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Acute and chronic effects of exercise on inhibitory control in patients with coronary artery disease: a pilot study

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Abstract: Cardiovascular disease is associated with increased risk of cognitive decline and impaired executive functions, particularly inhibitory control, in patients with coronary artery disease (CAD). Exercise-based cardiac rehabilitation enhances cardiorespiratory fitness and may benefit cognition by improving cerebral perfusion and promoting neuroplasticity. This pilot study aimed to examine both the acute (pre- vs. post-exercise) and chronic (pre- vs. post-intervention) effects of aerobic exercise on inhibitory control in patients with CAD. This manuscript presents pilot data from the first 10 participants enrolled in a larger prospective, randomized, single-blind, multicenter trial. In this preliminary phase, ten clinically stable patients with CAD completed a 12-week aerobic exercise-based cardiac rehabilitation program. Peak oxygen uptake (VO_2 peak) was measured by cardiopulmonary exercise test (CPET). Cognitive inhibitory control was assessed using a computerized Stroop task at two time points (pre- and post-intervention) and at two time points within each assessment (rest vs. 15 min post-CPET), allowing evaluation of both chronic and acute effects. Reaction time and accuracy were analyzed using a two-way repeated-measures analysis of variance (ANOVA) with two factors: Acute (rest vs. post-CPET) and Chronic (pre- vs. post-intervention). VO_2 peak increased significantly after the intervention (mean difference = $3.4 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; $p = .006$; $d = 1.14$; 95% CI [0.31, 1.93]). Accuracy remained at ceiling across conditions (88–100%). Acute exercise consistently improved reaction time in all Stroop conditions (η^2p range: .450–.770). Only in the incongruent condition—the trial with the highest inhibitory demand—was chronic improvement observed ($\eta^2p = .434$), indicating enhanced cognitive efficiency after the training program. Interaction effects were not statistically significant, although effect sizes suggested clinically meaningful changes. Aerobic exercise produces acute improvements in inhibitory control and may induce selective chronic benefits under high executive demand. These preliminary findings support the feasibility of the protocol and justify a fully powered trial to determine the extent of exercise-induced cognitive adaptations in this clinical population.

Keywords: Cognitive function, Physical exercise, Cardiovascular disease, Peak oxygen uptake.



1. Introduction

Cardiovascular diseases (CVD) remain the leading global cause of death, primarily driven by the high prevalence of coronary artery disease (CAD) (Chong et al., 2025). This condition is characterized by reduced blood flow to the myocardium due to obstruction of the coronary arteries, leading to clinical manifestations such as myocardial infarction and ischemic cardiomyopathy (Stark et al., 2024). The incidence and prevalence of CVD are expected to continue rising, driven not only by the increasing rates of obesity, diabetes, and metabolic syndrome but also by the progressive aging of the population (Shi et al., 2025).

CVD predisposes individuals to cerebrovascular damage, and its incidence increases markedly with age. Patients with CAD are particularly vulnerable to cognitive and functional decline, showing a higher risk of developing dementia compared to age-matched adults without CVD (Taylor, 2023; Toval et al., 2024). This association is partly explained by shared cardiovascular risk factors such as hypertension, diabetes, dyslipidemia, and obesity, as well as by standard pathophysiological mechanisms, including cerebral hypoperfusion and endothelial dysfunction, which may compromise the delivery of oxygen and nutrients to neural tissue (Alagiakrishnan et al., 2018). Consequently, the coexistence of cardiovascular and cerebrovascular alterations may accelerate neurodegenerative processes and cognitive decline in this population (Taylor, 2023).

As indicated by previous literature in healthy and older adults, a single session of physical exercise can produce measurable

improvements in reaction time, attention, and executive control (Kamijo et al., 2009; McSween et al., 2019). These acute cognitive benefits have been consistently demonstrated through tasks such as the Stroop and Flanker tests, which assess inhibitory control and cognitive flexibility, and are typically reflected in faster response times and enhanced task performance (Davranche et al., 2009; Hsieh et al., 2018). However, despite the growing body of evidence in non-clinical populations, these effects have been scarcely examined in patients with CVD, a group particularly vulnerable to both cardiovascular and cognitive dysfunction.

Cardiac rehabilitation (CR) represents a key therapeutic strategy in the management of patients with CVD. This multidisciplinary intervention combines exercise training, health education, and psychological support to optimize functional recovery, reducing cardiovascular mortality, recurrent cardiac events, and hospitalizations (Dibben et al., 2023). Among these approaches, exercise-based CR programs have demonstrated strong efficacy in improving functional capacity, alleviating symptoms, and reducing mortality rates in patients with cardiovascular and heart failure conditions (Tegegne et al., 2022).

