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Effects of exercise training intensity on cardiac autonomic regulation in habitual smokers

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Background: The sympathoexcitatory effects of cigarette smoking cause an autonomic imbalance that may lead to cardiovascular disease. Aerobic training improves autonomic function by developing cardiorespiratory fitness; however, it is still uncertain whether aerobic training ameliorates the compromised autonomic modulation in smokers. This study aimed to investigate the effects of 8 weeks' aerobic training at different exercise intensities on autonomic regulation in habitual smokers.

Methods: Healthy males ($n = 34$) were randomly assigned to a moderate-intensity aerobic training (MAT, 60% of heart rate reserve [HRR]), a high-intensity training group (HAT, 75% HRR), or a control group (CG). Training groups performed 8 weeks' aerobic training on a treadmill (3 times/week), but all subjects continued to smoke cigarettes as usual. Heart rate variability was monitored to evaluate the effect of aerobic training on autonomic regulation.

Results: Aerobic training improved autonomic balance despite the continued smoking. In the time domain, rMSSD and pNN50 were significantly increased in HAT than in CG. On spectral analysis, the absolute and normalized units of high frequency (HF) were significantly increased in HAT, whereas the LF/HF ratio and the normalized unit of LF were significantly decreased compared to that in CG. SD1 and the SD1/SD2 ratio of the Poincaré plot analysis were significantly increased compared to CG. Although MAT showed a similar tendency to HAT in nonlinear indexes, there were no significant differences compared to CG.

Conclusion: Aerobic training, particularly high-intensity training, increases the parasympathetic contribution to the sympathovagal system, leading to an improvement in autonomic balance despite continued cigarette smoking.

KEYWORDS

aerobic training, autonomic imbalance, cigarette smoking, heart rate variability

1 | INTRODUCTION

Although the World Health Organization (WHO) has implemented the Framework Convention on Tobacco Control as a part of its sustainable development goals, with a view to reducing cigarette smoking, according to the annual World Health Statistics reported in 2016 there are approximately 1.1 billion current smokers worldwide (World Health Organization, 2016). The Surgeon General's report included cigarette smoke as a major cause of death, implicated in

12 types of cancer, six types of cardiovascular disease (CVD), diabetes, chronic obstructive pulmonary disease, pneumonia, and influenza (U.S. Department of Health and Human Services, 2014). In addition, cigarette smoking was listed as a relative risk factor for the occurrence of common diseases, being highly correlated with renal failure, intestinal ischemia, hypertensive heart disease, various respiratory diseases, breast cancers, and prostate cancers (Carter et al., 2015). Meanwhile, the Centers for Disease Control and Prevention (CDC) evaluated the success rate of smoking cessation over one

decade in the United States, based on the National Health Interview Survey. The results showed that 68.8% of all smokers had a positive attitude toward smoking cessation, while 52.4% attempted to quit smoking during the study. However, only 6.2% had succeeded in quitting smoking by the end of the study in 2010 (Centers for Disease Control and Prevention, 2011). In general, smokers suffer from nicotine addiction, which induces negative withdrawal symptoms such as sadness, irritability, anxiety, frustration, poor sleep quality, and change in appetite (Piasecki, 2006). These symptoms make it hard for smokers to quit permanently and easy for them to restart smoking. Thus, preventive healthcare is necessary for habitual smokers, since the smoking relapse rate is higher than the success rate for smoking cessation.

The Framingham Heart Study (examination 3, 1983–1987) investigated the risk factors for metabolic risks, CVD, diabetes, and mortality over a 12-year period. Resting heart rate (HR) and autonomic imbalance were not only identified as significant predictive factors in the diagnosis of hypertension, hyperglycemia, and diabetes but were also revealed as risk factors for CVD and early mortality (Wulsin, Horn, Perry, Massaro, & D'Agostino, 2015). In fact, the control of resting HR depends upon the autonomic nervous system and its two branches, the sympathetic and parasympathetic systems. Sympathetic hyperactivity and parasympathetic withdrawal as a result of intrinsic and/or extrinsic factors induce an autonomic imbalance, whose effects include an increase in resting HR (Thayer, Yamamoto, & Brosschot, 2010).

