise interoception and potential role of PQQ and NMN in regulating internal body states and their positive effects on endurance performance, this study aimed to evaluate the effects of PQQ and NMN supplementation on interoception following acute exhaustive exercise, to identify potential nutritional strategies for improving exercise interoception, and explore new approaches for enhancing interoceptive abilities.

Materials and methods

Study design and participants

This study employed a randomized, double-blind, placebo-controlled design. Participants were recruited from male students majoring in physical education at Beijing Sport University, China. The recruitment criteria included individuals aged 18 to 28 years. The International Physical Activity Questionnaire (IPAQ) was used to assess participants' habitual physical activity levels.

Sample size estimation was conducted using G*Power software (version 3.1.9.7; Heinrich Heine University, Düsseldorf, Germany). An a priori effect size (f) of 0.25 was specified, with a significance level of $\alpha = 0.05$ and a statistical power of 0.80. The design included four groups and two repeated measurements. Based on these inputs, G*Power estimated a required total sample size of 48 participants (12 per group). To account for potential dropouts, an additional 3 participants were recruited for each group.

The inclusion criteria were as follows: (a) a Body Mass Index (BMI) between 18.5 and 24 kg/m²; (b) regular exercise habits over the preceding three months, defined as engaging in physical exercise at least three times per week, with each session lasting at least 30 min and of moderate or higher intensity; (c) non-consumption of coffee, tobacco products, and alcohol; (d) absence of cardiopulmonary disease; (e) absence of metabolic diseases such as endocrine, kidney, or gastrointestinal disorders; (f) absence of sports-related injuries and movement disorders; (g) no medication use in the month prior to enrollment; and (h) no participation in any other clinical nutrition research trials.

All participants provided written informed consent after receiving a detailed explanation of the study's purpose and procedures. The study protocol was approved by the Scientific Ethics Committee at Beijing Sport University (approval number: 2023286H, approval date: 14 November 2023). This study was retrospectively

registered in the Chinese Clinical Trial Registry (ChiCTR2500112623) on 17 November 2025. Baseline data, including age, sex, athletic classification, smoking status, alcohol consumption habits, and general health status, were collected via a baseline survey and physical examination. Sixty participants met the eligibility criteria and were subsequently enrolled in the study. Participants were randomly assigned to one of four treatment groups using a computer-generated random allocation sequence: the PQQ supplement group (PQQ, $n = 15$), the NMN supplement group (NMN, $n = 15$), the PQQ with NMN supplement group (PN, $n = 15$), or the placebo group (PLC, $n = 15$). Figure 1 shows the process of participant selection and group allocation.

To ensure compliance and dietary consistency, participants were instructed to abstain from vitamins, minerals, coffee, tea, and other supplements throughout the study period. All participants completed a 48-h dietary recall questionnaire and were required to complete for 12-h overnight fast prior to the experimental trial. Participants arrived at the laboratory in the morning. After a 5-min rest period, they completed the baseline interoception questionnaire assessment. Subsequently, they consumed the assigned nutritional supplement along with a standardized breakfast (a 400 kcal hamburger and 250 mL of milk). After one hour, participants performed an acute exhaustive exercise test. Upon completion of the exercise, participants walked on a treadmill at 3 km/h for 3 min, followed by a second interoception questionnaire assessment. Figure 2 presents an illustration of the experimental protocol for testing sessions in the lab.

Acute exhaustion exercise protocol

All participants in the four intervention groups completed an acute exhaustion exercise test following the Bruce incremental loading protocol on a treadmill (RUN 7410, Runner, Italy). Expired gases were continuously monitored using a gas analyser (Metalyzer 3B, CORTEX Biophysik, Germany). Heart rate was continuously recorded using a Firstbeat Sports Heart Rate Band (Firstbeat Sports, Firstbeat Technologies, Finland). The protocol consisted of running on the treadmill until volitional exhaustion.

The treadmill started at an initial speed of 2.74 km/h with a 10% slope. Speed and slope were increased incrementally every 3 min²⁹. At the point of exhaustion, participants verbally reported their perceived level of fatigue using the Borg 6–20 Rating of Perceived Exertion (RPE) scale.

The experiment was terminated immediately when participants reached volitional exhaustion. The criteria for determining exhaustion were as follows: (1) participant reported feeling exhausted and was unable to continue the exercise despite verbal encouragement; (2) oxygen uptake had plateaued (no longer changed or decreased) with further increases in the exercise workload; (3) the participant's heart rate (HR) was at or near their predicted maximal heart rate (HR_{max}); and (4) the respiratory exchange ratio (RER) was ≥ 1.10 .