Among its components, exercise training serves as the cornerstone, promoting favorable adaptations in cardiorespiratory, metabolic, and vascular function (Manresa-Rocamora et al., 2022). Beyond its cardiovascular benefits, growing evidence suggests that exercise may also exert positive effects on cognitive function by enhancing cerebral perfusion, neuroplasticity, and neurovascular regulation (Alagiakrishnan et

al., 2018). Therefore, CR not only supports physical recovery but may also play an important role in preserving brain health and maintaining cognitive reserve in this population.

The relevance of exercise-based interventions is best understood within the broader framework of cognitive reserve, defined as the brain's capacity to maintain functional performance despite age-related or pathological changes (Pettigrew & Soldan, 2019). Regular physical exercise serves as a key contributor to this reserve by inducing long-term improvements in cognitive domains such as executive function, memory, and attention (Zhang et al., 2023); these benefits are likely mediated by a convergence of physiological mechanisms, where exercise not only promotes neurovascular health, synaptic plasticity, and neurogenesis (Dhahbi et al., 2025), but also sustains improvements in cardiorespiratory fitness and endothelial function (Moriarty et al., 2020). Consequently, incorporating exercise into CR programs supports long-term brain resilience in individuals with cardiovascular disease through these multifaceted neuroprotective and vascular adaptations. However, the long-term impact on this population remains to be fully elucidated.

To better understand this relationship, it is essential to consider the influence of specific training variables, including frequency, intensity, time, type, volume, and progression (FITT-VP principle). Among these, intensity has been identified as a key determinant of both physiological (Fuertes-Kenneally et al., 2023) and cognitive adaptations (Oberste et al., 2019). In CR programs, moderate-intensity

aerobic exercise has traditionally been the primary modality due to its well-documented benefits, including improvements in cardiorespiratory fitness, an independent predictor of mortality, along with reductions in cardiovascular risk and enhancements in quality of life (Calverley et al., 2020; Fujiyoshi et al., 2020). However, in recent years, there has been growing interest in high-intensity interval training (HIIT) as a safe and effective alternative for patients with CAD. Several studies have shown that HIIT can elicit greater improvements in cardiorespiratory fitness and vascular function than moderate-intensity training (MIT), thereby contributing to a more efficient rehabilitation process (Manresa-Rocamora et al., 2021; Toval et al., 2024).

In parallel, research conducted in healthy adult populations has demonstrated that exercise intensity also modulates cognitive responses. Specifically, HIIT has been associated with superior improvements in executive functions, particularly inhibitory control, followed by vigorous continuous exercise, whereas the effects of moderate-intensity training tend to be more modest (Hsieh et al., 2021; W. Zhang et al., 2025). However, whether these cognitive benefits extend similarly across different training modalities or are influenced by the specific exercise method remains unclear, especially in clinical populations such as patients with CAD.

Despite growing evidence that exercise benefits cognitive function, most studies in cardiac populations have evaluated either the chronic effects of structured training or the acute effects of a single exercise bout, but not both within the same intervention framework. Acute aerobic

exercise has been shown to transiently enhance executive performance, likely through increases in cerebral blood flow, catecholamines, lactate availability, and neurotrophic factors such as BDNF (Boyne et al., 2019; Kamijo et al., 2009; McSween et al., 2019). In contrast, chronic improvements in cognition appear to be mediated by long-term physiological adaptations such as enhanced cardiorespiratory fitness, neurovascular coupling, and synaptic plasticity (Alagiakrishnan et al., 2018; Patti et al., 2021). However, to our knowledge, no study has evaluated the acute and chronic effects of exercise on inhibitory control within the same CR program, nor has it examined cognitive responses immediately before and after a standardized cardiopulmonary exercise test (CPET).

Therefore, the primary aim of this pilot study was to examine the effect of exercise on inhibitory control in patients with CAD by testing: (a) the acute effect of exercise (rest vs. post-CPET); and (b) the chronic effect after a 12-week CR program (pre- vs. post-intervention). A secondary aim was to generate effect size estimates to inform sample size and methodological decisions for a future fully powered trial.

2. Materials and Methods

Study design - The study was conducted in accordance with the principles outlined in the Declaration of Helsinki and received approval from the Ethics Committee of the Universidad Miguel Hernández de Elche (DCD.JMSM.240126).