Cigarette smoking is known to be a major factor causing autonomic imbalance via its sympathoexcitatory effect (Cagirci et al., 2009; Middlekauff, Park, & Moheimani, 2014). Physiologically, the nicotine within cigarettes induces the release of catecholamines from adrenergic nerve terminals when it is inhaled (Najem et al., 2006); moreover, smoke resulting from the combustion of organic particulate matter within cigarettes also causes autonomic imbalance (Pope et al., 2004). In the Copenhagen Holter Study of middle-aged men and women ($n = 775$), heart rate variability (HRV) was analyzed in terms of 5 min of RR intervals. HRV has proved itself in many clinical studies as a useful method for evaluating autonomic balance and function. HRV indexes have been inversely associated with cigarette smoking; however, they were positively related with physical activity (Sajadieh et al., 2004).

A high level of cardiorespiratory fitness is a modifiable factor that improves the overall state of health, as well as reducing CVD and all-cause mortality. In fact, 12 weeks' aerobic training in sedentary subjects ($n = 34$) induced an increase in vagal-mediated HRV parameters (Albinet et al., 2010), implying that the cardiorespiratory fitness level is not only associated with autonomic regulation, but also promotes autonomic balance and function (Hautala, Kiviniemi, & Tulppo, 2009).

Despite the positive effect of aerobic training on autonomic balance and function, little is known about the effects of aerobic training on autonomic regulation in habitual smokers. It is clinically important to investigate training interventions for habitual smokers, since the success rate of smoking cessation is lower than the rate of smoking relapse. Therefore, this study was aimed at investigating the effect of 8 weeks' aerobic training with different

exercise intensities on autonomic regulation in habitual male smokers.

2 | METHODS

2.1 | Study population

Healthy young males ($n = 34$, age 23.6 ± 0.3 years, mean $\pm$ SE) participated in this study. We included subjects who met the following criteria: (i) age ≥ 18 , but < 29 years; (ii) no history of CVD and/or orthopedic disease; (iii) a regular smoker, ≥ 10 cigarettes/day for at least three consecutive years; (iv) sedentary, not performing regular physical activity over the previous 6 months; and (v) under no medication during the previous 2 weeks. This study was approved by the Ethics Committee of Kyungpook National University [20140066].

2.2 | Study design

All subjects were asked to refrain from any caffeinated and alcoholic beverages for at least 24 hr, any kind of food (overnight fasting) for at least 12 hr, strenuous exercise for at least 48 hr, and any medication for at least 2 weeks. They were also asked to limit cigarette smoking, including second-hand smoke and/or electronic cigarettes, for at least 12 hr prior to participation. Pre and posttraining evaluations were performed between 9:00 and 11:00 a.m. to avoid circadian variation (Buchheit, Haddad, Laursen, & Ahmaidi, 2009). All subjects completed the Physical Activity Readiness (PAR-Q) Questionnaire, the Health/Fitness Facility Preparticipation Screening Questionnaire from the American Heart Association, and an informed consent form following the American College of Sports Medicine (ACSM) guidelines (American College of Sports Medicine, 2013). In addition, the Cigarette Dependence Scale-12 (CDS-12) questionnaire was evaluated to assess smoking status (Etter, Le Houezec, & Perneger, 2003). Subjects were assigned to one of three groups by randomization: moderate-intensity aerobic training (MAT, $n = 12$), high-intensity aerobic training (HAT, $n = 12$), and a control group (CG, $n = 10$). All subjects were instructed to maintain their usual smoking habits. To ensure smoking and exercise status, the experimenters tracked participants' detailed daily routine through telephone interviews.

2.2.1 | Anthropometry and hemodynamic measurements

Weight and height were measured to the nearest 0.01 kg and 0.1 cm, respectively, using an automatic digital stadiometer (GL-150; G-Tech International Co., Gyeonggi-do, Korea). Body mass index (BMI, kg/m^2) was calculated by dividing weight (kg) by the square of height (m^2). Waist circumference (cm) and hip girth (cm) were measured to calculate the waist-to-hip ratio (WHR). Blood pressure (BP) was obtained using an automatic digital BP monitor (UA-772C; A&D, Tokyo, Japan) on the nondominant arm with the subject in a seated position. Systolic (SBP) and diastolic (DBP) pressures were recorded,

and mean arterial pressure (MAP) was calculated using the equation, $MAP = (2 \times DBP + SBP)/3$. All measurements were consecutively taken twice and the average value was used.