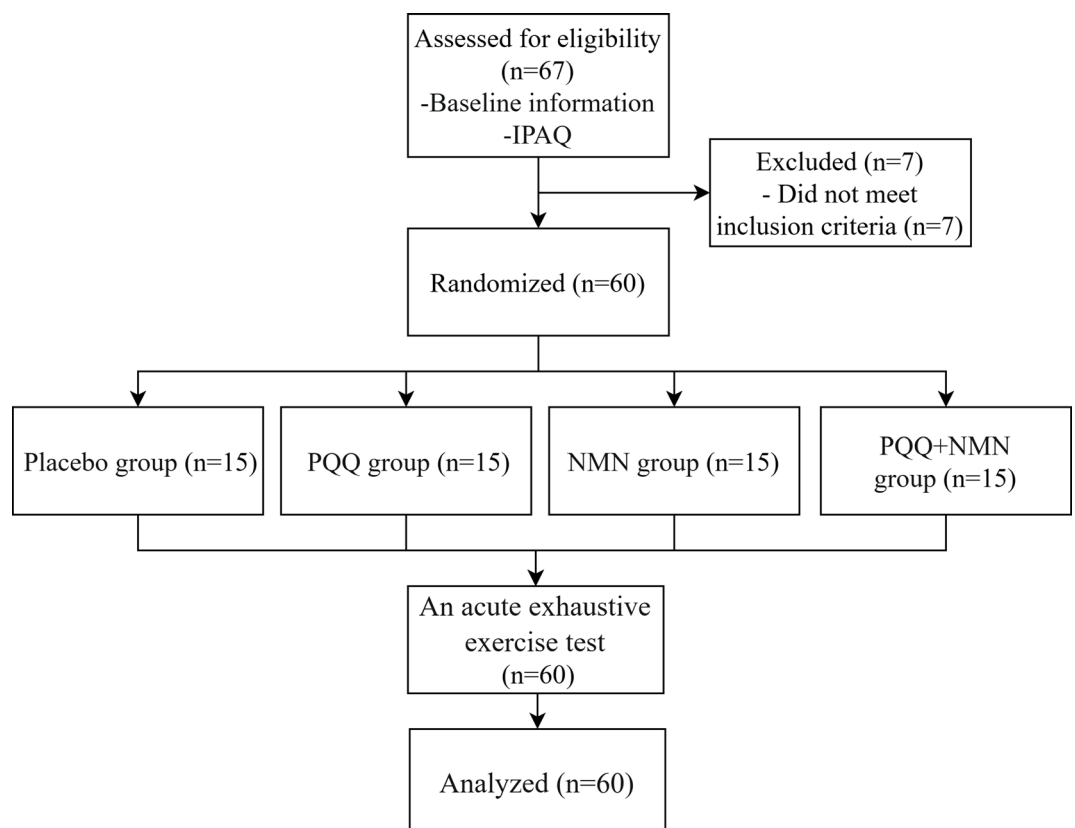


Fig. 1. The process of participant selection and group allocation.

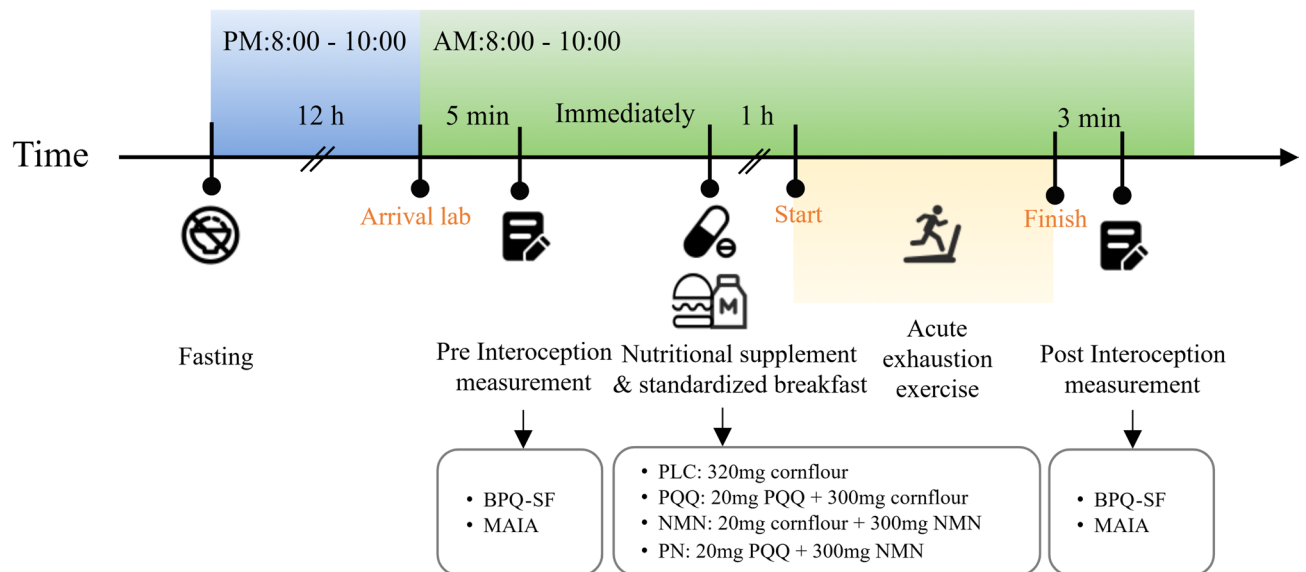


Fig. 2. The experimental protocol.