This manuscript reports the pilot phase of the trial, consisting of the first 10 participants enrolled in the larger randomized study. These preliminary data

were analyzed to evaluate feasibility, estimate effect sizes, and refine methodological and statistical parameters for the fully powered trial. Because of the reduced and imbalanced group distribution in this pilot phase (MIT = 5, HIIT-Short = 2, HIIT-Long = 3), all analyses were conducted on the whole sample as a single group. Recruitment takes place across several hospital centers, including Vinalopó University Hospital, General University Hospital of Elche, and Dr. Balmis General University Hospital of Alicante. Eligible individuals are contacted by telephone and voluntarily enrolled after receiving detailed information about the study procedures.

Those who agreed to participate came to the laboratory to provide written informed consent and complete a familiarization session with the Stroop test, performing it five times to minimize potential learning effects.

On the day of the CPET, participants completed the Stroop test immediately before the exercise and again 15 min after its completion (Chang et al., 2012) to examine the acute effects of exercise on cognitive performance. This procedure was repeated at baseline (pre-intervention), and at the end of the 12-weeks of intervention (post-intervention assessment). In addition, a CPET was conducted at week 6 of the program to update training intensities based on the new ventilatory threshold values. All Stroop tests were conducted under identical environmental conditions (i.e., same room, table, and chair).

Patients were randomly assigned to one of three experimental groups: HIIT with long intervals (HIIT-Long), HIIT with short intervals (HIIT-Short), or MIT. All programs

were performed on a cycle ergometer, three days per week, over 12 weeks (36 supervised sessions). To ensure comparability between groups, the protocols were designed to be isocaloric, with the MIT group's work duration individualized to match the estimated energy expenditure of the HIIT sessions (Table 1).

For each participant in the HIIT groups, the energetic cost of the HIIT sessions—including both high-intensity intervals and active recovery periods—was first determined. This was accomplished by applying the individual linear regression model for energy expenditure (EE) vs. power output (PO), which was established during the baseline CPET.

The prescribed PO intensities (above VT2 for intervals and below VT1 for recovery phases) were converted into the corresponding EE using this model. The calculated total caloric cost of the HIIT sessions for a given training block served as the reference to adjust the duration of the MIT sessions.

MIT was performed continuously between VT1 and VT2. Session durations were individualized by using the individual PO-EE linear regression model to ensure they precisely matched the total caloric cost of the corresponding weekly HIIT protocol. This isocaloric approach ensured that, despite differences in intensity distribution, all three training modalities imposed equivalent energetic demands.

Training intensities were updated after the mid-intervention CPET, allowing recalibration of the PO-EE linear regression model. Accordingly, MIT session durations were adjusted as needed to maintain isocaloric comparability. At the same time,

progressive overload was applied by modifying either the number of intervals in the HIIT protocols or the duration in the MIT condition, consistent with the periodization presented in Table 1.

Across all training modalities, progressive overload was applied throughout the intervention to promote physiological adaptations while ensuring participant safety. Adjustments after the mid-intervention CPET allowed for individualized recalibration of training intensities based on updated ventilatory thresholds, complementing the adjustments already made to maintain isocaloric comparability.

Subjects - The study's recruitment target is 50 participants per group. However, the current pilot phase includes 10 individuals (2 females and 8 males). All participants meet the inclusion criteria and are medically stable at the time of assessment. The sample is distributed as follows: five participants in the MIT group, two in the HIIT-Short group, and three in the HIIT-Long group. Descriptive data are presented in Table 2.

The inclusion criteria for the study are as follows: (a) male and female participants; (b) aged between 45 and 75 years; (c) diagnosed with acute myocardial infarction or stable angina pectoris, treated by percutaneous coronary intervention, coronary artery bypass graft surgery, or conservative medical therapy; (d) the cardiac event or intervention occurred within 3 to 12 months prior to study enrollment; (e) absence of physical limitations preventing the performance of exercise; and (f) completion of the in-hospital phase of cardiac rehabilitation and/or medical discharge authorization.

Table 1. Exercise training program.

Block	Week	HIIT-Long			HIIT-Short				MIT	
		Reps x work duration	Intensity	Relief	Reps x work duration	Sets	Intensity	Relief / Recovery	Time	Intensity
1	1	2 x 4 min	> VT2W	4 min	4 x 1 min	2	> VT2W	1 min / 3 min	Equivalent Isocaloric energy expenditure	VT1W - VT2W
	2									
	3									
2	4	3 x 4 min				3				
	5									
	6									
Mid-intervention assessment (adjust the intensity to the new CPET values)										
3	7	3 x 4 min	> VT2W	4 min	4 x 1 min	3	> VT2W	1 min / 3 min	Equivalent Isocaloric energy expenditure	VT1W - VT2W
	8									
	9									
4	10	4 x 4 min				4				
	11									
	12									

MIT = moderate-intensity continuous training; HIIT-Long = high-intensity interval training with long intervals; HIIT-Short = high-intensity interval training with short intervals; VT1 = first ventilatory threshold; VT2 = second ventilatory threshold; W = power output associated to each threshold; Recovery = active recovery performed at 10% below of power at VT1 unless otherwise stated. Energy expenditure per session (kcal) was estimated from individual VO_2 data as described in Methods.