2.2.2 | Assessment of carbon monoxide (CO) and carboxyhemoglobin (COHb)

A portable CO monitor, Pico + Smokerlyzer (Bedfont Scientific Ltd., Kent, United Kingdom) was used to assess exhaled CO and COHb. Before the test, a breath sampling D-piece and a clean cardboard mouthpiece were attached to the CO monitor. Subjects were asked to inhale deeply and hold their breath for a 15 s countdown displayed on screen. To exhale completely, subjects were coached to blow through mouthpiece slowly and fully as soon as the CO monitor started beeping (Al-Sheyab, Kheirallah, Mangnall, & Gallagher, 2015).

2.2.3 | Heart rate variability (HRV) assessment and analysis

HRV monitoring was performed in a quiet and dimly lit room at a temperature of 22–24°C. The resting RR interval was monitored for 10 min with the subject in a seated position, using a wearable wireless chest strap (two-lead) connected to a Polar RS800CX device (Polar Electro Oy, Kempele, Finland). The metronome was set to a rate of 15/min (0.25 Hz) to control the frequency of respiration (Strano et al., 1998). Obtained RR interval data were extracted as text files using Protrainer Polar 5 software (version 5.40.171, Polar Electro), then transferred into HRV analysis software (Kubios version 2.0, 2008, Biosignal Analysis And Medical Imaging Group, University of Kuopio, Finland, MATLAB) published by Tarvainen et al., 2014). Before analysis, ectopic beats were excluded through artifact correction, successive interbeat intervals (IBIs) in 256 points/Hz were selected, and smoothness priors (Lambda 500) technique applied IBIs for detrend. Time, frequency, and nonlinear domains were analyzed using the standard short-term HRV protocol (Grant, Viljoen, Janse van Rensburg, & Wood, 2012). In the time domain, rMSSD and pNN50 were determined as major indicators of parasympathetic activation. In power spectrum density analysis using fast Fourier transforms, absolute units of high frequency (HF, 0.15–0.40 Hz) and low frequency (LF, 0.04–0.15 Hz) spectral power, and the LF/HF ratio were determined as main indexes in the frequency domain. In addition, normalized units of HF (HF nu) and LF (LF nu) were computed. To interpret the nonstationary data, SD1 and the SD1/SD2 ratio of the Poincaré plot analysis were determined.

2.2.4 | Exercise test

Cardiorespiratory fitness level was assessed using the Bruce protocol stress test, which was performed for a more accurate evaluation of cardiorespiratory fitness. The test was started at 1.7 mph and at a gradient of 10% on the treadmill. Both gradient and speed were increased automatically. The gradient was increased by 2% every 3 min, and treadmill speed was gradually increased to 2.5, 3.4, 4.2, 5.0, 5.5, 6.0, 6.5, 7.0,

and 7.5 mph. The test was stopped if subjects were unable to continue because of fatigue, pain, and/or other medical indications. The total time completed was recorded and converted to a test score (T) in minutes (e.g., total time completed, 9 min 15 s = test score, 9.25 min). Estimated VO_{2max} was calculated using the following formula:

$$VO_{2max} (ml^{-1}kg^{-1}min^{-1}) = 14.76 - (1.379 \times T) + (0.451 \times T^2) - (0.012 \times T^3).$$

2.3 | Aerobic training protocol

Training groups performed supervised aerobic exercise on a treadmill (MAHA3, TAEYOUNG Inc., Daegu, Korea) 3 times/week for 8 weeks. Subjects in the MAT group trained at 60% of heart rate reserve [HRR], while HAT subjects trained at 75% of HRR (Garber et al., 2011). Each session consisted of a 5 min warm-up, 30 min of walking and/or running during the 1st to 4th weeks, and 5 min of cool-down. Exercise duration was increased up to 50 min/session during the 5th to 8th weeks. Treadmill speed (km/hr) was adjusted every 2 weeks.