Supplementation protocol and blinding

In a double-blind fashion, participants were randomly assigned to orally ingest 320 mg of cornflour (PLC), 20 mg of PQQ with 300 mg of cornflour (PQQ), 300 mg of NMN with 20 mg of cornflour (NMN), or 20 mg of PQQ with 300 mg of NMN (PN). The PQQ used was provided in the form of PQQ disodium. All supplements were manufactured to be identical in size, shape, and colour. One researcher, who alone was aware of the allocation, distributed the supplements in a randomised manner and kept the records. This researcher was not involved in testing or data analysis, thereby ensuring blinding of both participants and investigators. Study personnel distributed the respective supplement to each participant 60 min before the exercise session.

Interoception measurement

Interoceptive sensitivity was measured using subjective self-report questionnaires. The Body Perception Questionnaire (BPQ) and the Multidimensional Assessment of Interoceptive Awareness (MAIA) are two commonly cited questionnaires in interoception research³⁰. Moreover, both questionnaires have been validated for reliability and validity in Chinese university student populations^{31,32}. Therefore, interoception was measured using the BPQ and MAIA questionnaires.

The body perception questionnaire-short form (BPQ-SF)

The BPQ-SF is a shortened version of the BPQ's Body Awareness subscale³³. The BPQ-SF consists of 46 items measuring sensitivity to internal bodily sensations and autonomic nervous responses. Item responses are scored on a 5-point ordinal scale ranging from 1 (*never*) to 5 (*always*). The overall BPQ-SF score was calculated by summing all item scores.

The multidimensional assessment of interoceptive awareness (MAIA) 2nd edition

The MAIA consists of 37 items divided into eight subscales: *Noticing*, *Not-Worrying*, *Not-Distracting*, *Attention Regulation*, *Emotional Awareness*, *Self-Regulation*, *Body Listening*, and *Trusting*³⁴. Each item is scored on a 6-point Likert scale ranging from 0 (*never*) to 5 (*always*), with higher scores indicating greater self-reported interoceptive awareness. The *Not-Worrying* and *Not-Distracting* subscales are reverse-scored. Scores for each MAIA subscale were determined by averaging the scores of all items within the respective subscale.

Exercise capacity measurement

Gas analysers (Metalyzer 3B, CORTEX Biophysik, Germany) were used to measure exercise capacity during the acute exhaustive exercise test. Baseline values were obtained from an exhaustive exercise test using the same treadmill protocol as in the formal experiment, administered during the participant recruitment phase. Participants underwent the Bruce protocol to determine their time to exhaustion (TTE), time to the anaerobic threshold (AT), peak respiratory exchange ratio (RER), maximal oxygen uptake ($\text{VO}_{2\text{max}}$), VO_2 at AT, VO_2 utilisation (VO_2 at AT/ $\text{VO}_{2\text{max}}$), and respiratory efficiency ($\text{VE}_{\text{max}}/\text{VO}_{2\text{max}}$). These variables were used as indicators of exercise capacity.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences software (SPSS Version 25.0, IBM Corporation, Armonk, NY, USA). Normality and homogeneity of variance were tested ($p > 0.05$). A chi-square test and one-way analysis of variance (ANOVA) were used to examine differences in participants' characteristics (age, BMI, and athletic classification) across the study groups. A mixed-design ANOVA was then applied to

assess differences in interoception between the four groups, both before and after exercise. Analysis of covariance (ANCOVA) was used to examine the differences in exercise capacity indicators among the four groups after adjusting for baseline exercise capacity, age, BMI, and athlete classification. Indicators with significant differences among the groups were further analyzed using Bonferroni post-hoc multiple comparisons to assess pairwise differences between the two groups. Partial correlation analysis was conducted to explore the correlation between exercise performance (RPE, VO_{2max} , and HR_{max}) and changes in interoception (post values minus pre values), while adjusting for the groups, age, BMI, and athlete classification. In addition, Partial eta square (η^2) effect sizes (ES) were calculated to compare the magnitude of differences in interoception among the groups. η^2 thresholds of 0.01, 0.06, and 0.14 were interpreted as small, moderate, and large effects, respectively. The level of significance was set at $\alpha = 0.05$.

Results

Table 1 presents the baseline characteristics of the participants. The mean age of the participants was 19.0 ± 0.7 years. Of the 60 participants, 15% were classified as first-class athletes, and 63.3% were classified as second-class athletes.