Table 2. Sample description.

Characteristic	All patients (n = 10)
Sex (Male/Female)	10 (8♂/2♀)
Age (years)	60 ± 10
BMI ($kg \cdot m^{-2}$)	28.0 ± 4.2
VO_2 peak ($ml \cdot kg^{-1} \cdot min^{-1}$)	25.0 ± 4.3

BMI: Body Mass Index; VO_2 peak: Peak of oxygen uptake achieved during the pre-intervention CPET.

The exclusion criteria are: (a) acute heart failure; (b) complex ventricular arrhythmias; (c) left ventricular ejection fraction below 50%; (d) uncontrolled arterial hypertension; (e) myocarditis or pericarditis; (f) severe aortic stenosis, left ventricular outflow tract obstruction, or aortic dissection; (g) current use of nitrates as part of pharmacological treatment; and/or (h) the

presence of ischemic symptoms during the CPET performed prior to the intervention.

Measurements - Cognitive inhibition -

The Stroop test (Stroop, 1935) is a widely used neuropsychological assessment that measures executive functioning, selective attention, and inhibitory control (Chang et al., 2019; Golden, 1994). In the present study, cognitive inhibition was evaluated as one of the primary domains of cognitive function.

In the present study, we utilize a computerized version of the Stroop test (UMH-MEMTRAIN, as described by Pastor et al., 2018), which adheres to the standardized methodology outlined by Golden et al. (1994). This version enables the accurate assessment of reaction time and response accuracy, as previously validated

by Ballester-Ferrer et al. (2022a). All tests are conducted on a tablet device (Samsung Galaxy Tab A9+) to ensure standardized digital administration.

The task includes three progressively challenging stages. The initial stage represents the congruent condition, the second represents the neutral condition, and the third corresponds to the incongruent condition, as explained below. During each stage, one of four stimuli, “red”, “blue”, “yellow”, or “green” (in Spanish) or the sequence “XXXX” is presented in the center of a white screen.

At the bottom of the screen, four buttons are displayed, corresponding to the options “red”, “blue”, “yellow”, and “green”. In the congruent condition (first test), the four-color words appear in black font, and participants are instructed to read the word and select the matching option.

In the neutral condition, four “XXXX” symbols are presented in a specific color, and participants must identify the font color and press the corresponding button.

Finally, in the incongruent condition, a color word is shown in a font color that does not match its meaning. In this case, participants must ignore the word’s meaning and select the color of the letters.

Participants are instructed to respond as quickly and accurately as possible. Each condition is administered for 45 s, during which participants complete as many stimuli as possible without sacrificing accuracy; therefore, the number of trials varies across individuals depending on their execution speed. For each block, reaction time is calculated as the mean of all responses, with no anticipatory responses detected and no outlier removal applied.

Both correct and incorrect responses are recorded, and a 25 s inter-condition rest interval is included before proceeding to the subsequent task. Five familiarization trials of the Stroop task are administered prior to the experimental phase to account for potential learning effects. This number is selected based on previous findings, which report that five trials are sufficient to decrease intra-block variability to below 5% (Ballester-Ferrer et al., 2022a).

Cardiopulmonary exercise test - participants were instructed to refrain from performing intense physical activity for at least 24 hours before each assessment and to avoid consuming alcohol and caffeine for at least 4 hours prior to testing. A cardiopulmonary exercise test (CPET) is conducted for all participants using a cycle ergometer (SanaBike 500 easy, Truchtelingen, Germany) under continuous medical supervision. The CPET protocol consists of several sequential stages. Participants first remain seated at rest on the ergometer for 5 minutes to record baseline values, followed by a 3-minute warm-up phase at a workload of 10 W. Subsequently, an individualized ramp protocol is applied, with power output increasing continuously between 4 and 20 W·min⁻¹ according to each participant’s estimated peak oxygen uptake. The protocol is designed to reach volitional exhaustion within approximately 8 to 12 minutes (Manresa-Rocamora et al., 2023) while maintaining a pedalling cadence between 60 and 70 revolutions per minute. The test concludes with a 5-minute active recovery phase at a power output of 10 W.