2.4 | Statistical analysis

All data were presented as mean $\pm$ SE and analyzed using SPSS 22.0 (Statistical Package for the Social Sciences Software, Version 22.0, Chicago, IL, USA). One-way analysis of variance (ANOVA) followed by a Bonferroni post hoc test was used to evaluate the changes between pre and post aerobic training. Training-induced changes were analyzed by repeated measures ANOVA with time and group. Significance was set at $p < .05$.

3 | RESULTS

3.1 | Changes in clinical characteristics at posttraining

There were no significant differences among CG, MAT, and HAT in smoking duration, daily cigarette use, or CDS-12 score at baseline ($p < .05$). Nor were there any significant differences in clinical characteristics, including age and BMI ($p > .05$). Eight weeks' aerobic training while cigarette smoking was continued had no effect on hemodynamic indexes, with no significant between-group differences in SBP, DBP, or MAP ($p > .05$). In contrast, mean HR showed significant differences among groups ($p > .05$). The HAT group showed a significant decrease in mean HR compared to CG ($p < .05$); mean HR also decreased in the MAT group, but the difference from CG was not statistically significant ($p > .05$) (Table 1).

3.2 | Changes in cardiorespiratory fitness level at posttraining

The results of the QCT showed that VO_{2max} differed significantly among the MAT, HAT, and CG groups ($p < .05$). In particular, HAT showed a significant increase compared to CG ($p < .05$), whereas there

TABLE 1 Clinical characteristics and cardiorespiratory fitness at pre- and posttraining in all groups

Variables	CG (n = 10)		MAT (n = 12)		HAT (n = 12)		p
Smoking status							
Smoking duration (month)	33.60 ± 2.63		32.92 ± 2.01		32.75 ± 1.53		–
Cigarettes day (number)	15.33 ± 1.32		12.67 ± 1.13		12.25 ± 1.28		–
Cigarette dependence scale-12 (score)	69.60 ± 9.09		61.00 ± 5.21		71.00 ± 7.60		–
Clinical characteristics	Pre	Post	Pre	Post	Pre	Post	–
Age (years)	23.30 ± 0.47	–	24.08 ± 0.62	–	23.25 ± 0.63	–	–
Body mass index (kg/m ²)	23.04 ± 1.07	23.39 ± 1.17	23.23 ± 1.31	23.05 ± 1.22	24.18 ± 0.81	23.99 ± 0.81	.120
Systolic blood pressure (mm Hg)	112.40 ± 4.41	112.60 ± 4.85	114.83 ± 2.99	111.75 ± 2.38	117.00 ± 2.46	114.50 ± 1.74	.593
Diastolic blood pressure (mm Hg)	69.90 ± 3.17	71.50 ± 3.78	70.42 ± 2.96	70.25 ± 2.18	71.33 ± 1.83	67.67 ± 2.66	.384
Mean arterial pressure (mmHg)	84.07 ± 3.50	85.20 ± 4.05	85.22 ± 2.77	84.08 ± 2.09	86.56 ± 1.61	83.28 ± 2.17	.414
Mean heart rate (beats/min)	70.32 ± 2.09	74.14 ± 2.63	64.48 ± 1.65	61.71 ± 2.24	70.40 ± 1.89	62.71 ± 2.35**	.005*
Vital capacity (L)	4.68 ± 0.18	4.80 ± 0.17	4.29 ± 0.20	4.51 ± 0.18	4.82 ± 0.17	4.93 ± 0.17	.793
Forced vital capacity (L)	4.23 ± 0.11	4.42 ± 0.18	3.86 ± 0.18	3.95 ± 0.17	4.24 ± 0.18	4.31 ± 0.20	.840
Maximal voluntary ventilation (L/min)	133.54 ± 5.97	133.98 ± 6.26	125.86 ± 6.22	130.62 ± 4.21	137.70 ± 6.88	142.18 ± 6.03	.737
Exhaled carbon monoxide (ppm)	11.00 ± 1.51	7.30 ± 1.05	10.92 ± 0.95	9.17 ± 1.10	8.92 ± 1.12	6.83 ± 0.79	.507
Carboxyhemoglobin (%)	2.37 ± 0.25	1.81 ± 0.17	2.40 ± 0.15	2.09 ± 0.17	2.07 ± 0.18	1.74 ± 0.13	.621
Cardiorespiratory fitness							
VO _{2max} (ml kg ^{−1} min ^{−1})	46.19 ± 1.53	45.63 ± 1.26	47.67 ± 1.56	49.94 ± 1.93	46.45 ± 1.45	51.97 ± 0.85**	.001*

CG, control; MAT, moderate-intensity aerobic training group; HAT, high-intensity aerobic training group.