Table 2 and Fig. 3 present the effects of the nutritional supplements on interoception during the acute exercise protocol, as measured by the BPQ and MAIA questionnaires. No significant differences in interoception scores during exercise were observed among the groups (all p values > 0.05), indicating relatively comparable interoception scores across the control, PQQ, NMN, and PN groups. However, when examining the time effect (pre vs. post-exercise), significant improvements were observed in BPQ scores (89.45 vs. 95.08 , $p = 0.006$), Self-Regulation (2.79 vs. 3.02 , $p = 0.015$), Body Listening (2.36 vs. 2.76 , $p < 0.001$), and Trusting (2.97 vs. 3.21 , $p = 0.031$). No significant changes over time were observed in the remaining MAIA subscales ($p > 0.05$).

Furthermore, body listening was the only domain to have exhibited a significant group $\times$ time interaction effect ($p = 0.016$) (Fig. 3I), indicating group-specific differences over time. Within-group pre-post comparisons revealed no significant change in the placebo group ($p = 0.380$), a significant improvement in the PQQ group ($p < 0.001$), no significant change in the NMN group ($p = 0.102$), and a significant improvement in the PN group ($p = 0.011$).

Table 3 shows the effects of nutritional supplements on exercise capacity during acute exercise. No significant differences were observed in exercise capacity indicators ($p > 0.05$).

The results of the partial correlation analysis are shown in Fig. 4. Significant positive correlations are observed between RPE scores, VO_{2max} , and changes in BPQ score ($p = 0.005$; $p = 0.034$).

Discussion

The primary aim of this study was to determine whether PQQ and NMN supplementation could effectively improve interoception following acute exhaustive exercise. The findings suggest that interoception scores were generally comparable across all groups (control, PQQ, NMN, and PN). However, examination of the time effect (pre vs. post-exercise) revealed significant improvements in BPQ, Self-Regulation, Body Listening, and Trusting. Notably, body listening was the only domain to exhibit a significant group $\times$ time interaction ($p = 0.016$), indicating that, while improvements in BPQ, Self-Regulation, and Trusting were consistent across all groups, Body Listening improved significantly only within the PQQ group. These findings suggest that nutritional supplementation may offer an avenue for enhancing interoception and provide novel strategies for improving interoception in exercise environments.

During high-intensity exercise, there is a proposed shift from descending cognitive processes to ascending interoceptive cues³. Accordingly, athletes must attend to and interpret their physiological signals to make appropriate adjustments. Based on the positive feedback loop between exercise and interoception, maintaining and improving interoception may assist athletes in better regulating their exercise status, preventing injuries, and enhancing performance. During maximal-intensity exercise, the oxidative metabolism increases, resulting in elevated levels of reactive oxygen and nitrogen species, which generate oxidative stress. Simultaneously, the release of inflammatory factors intensifies, further aggravating the degree of oxidative stress³⁵. Neurons are

	PLC (n = 15)	PQQ (n = 15)	NMN (n = 15)	PN (n = 15)	Total (n = 60)	F/ χ^2	p
Age (year)	19.1 $\pm$ 0.9	19.2 $\pm$ 0.7	18.9 $\pm$ 0.5	19.1 $\pm$ 0.8	19.0 $\pm$ 0.7	0.58	0.63
Athlete classification, n (%)						4.91	0.56
First-class athlete	4 (26.7)	2 (13.3)	1 (6.7)	2 (13.3)	9 (15.0)		
Second-class athlete	10 (66.7)	10 (66.7)	9 (60.0)	9 (60.0)	38 (63.3)		
No athletic classification	1 (6.7)	3 (20.0)	5 (33.3)	4 (26.7)	13 (21.7)		
BMI (kg/m ²)	21.7 $\pm$ 1.0	21.9 $\pm$ 0.8	21.6 $\pm$ 0.8	21.8 $\pm$ 0.6	21.7 $\pm$ 0.6	0.32	0.81
MVPA (min/week)	628.0 $\pm$ 415.8	702.7 $\pm$ 372.5	670.0 $\pm$ 485.3	714.7 $\pm$ 426.9	678.8 $\pm$ 417.4	0.12	0.95
SB (min/week)	1426.7 $\pm$ 504.2	1640.0 $\pm$ 640.1	1513.3 $\pm$ 459.6	1390.0 $\pm$ 609.2	1492.5 $\pm$ 552.4	0.59	0.62
RPE	18.9 $\pm$ 1.4	18.9 $\pm$ 0.7	19.1 $\pm$ 1.1	18.4 $\pm$ 1.4	18.8 $\pm$ 1.2	1.04	0.38
HR _{max} (bpm)	192.0 $\pm$ 8.8	195.3 $\pm$ 7.5	195.5 $\pm$ 6.3	191.1 $\pm$ 7.4	193.5 $\pm$ 7.6	1.36	0.27

Table 1. Participant characteristics. The values are presented as the number (%) or mean $\pm$ SD. BMI Body mass index, MVPA Moderate-to-vigorous physical activity, SB Sedentary behavior, SD Standard deviation.