Throughout the procedure, respiratory gas exchange is measured breath-by-breath using a metabolic cart (Metalyzer

3B, CORTEX Biophysik GmbH, Leipzig, Germany), and heart rate is continuously monitored through a 12-lead electrocardiogram (Norav PC-ECG 1200, Mainz-Kastel, Germany). Electrodes are positioned in standard anatomical locations, and filters are applied to eliminate 50 Hz electrical interference and electromyographic noise (35 Hz). Ventilatory data are averaged in 10-second intervals for subsequent analysis.

To verify that the CPET represented a maximal effort, the primary criterion assessed was the presence of a VO_2 plateau, defined as an increase in oxygen uptake of $<150 \text{ ml}\cdot\text{min}^{-1}$ despite an increase in workload. If the VO_2 plateau was not achieved, the test was considered maximal only if any of the following criteria were met: (1) a respiratory exchange ratio (RER) ≥ 1.10 ; (2) a post-exercise (1-minute) capillary blood lactate concentration $\geq 8 \text{ mmol}\cdot\text{L}^{-1}$. When primary or secondary criteria were satisfied, the test was classified as maximal or symptom-limited.

After test termination, participants completed a 3-minute passive recovery phase before proceeding with post-exercise assessments.

Calculation of ventilatory thresholds - Ventilatory thresholds are determined using a combined approach to improve their accuracy and consistency (Keir et al., 2022). Ventilatory data are analyzed and independently reviewed by experienced investigators to identify the first (VT1) and second (VT2) ventilatory thresholds. For each threshold, corresponding values of oxygen uptake (VO_2), heart rate (HR), and power output (PO) are obtained. HR and PO at VT1

and VT2 are calculated through temporal interpolation.

Sample size calculation - The sample size was estimated using G*Power software based on a two-way repeated-measures ANOVA (2×2 design) with acute (resting-post CPET) and chronic effect (pre-post program) as factors. Considering the reaction time in the Stroop test as the primary outcome, an expected large effect size ($f = 0.35$) derived from the previous studies (Ballester-Ferrer et al., 2022b), a statistical power of 0.80, and an alpha level of .05, the required sample size was calculated to be 35 participants. Accounting for a potential dropout rate of approximately 20%, the total number of participants to be recruited for the main trial was set at 42 (14 per training group).

This pilot study was designed to provide preliminary data that will be used to validate or adjust the estimated effect size for the subsequent full-scale clinical trial. The findings obtained from this initial sample will help refine the statistical assumptions and ensure that the final sample size calculation accurately reflects the expected variability and magnitude of the intervention effects in the target population.

Data analyses - Although participants were randomly allocated to three training modalities (HIIT-Long, HIIT-Short, and MIT), statistical analyses were performed on the whole sample as a single group. Due to the exploratory nature of this pilot study and the small sample size per condition, subgroup comparisons would lack statistical power and increase the risk of Type II error.

Therefore, analyses focused on the overall effect of exercise on cognitive

outcomes, rather than on between-group comparisons.

A two-way repeated-measures ANOVA (2×2) was performed, with two within-subject factors: acute effect (resting vs. post-CPET) and chronic effect (pre-intervention vs. post-intervention). The model tested the main effects of the two repeated factors and the interaction (acute $\times$ chronic).

Prior to analysis, assumptions of normality of residuals (Shapiro–Wilk), homogeneity of variances (Levene), and sphericity (Mauchly) were evaluated. When sphericity was violated, the Greenhouse–Geisser correction was applied. If normality assumptions were not met, logarithmic or square-root transformations were considered. For the percentage of correct responses, due to its bounded nature (0–100%), the distributional properties were examined. If substantial skewness persisted, an arcsine–square-root transformation was used (Little & Rubin, 2019).

When significant main or interaction effects were found, pairwise comparisons with Bonferroni adjustment were performed. Effect sizes were reported as partial eta-squared (η^2_p) for ANOVA effects and Cohen's d for t-test and pre-post pairwise comparisons. The interpretation thresholds used were for η^2_p (Cohen, 2013; Richardson, 2011): small: ≥ 0.01 , medium: ≥ 0.06 , and large: ≥ 0.14 ; for Cohen's d (Cohen, 2013; Lakens, 2013) trivial: < 0.20 , small: 0.20 – 0.49 , medium: 0.50 – 0.79 , and large: ≥ 0.80 .

All data are presented as mean $\pm$ standard deviation (SD), along with mean differences (MD) and their corresponding 95% confidence intervals (95% CI). Statistical analyses were conducted using JASP

software, version 0.95.4 (intel) (JASP Team, 2025; University of Amsterdam, The Netherlands). The Statistical significance threshold was set at $p < .05$, and trends approaching significance ($p < .10$) were also reported, given the exploratory nature of the pilot study.