Values are means ± SEM.

* $p < .05$, significant difference between CG, MAT, or HAT by one-way analysis of variance (ANOVA);

** $p < .05$, significant difference between CG and other groups resulted from Bonferroni post hoc test.

was no significant difference in VO_{2max} between MAT and CG. The Bruce protocol test gave similar results, with a significant increase in VO_{2max} in the HAT group than in the CG ($p < .05$), but no significant difference between MAT and CG (Table 1).

3.3 | Changes in time domain indexes at posttraining

The changes in both rMSSD and pNN50 showed significant differences among CG, MAT, and HAT ($p < .05$). Both parameters showed a significant increase in the HAT ($p < .05$) than in the CG, but no significant difference between MAT and CG ($p > .05$). Furthermore, there was a significant time-group interaction in the changes in rMSSD and pNN50 ($p < .05$) (Figure 1).

3.4 | Changes in spectral analysis of frequency indexes at posttraining

The changes in HF power and LF/HF ratio differed significantly among the CG, MAT, and HAT groups ($p < .05$). HF power showed a significant increase in the HAT group compared to CG, while the LF/HF ratio

showed a significant decrease ($p < .05$). However, the changes in HF power and LF/HF ratio in MAT did not differ significantly compared to CG ($p > .05$). In addition, there was a significant time-group interaction in the changes in HF power and LF/HF ratio ($p < .05$) (Figure 2).

3.5 | Changes in normalized units of spectral indexes at posttraining

The changes in LF nu and HF nu showed significant differences among CG, MAT, and HAT ($p < .05$). LF nu decreased significantly in the HAT group, while HF nu showed a significant increase in HAT compared to CG ($p < .05$). Furthermore, there was a significant time-group interaction ($p < .05$) in the changes in LF nu and HF nu (Figure 3). In contrast, the changes in LF nu and HF nu in MAT did not differ significantly compared to CG ($p > .05$).

3.6 | Changes in nonlinear indexes at posttraining

The changes in SD1 and SD1/SD2 ratio showed significant differences among CG, MAT, and HAT ($p < .05$). Both SD1 and SD1/SD2 ratio

FIGURE 1 Change rate (Δ) in time domain at rest after 8-week aerobic training CG, control; MAT, moderate-intensity aerobic training group; HAT, high-intensity aerobic training group; rMSSD, square root of the mean squared differences between successive RR intervals; pNN50, NN50 (Number of successive RR interval pairs that differ more than 50 ms) divided by the total number of RR intervals

increased significantly in HAT compared to CG ($p < .05$). Furthermore, both indexes showed a significant time-group interaction ($p < .05$) (Figure 4). Although the SD1 and SD1/SD2 ratio increased in MAT subjects, there was no significant difference compared to CG ($p > .05$).

4 | DISCUSSION

Nicotine and fine particulate organic matter within cigarettes cause an autonomic imbalance that contributes to an increase in all-cause morbidity and mortality, including that from CVD. On the other hand, the autonomic balance gradually recovers to the normal range after smoking cessation. Many smokers attempt to quit smoking, since they recognize the negative effects of the habit, but the actual success rate of smoking cessation is very low because of the high relapse rate. Thus, a specific clinical strategy for habitual smokers is necessary to improve their

damaged autonomic balance and function. Given that regular physical activity, such as aerobic exercise, helps improve cardiac autonomic regulation, this study investigated the effect of 8 weeks' aerobic training at different intensities on autonomic regulation in habitual young smokers.