Variable	Group effect					Time effect			Interaction effect
	Control Mean (95% CI)	PPQ Mean (95% CI)	NMN Mean (95% CI)	PN Mean (95% CI)	p-value	Pre Mean (95% CI)	Post Mean (95% CI)	p-value	
BPQ	93.47 (81.70, 105.23)	87.13 (75.37, 98.90)	91.73 (79.97, 103.50)	96.73 (84.97, 108.50)	0.708	89.45 (83.43, 95.47)	95.08 (88.71, 101.46)	0.006	0.838
MAIA score	97.87 (90.46, 105.27)	99.90 (92.49, 107.31)	107.37 (99.96, 114.77)	98.77 (91.36, 106.17)	0.259	99.88 (96.08, 103.69)	102.07 (97.98, 106.15)	0.114	0.119
Noticing	2.81 (2.28, 3.33)	3.18 (2.65, 3.70)	3.45 (2.92, 3.98)	3.02 (2.49, 3.54)	0.375	3.13 (2.83, 3.43)	3.09 (2.81, 3.37)	0.729	0.711
Not-Distracting	2.54 (2.08, 2.99)	2.23 (1.78, 2.69)	2.26 (1.81, 2.72)	2.40 (1.94, 2.86)	0.768	2.42 (2.16, 2.30)	2.30 (2.06, 2.53)	0.238	0.953
Not-Worrying	2.63 (2.29, 2.97)	2.55 (2.21, 2.89)	2.47 (2.13, 2.81)	2.32 (1.98, 2.66)	0.620	2.53 (2.34, 2.46)	2.46 (2.26, 2.65)	0.415	0.442
Attention Regulation	2.51 (2.11, 2.91)	2.58 (2.18, 2.98)	2.96 (2.56, 3.36)	2.52 (2.12, 2.92)	0.336	2.61 (2.41, 2.81)	2.68 (2.45, 2.91)	0.413	0.446
Emotional Awareness	2.81 (2.40, 3.22)	2.85 (2.44, 3.26)	3.15 (2.74, 3.56)	3.05 (2.64, 3.46)	0.589	2.96 (2.72, 3.19)	2.98 (2.78, 3.18)	0.785	0.440
Self-Regulation	2.58 (2.17, 3.00)	2.98 (2.56, 3.39)	3.20 (2.78, 3.62)	2.86 (2.44, 3.28)	0.219	2.79 (2.56, 3.02)	3.02 (2.79, 3.25)	0.015	0.464
Body Listening	2.41 (1.98, 2.85)	2.54 (2.11, 2.98)	2.75 (2.31, 3.18)	2.54 (2.11, 2.98)	0.750	2.36 (2.12, 2.61)	2.76 (2.52, 3.01)	<0.001	0.016 PLC: pre vs. post (p-value=0.380) PQQ: pre vs. post (p-value<0.001) NMN: pre vs. post (p-value=0.102) PN: pre vs. post (p-value=0.011)
Trusting	3.02 (2.58, 3.46)	3.06 (2.61, 3.50)	3.37 (2.93, 3.81)	2.91 (2.47, 3.35)	0.505	2.97 (2.74, 3.19)	3.21 (2.95, 3.48)	0.031	0.540

Table 2. The effects of nutritional supplements on interoception during acute exercise are measured by the BPQ and MAIA. *CI* Confidence interval.

particularly susceptible to damage from oxidative stress³⁶, which may affect the perception and transmission of internal bodily signals, as well as the brain's interpretation of these signals. Maximal intensity exercise can trigger negative emotions, potentially leading to reduced accuracy and sensitivity of interoception. Previous research has indicated that acute physical activity momentarily increases interoceptive accuracy, as measured by cardiac counting experiments, when measured immediately after the cessation of exercise⁴. The strength of the MAIA lies in its ability to assess various aspects of interoception awareness in a multi-dimensional manner³⁴. The MAIA focuses more on the correlation between internal bodily signals and health functions, emphasizing positive emotion evaluation, whereas the BPQ-SF is a unidimensional interoception assessment scale that covers bodily awareness related to sympathetic nervous system activation and stress, focusing on the evaluation of internal signals associated with stress and negative emotions. The increase in BPQ-SF scores following exhaustive exercise is potentially due to the enhanced excitability of the sympathetic nervous system and the increased secretion of catecholamines³⁷, leading to a series of physiological and psychological changes, including increased heart rate, elevated blood pressure, and increased physical and mental stress and negative emotions³⁵. These results indicate that interoception sensitivity levels generally decrease following exhaustive exercise, while interoception of negative emotions increases. Some studies have suggested that, for assessing the ability to perceive signals from within the body, the MAIA Noticing subscale might be the preferred choice³⁸.