3. Results

Cardiorespiratory fitness – A significant improvement in aerobic capacity was observed after the intervention. $\text{VO}_{2\text{peak}}$ increased from pre- to post-intervention (MD = $3.4 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$; 95% CI = 1.3, 5.5; $p = .006$, $d = 1.14$). Figure 1 shows individual trajectories according to exercise modality (MIT, HIIT-Short, and HIIT-Long). Given the reduced and imbalanced distribution of participants across groups in this pilot phase (MIT = 5, HIIT-Short = 2, HIIT-Long = 3), these data are presented for descriptive purposes only, and no formal between-group statistical comparisons were performed. Figure 1 illustrates individual changes in $\text{VO}_{2\text{peak}}$ across the three exercise modalities, showing improvements in aerobic capacity in participants from all intervention groups.

No significant effects were observed for the chronic factor or any interactions ($p > .05$). In the neutral condition, a similar pattern was noted, with a significant acute effect ($F(1,7) = 9.96$, $p = .016$, $\eta^2_p = 0.59$), suggesting faster responses post-exercise but no significant differences across groups ($F(2,7) = 0.81$, $p = .484$, $\eta^2_p = 0.19$). Finally, in the incongruent condition, the acute effect again reached significance ($F(1,7) = 24.29$, $p = .002$, $\eta^2_p = 0.78$). In contrast, a marginal effect was detected for the chronic factor ($F(1,7) = 5.28$, $p = .055$, $\eta^2_p = 0.43$), reflecting a trend

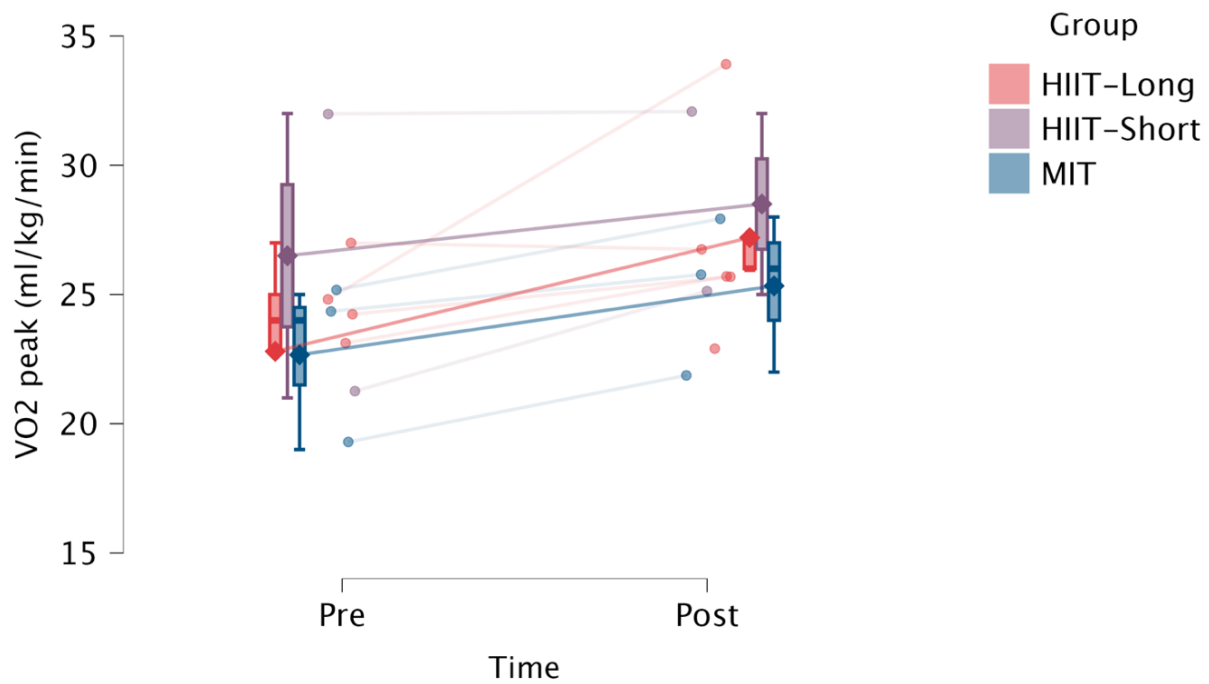


Figure 1. Individual trajectories and box plots of VO_2peak ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) at pre- (baseline) and post-intervention (12 weeks).

toward long-term improvement in inhibitory control. Across all conditions, the absence of significant group or interaction effects ($p > .05$) indicates that, although acute improvements in cognitive performance were evident, the small group sizes ($n = 3\text{--}5$ per group) may have limited statistical power to detect between-group differences.