The training groups showed a tendency to a lower resting HR at posttraining, independently of exercise intensity, although there were no significant differences in weight and BMI among groups. HAT subjects showed a significant decrease in resting HR, while the difference in the MAT group was not significant compared to CG. In addition, 8 weeks' aerobic training induced significant changes in HRV indexes that reflect autonomic regulation. The training groups showed an increase in rMSSD and pNN50, time domain indexes indicating parasympathetic activation; the increases in both indexes were statistically significant in the HAT group, but not in the MAT group, compared to CG. Spectral analysis revealed that the training groups also showed an increase in the absolute units of HF at posttraining, reflecting

FIGURE 2 Change rate (Δ) in spectral index at rest after 8-week aerobic training CG, control; MAT, moderate-intensity aerobic training group; HAT, high-intensity aerobic training group; HF, high frequency band power, 0.15–0.4 Hz; LF/HF ratio, ratio of LF (low frequency band power, 0.04–0.15 Hz) and HF

parasympathetic activation. Again, the increase was significant in the HAT group, whereas there was no significant difference between MAT and CG. On the other hand, the training groups showed a decrease in the LF/HF ratio, which indicates sympathetic activation; the decrease was significant in HAT subjects, but not in MAT subjects, compared to CG. Similarly, the training groups showed a decrease in LF nu, an index of sympathetic predominance in the cardiac sympathovagal balance. Again, the decrease was significant compared to CG for the HAT group, but not for the MAT group. In contrast to LF nu, HF nu increased after training, reflecting parasympathetic predominance. As with the other parameters, the change was significant for the HAT group compared to CG, but not for MAT subjects. Finally, in the non-linear domain, at posttraining the training groups showed an increase in both SD1 and the SD1/SD2 ratio, which reflect parasympathetic activation. Both increases were significant in the HAT group compared to CG, but there was no significant difference between MAT and CG.

A poor cardiorespiratory fitness level and/or high resting HR are associated with a greater incidence of CVD and all-cause mortality

(Saxena et al., 2013). Along with the increase in resting HR, a decrease in HRV is a powerful predictor of hypertension, hyperglycemia, and diabetes, and both changes are acknowledged as significant risk factors for CVD and all-cause mortality (Wulsin et al., 2015). Generally, a decrease in resting HR is noted after endurance training, as a result of a reduction in the rhythmicity of the heart, an increase in parasympathetic predominance, and a reduction in the sympathetic contribution to HR. The main reason for a lack of change in resting HR and autonomic modulation is exercise load (Borresen & Lambert, 2008).

Tulppo et al. (2003) studied 55 males (age 35 ± 10 years), who were nonsmokers with high BMI (≥ 30 kg/m²), were free of diabetes, asthma, and/or CVD, and underwent 8 weeks' aerobic training (6 times/week) at 70%–80% HR_{max} with different intensities on a treadmill. The moderate-intensity protocol used 30-min sessions, whereas the high-volume training group exercised for 60 min/session. At posttraining, both exercise groups showed significant decreases in mean HR, from 70 ± 7 to 64 ± 8 beats/min and from 67 ± 5 to 60 ± 6 beats/min for the moderate- and high-intensity groups, respectively (Tulppo et al.,

Repeated measured ANOVA
Interaction
Time $\times$ Group
 $p = .026^{\dagger}$

Repeated measured ANOVA
Interaction
Time $\times$ Group
 $p = .026^{\dagger}$

FIGURE 3 Change rate (Δ) in normalized unit of spectral index at rest after 8-week aerobic training CG, control; MAT, moderate-intensity aerobic training group; HAT, high-intensity aerobic training group; LF nu, normalized unit of LF; HF nu, normalized unit of HF. * $p < .05$, significant difference between CG, MAT, or HAT resulted from Bonferroni post hoc; $\dagger p < .05$, significant difference from repeated measured ANOVA

2003). As in our study, the difference was significant for HAT compared to CG, but not for MAT. The difference between the previous study and our study was the training intensity; however, the ACSM guidelines classify both 77%–95% HR_{max} and 60%–84% HRR as high-intensity exercise. Therefore, even though there were also differences in the subjects' age and smoking status, both studies yielded similar findings.

Furthermore, both studies observed significant changes in HRV indexes, as well as resting HR. High-intensity aerobic training led to a significant increase in HF power and a decrease in the LF/HF ratio on spectral analysis, whereas for moderate-intensity exercise the increase was not significant. Thus, high-intensity, rather than moderate-intensity aerobic training is required in habitual smokers for improvement of their parasympathetic activation.