This research has shown that PQQ supplementation effectively enhances Body Listening levels. However, studies on the effects of nutritional supplements on interoception remain limited. A recent randomised controlled trial demonstrated that four weeks of probiotic supplementation did not affect MAIA scores in healthy adults³⁹. This study is among the first to find improvements in interoceptive sensitivity attributable to PQQ supplementation, particularly in the domain of Body Listening, following exhaustive exercise. Body listening reflects the tendency to attend to internal bodily sensations to gain insight and understanding⁴⁰. Together with interoceptive sub-component Self-Regulation, it represents regulatory aspects and skills of interoceptive awareness or attention styles of interoceptive sensibility⁴¹, which underlie adaptive decision-making and emotional awareness. In the exercise environment, higher body listening ability facilitates more sensitive insight into functional states and fatigue, enabling individuals to modulate performance and recovery more effectively. Accordingly, as an effective nutritional intervention for enhancing bodily awareness and Self-Regulation, PQQ supplementation may serve as a nutritional strategy to optimize interoceptive regulation and resilience under physiological stress. PQQ may protect against interoceptive disturbances induced by maximal-intensity exercise through its potent antioxidant and neuroprotective mechanisms. Neurons are particularly vulnerable to oxidative stress generated during exhaustive exercise, which can impair neural signalling related to interoception. By activating the Nrf2/ARE pathway, PQQ strengthens endogenous antioxidant defences^{11,12},

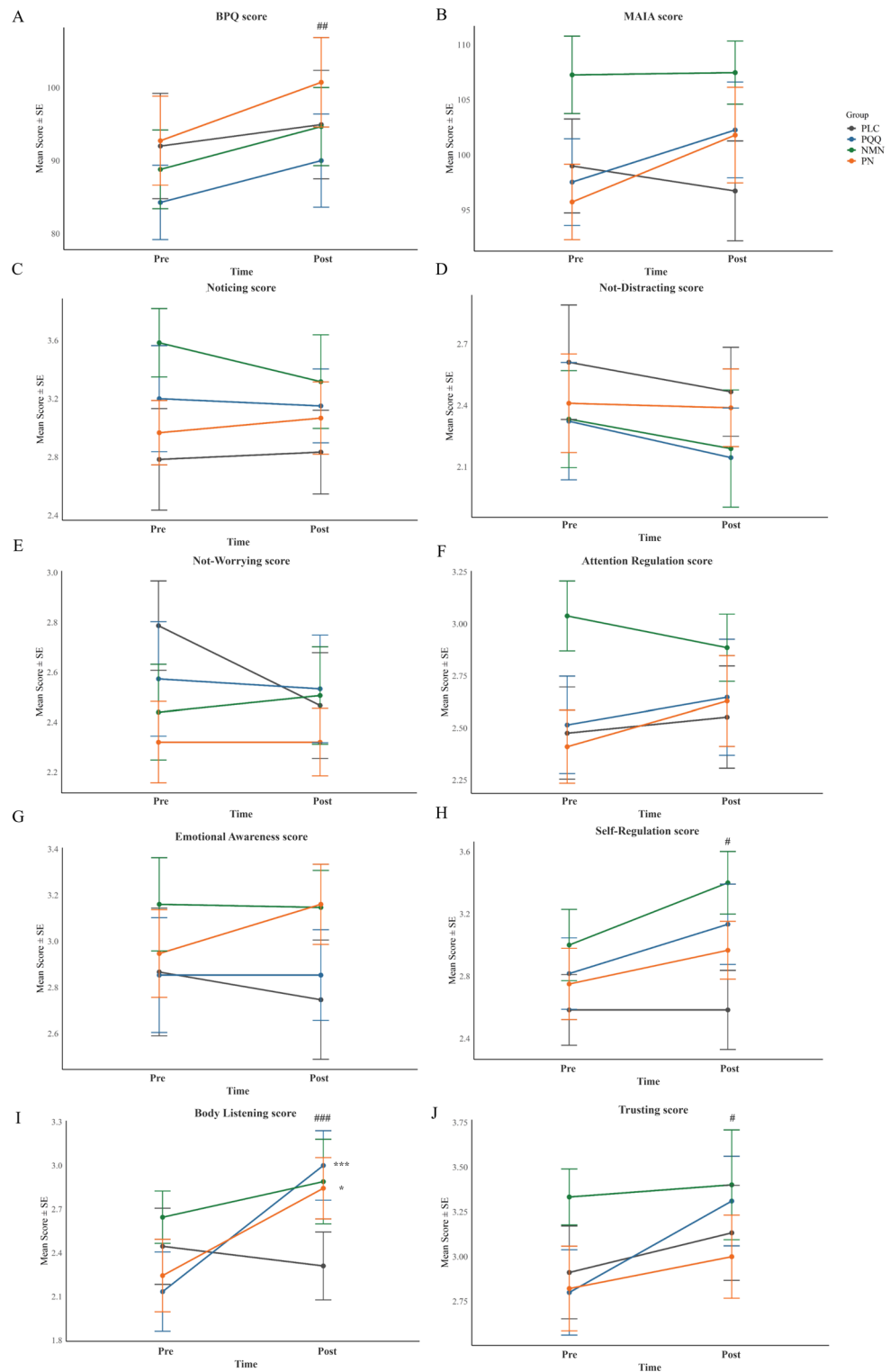


Fig. 3. Group x Time Effect of interoception.