Cognitive performance — accuracy (% correct). Accuracy remained consistently high across all conditions (range = 88–100%). The repeated-measures ANOVA showed no significant chronic effect (pre- vs post-intervention) on accuracy ($p = .608$, $\eta^2p =$

0.030). A trend toward an acute effect of exercise (rest vs post-CPET) was observed ($F(1,9) = 4.118$, $p = .073$, $\eta^2p = 0.314$). No significant Acute $\times$ Chronic interaction was detected ($F(1,9) = 1.658$, $p = .230$, $\eta^2p = 0.156$).

Cognitive performance — reaction time. Descriptive values are presented in Table 3, and the acute and chronic effect of the incongruent condition is shown in Figure 2 and 3. The statistical outcomes of the acute and chronic effects are summarized in Table 4. Reaction time results are reported separately for each Stroop condition.

Table 3. Reaction time (ms) in resting and post-CPET for each Stroop test condition.

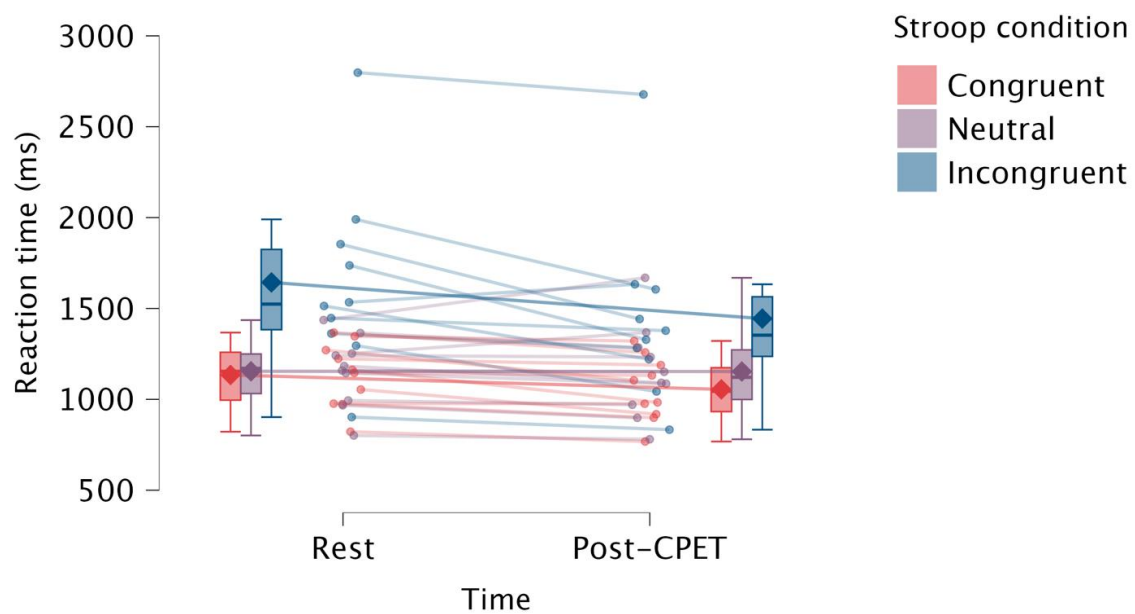
Condition	Pre-intervention		Post-intervention	
	Resting	Post-CPET	Resting	Post-CPET
Congruent	1134 $\pm$ 177	1055 $\pm$ 175	1159 $\pm$ 224	1028 $\pm$ 175
Neutral	1154 $\pm$ 191	1153 $\pm$ 254	1168 $\pm$ 256	1085 $\pm$ 187
Incongruent	1643 $\pm$ 508	1444 $\pm$ 496	1504 $\pm$ 513	1386 $\pm$ 436

CPET, Cardiopulmonary exercise test. Values are reported as mean and standard deviation.

Table 4. Principal effects of repeated-measures factors (acute and chronic effects) for each Stroop test condition.

	MD	95%CI (lower, upper limit)	<i>p</i>	η^2_p
Acute effect (<i>post-CPET vs resting</i>)				
Congruent	-105	-59, -152	<.001*	0.746
Neutral	-42	-77, -7	.024*	0.450
Incongruent	-158	-224, -93	<.001*	0.770
Chronic effect (<i>post- vs pre-intervention</i>)				
Congruent	-1	-54, 52	.960	<0.001
Neutral	-28	-19, 74	.210	0.169
Incongruent	-99	-184, -14	.027*	0.434

95%CI, 95% confidence interval; *Statistical significance was reached ($p \leq .050$).