Mourot, Bouhaddi, Perrey, Rouillon, and Regnard (2004) studied the effect of 6 weeks' aerobic training using a cycle ergometer on a healthy young man with no medical history of CVD or metabolic disorders. After training, maximal oxygen uptake (VO_{2max}) had significantly increased. The time domain indexes rMSSD and pNN50 and the SD1 of the Poincaré plot, all of which reflect parasympathetic activation,

showed significant increases (Mourot et al., 2004). Likewise, our study of habitual smokers, using 8 weeks' high-intensity aerobic training on a treadmill, indicated a significant increase in VO_{2max} (Bruce treadmill test, QCT). In addition, indexes of parasympathetic activity, such as rMSSD, pNN50, SD1, and the SD1/SD2 ratio, increased significantly in the HAT group (75% HRR) compared to CG, although the differences in VO_{2max} and HRV indexes between MAT and CG were not significant. These findings suggest that improving cardiorespiratory fitness through high-intensity aerobic training can contribute to the development of autonomic regulation, regardless of the exercise mode.

Power spectral analysis has been used to evaluate sympathovagal balance and to monitor sympathetic predominance in regular smokers. Lucini, Bertocchi, Malliani, and Pagani (1996) carried out a comparative study of nonsmokers and heavy smokers (age, 18 ± 2 years). Heavy smokers showed a significant increase in LF nu, which indicates a shift of the sympathovagal balance toward sympathetic predominance, but HF nu, which reflects parasympathetic predominance, was significantly decreased compared to nonsmokers after adjustment for age (Lucini et al., 1996).

FIGURE 4 Change rate (Δ) in nonlinear domain at rest after 8-week aerobic training CG, control; MAT, moderate-intensity aerobic training group; HAT, high-intensity aerobic training group; SD1, the standard deviation of the instantaneous beat-to-beat RR interval variability (minor axis of the ellipse); SD2, the standard deviation of the continuous long-term RR interval variability (major axis of the ellipse). $^*p < .05$, significant difference between CG, MAT, or HAT resulted from Bonferroni post hoc; $^\dagger p < .05$, significant difference from repeated measured ANOVA

Another study compared light, moderate, and heavy smokers ($n = 40$ in each group), based on daily cigarette use and total smoking duration. All groups showed a significant increase in LF nu and a significant decrease in HF nu compared to nonsmokers (Ferdousi, Ferdous, & Islam, 2014). Furthermore, heavy smokers had a significant increase in LF nu and a decrease in HF nu compared to light smokers. These findings are consistent with those of this study. Thus, high-intensity aerobic training using a treadmill appears to be an effective exercise mode for inducing a shift from sympathetic to parasympathetic predominance and restoring the sympathovagal balance in healthy male smokers.

4.1 | Limitations

This study had some limitations. We tested only healthy young men, without considering age and sex differences. For monitoring autonomic balance, HRV analysis is dependent upon age and sex (Voss, Schroeder, Heitmann, Peters, & Perz, 2015); however, this study demonstrated an improvement in autonomic function via parasympathetic

activation and sympathetic withdrawal within a homogenous group. In addition, we did not consider the effect on autonomic modulation of different types of exercise, such as aerobic training with a cycle ergometer or resistance training. Although cigarette smoking causes an autonomic imbalance, no previous clinical trial has tested the effect of exercise intervention on autonomic regulation in smokers. Our study found significant results as regards the improvement of autonomic balance and function through high-intensity aerobic training in habitual male smokers.

5 | CONCLUSIONS

In summary, this study indicated that 8 weeks' high-intensity aerobic training significantly reduced resting HR and induced positive changes in resting autonomic modulation by parasympathetic activation and sympathetic withdrawal in apparently healthy male smokers. Furthermore, HRV analysis is a useful technique for evaluating

the effect of high-intensity aerobic training on autonomic regulation. Our findings suggest that aerobic training could enhance cardiac autonomic balance and function, including resting HR, in habitual smokers even if they do not quit smoking; however, to promote this effect, high-intensity aerobic exercise intervention is required.

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