thereby mitigating oxidative stress-induced neuronal injury and preserving neuronal structure and function⁴². Moreover, PQQ promotes mitochondrial biogenesis and energy metabolism via the AMPK/PGC-1 α and SIRT1 pathways¹², which enhance cellular resilience to oxidative stress and sustain neuronal energy homeostasis. These mitochondrial benefits may be particularly relevant under high-intensity exercise conditions that increase reactive oxygen species production and energy demands. In addition, PQQ upregulates the expression of nerve growth factor (NGF) and its receptors¹³, supports neuronal growth and repair, and enhances neurotransmitter secretion—particularly norepinephrine—in the brain¹⁴. Through these integrated mechanisms, PQQ may

	PLC (n = 15)		PQQ (n = 15)		NMN (n = 15)		PN (n = 15)		F	p-value	η^2	ES
	Pre Mean (95% CI)	Post Mean (95% CI)	Pre Mean (95% CI)	Post Mean (95% CI)	Pre Mean (95% CI)	Post Mean (95% CI)	Pre Mean (95% CI)	Post Mean (95% CI)				
TTE (s)	963.20 (909.94, 1016.46)	957.33 (899.67, 1014.99)	940.00 (900.00, 980.00)	941.27 (885.28, 997.25)	972.13 (918.21, 1026.06)	939.60 (887.72, 991.48)	970.07 (916.88, 1023.26)	926.13 (888.43, 963.84)	0.665	0.578	0.037	S
AT (s)	528.53 (487.91, 569.16)	476.60 (410.17, 543.03)	508.67 (470.64, 546.69)	471.40 (403.54, 539.26)	530.40 (486.57, 574.23)	502.80 (433.52, 572.08)	489.00 (449.45, 528.55)	461.87 (398.07, 525.67)	0.855	0.470	0.047	S
Peak RER	1.10 (1.08, 1.13)	1.15 (1.10, 1.19)	1.09 (1.07, 1.11)	1.17 (1.14, 1.21)	1.10 (1.08, 1.11)	1.17 (1.14, 1.21)	1.10 (1.07, 1.12)	1.16 (1.11, 1.21)	1.311	0.281	0.070	M
VO ₂ ^{max} (mL/kg·min)	54.80 (53.08, 56.52)	56.40 (53.17, 59.63)	54.60 (53.01, 56.19)	54.47 (52.45, 56.48)	54.53 (52.81, 56.26)	54.67 (52.49, 56.84)	55.20 (53.51, 56.89)	54.73 (52.20, 57.27)	0.784	0.508	0.043	S
VO ₂ ^{AT} (mL/kg·min)	37.00 (34.25, 39.75)	35.47 (31.54, 39.39)	37.17 (34.92, 39.41)	34.20 (30.05, 38.35)	38.57 (35.34, 41.81)	37.87 (32.82, 42.91)	37.00 (34.17, 39.83)	34.60 (30.17, 39.03)	0.806	0.496	0.044	S
VO ₂ Utilization (%)	67.60 (62.51, 72.69)	66.28 (59.84, 72.71)	68.29 (63.58, 73.00)	68.40 (64.21, 72.59)	70.78 (65.00, 76.55)	70.35 (65.84, 74.86)	67.13 (61.84, 72.42)	68.05 (61.86, 74.25)	0.53	0.66	0.03	S
VE _{max} /VO ₂ _{max}	31.98 (30.20, 33.76)	32.42 (30.13, 34.71)	30.93 (29.20, 32.65)	31.57 (29.74, 33.41)	32.18 (30.69, 33.67)	32.37 (31.05, 33.70)	31.37 (29.75, 32.98)	31.56 (28.56, 34.56)	0.061	0.980	0.004	-

Table 3. The effects of nutritional supplements on exercise capacity. *TTE* Time to exhaustion, *AT* Anaerobic threshold, *RER* respiratory exchange ratio, *VO₂_{max}* maximal oxygen uptake, *VO₂_{AT}* *VO₂* at *AT*, *VO₂ Utilization* *VO₂* at *AT*/ *VO₂_{max}*.



Fig. 4. The correlation between the change of interoception and RPE, $\text{VO}_{2\text{max}}$, and HR_{max} .

maintain synaptic integrity, enhance sympathetic nervous system signaling, and stabilize interoceptive feedback loops during high-intensity physical exertion.

In contrast, NMN supplementation alone did not significantly influence interoception following exhaustive exercise. Although NMN increases intracellular NAD^+ concentrations, thereby supporting SIRT1-dependent pathways that promote mitochondrial biogenesis, neuronal survival, and anti-inflammatory activity^{20–22}, these effects are primarily substrate-driven rather than signal-initiated. Consequently, they may require sustained activation over a longer period to induce measurable neural adaptations. Given that the present experiment involved acute NMN administration one hour before exercise, the NAD^+ increase may not have been sufficient to elicit rapid transcriptional or neuroprotective responses. This contrasts with PQQ, which directly activates AMPK/PGC-1 α and SIRT1 signaling, allowing more immediate modulation of neuronal redox homeostasis during acute physiological stress. Previous research indicates that chronic NMN supplementation enhances aerobic endurance and elevates the ventilatory threshold²⁸, suggesting that NMN may contribute to long-term metabolic and neuronal stability rather than acute interoceptive modulation.

Interestingly, this study revealed that the PN group maintained stable scores across all dimensions of interoception following acute exhaustive exercise, suggesting a potential synergistic effect of combined supplementation on stabilizing interoception function. This mechanistic interaction is consistent with previous evidence demonstrating that concurrent activation of the PGC-1 α and SIRT1 pathways produces greater improvements in mitochondrial function, oxidative stress resistance, and neuronal survival than activation of either pathway alone^{43,44}. Therefore, while the present findings do not confirm a statistically significant synergistic effect, they are partially consistent with the mechanistic hypothesis that concurrent modulation of oxidative and metabolic stress pathways by PQQ and NMN could help stabilize interoceptive function under physiological stress. Future studies should further explore dose–response relationships, chronic supplementation effects, and neuroimaging-based correlates to elucidate the specific neural mechanisms underlying these potential synergistic benefits.

This study did not directly observe significant improvements in exercise capacity after nutritional supplementation. However, compared with the baseline, the PQQ group showed an upward trend in TTE and VO_2 Utilization after PQQ supplementation. The higher the ratio of VO_2 at the AT to $\text{VO}_{2\text{max}}$, the greater the efficiency of the athlete's aerobic metabolism, allowing them to maintain stable performance at higher intensities. PQQ may reduce fatigue perception during exercise by increasing the secretion of norepinephrine¹⁴, allowing the athlete to maintain executive ability even when perceiving a high-intensity workload, thereby sustaining

exercise for a longer duration. This study found a positive correlation between BPQ changes before and after exhaustive exercise with RPE and $\text{VO}_{2\text{max}}$. Recent research has indicated an interaction between interoception and RPE, which is modulated by visual cues. This research showed that higher interoceptive accuracy leads to a higher perceived effort in a virtual downhill environment under identical load conditions⁴⁵. This finding supports the possibility of a positive relationship between interoception and RPE. In the 1980s, Pennebaker et al. found that individuals focusing on interoceptive signals during exercise reported higher levels of RPE⁴⁶. When subjects ran at a constant speed on a treadmill, RPE scores were higher when listening to amplified breathing sounds compared to sounds that diverted attention (such as street noises). This suggests that subjective fatigue perception does not fully and accurately reflect the physiological state within the body but depends on the ability to accurately perceive and interpret signals within the body, a capacity determined by interoceptive sensitivity. This mismatch between perceived fatigue and actual physiological state can negatively affect exercise regulation³. The findings of this study demonstrate a link between the changes induced by PQQ in both interoception and exercise capacity, supporting the hypothesis that PQQ-induced improvement of interoception facilitated improved maintenance of exercise capacity.

This study has several limitations. First, only male participants were included. Previous research has confirmed sex differences in interoception⁴⁷, and males were selected to minimize potential confounding variables related to the sex. Future research should include a broader population to explore the effects of nutritional supplementation on interoception across diverse populations. Second, interoception was assessed immediately after acute exhaustive exercise, without considering changes at different time points. Future research could track interoception at various intervals to gain a more comprehensive understanding of the effects of nutritional supplementation on interoception. Third, the lack of follow-up data on the long-term effects of PQQ and NMN supplementation represents a limitation. Fourth, the neurobiological indicators associated with neural mechanisms of PQQ and NMN were not measured, and the precise mechanisms underlying PQQ's enhancement of interoception remain unverified. Finally, subjective self-reports were used as the measures of interoception, which may not accurately capture the subtle changes in interoception. Future research should investigate the long-term effects and mechanisms of nutritional supplementation on interoception.

Conclusion

Effective nutrients can optimize exercise interoception induced by acute exercise. While NMN alone does not affect exercise interoception, it has a potential synergistic effect when combined with PQQ enhancing interoception. It is necessary to undertake further investigation to explore available nutrition strategies for improving exercise interoception.

Data availability

The data presented in this study are available on request from the corresponding author.

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Author contributions

Conceptualization, G. W. and Y. Y.; methodology, G. W., Y. Y. and C. Z.; formal analysis, C. Z.; investigation, C. Z., B. W. and H. S.; data curation, C. Z., B. W. and H. S.; writing, original draft preparation, C. Z. and Y. Y.; writing review and editing, G. K., Y. Y.; supervision, Y. Y. and B. W.; funding acquisition, Y. Y. All authors have read and agreed to the published version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Institutional review board

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Scientific Ethics Committee at the Beijing Sport University (2023286H, Nov. 14, 2023).

Informed consent

Informed consent was obtained from all subjects involved in the study.

Additional information

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