**Figure 2.** Individual trajectories and box plots of reaction time (ms) for the three Stroop test conditions at rest and after the cardiopulmonary exercise test.

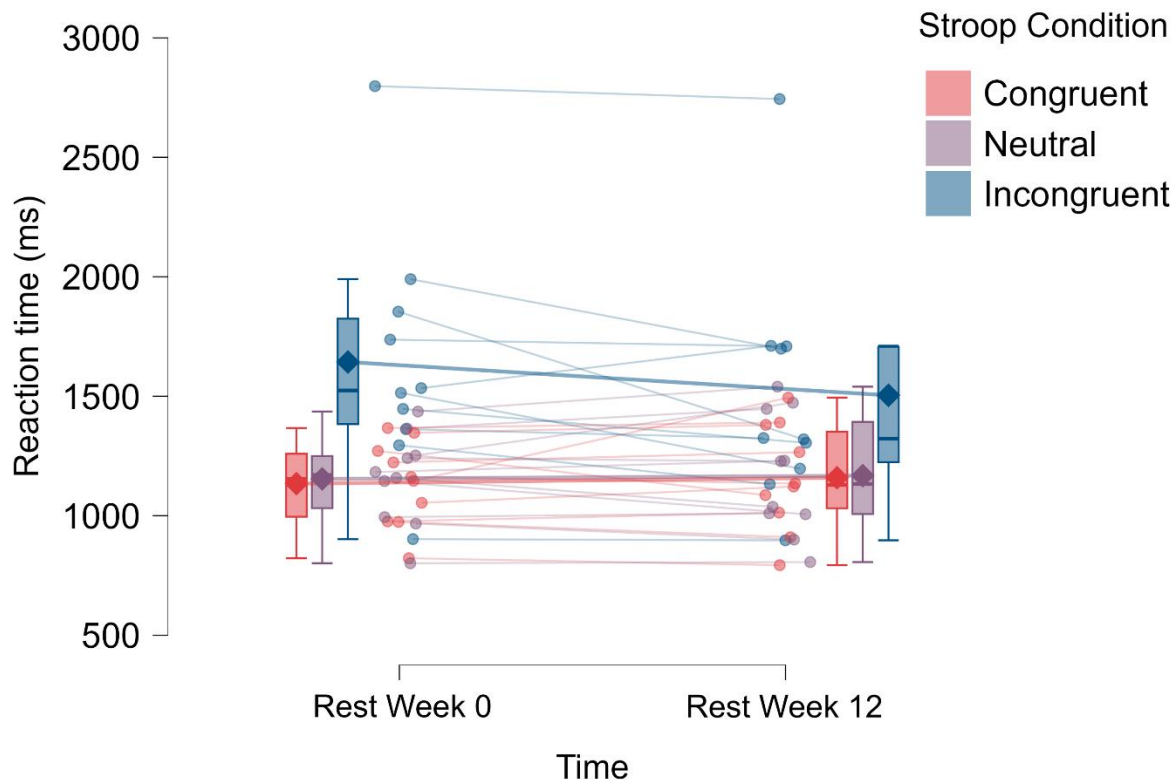


Figure 3. Individual trajectories and box plots of reaction time (ms) for the three Stroop test conditions at pre-intervention (baseline) and post-intervention (12 weeks)

Congruent condition - There was a significant acute effect, with faster responses after CPET ($F_{(1,9)} = 26.436, p < .001, \eta^2p = .746$). Neither a chronic effect ($F_{(1,9)} = 0.003, p = .960, \eta^2p < .001$), nor an interaction were observed ($F_{(1,9)} = 1.073, p = .327, \eta^2p = .106$).

Neutral condition - A significant acute effect was detected ($F_{(1,9)} = 7.366, p = .024, \eta^2p = .450$). No chronic effect ($F_{(1,9)} = 1.826, p = .210, \eta^2p = .169$) and no interaction were observed ($F_{(1,9)} = 2.176, p = .174, \eta^2p = .195$).

Incongruent condition - A significant acute effect was also found ($F_{(1,9)} = 30.091, p < .001, \eta^2p = .770$). Unlike the other conditions, a chronic effect of the training was observed ($F_{(1,9)} = 6.909, p = .027, \eta^2p = .434$), with faster responses following the intervention. No interaction was detected ($F_{(1,9)} = 1.225, p = .297, \eta^2p = .120$).

Sample size - Finally, data obtained from this pilot study were used to refine the

sample size estimation for a future fully powered trial. The original a priori calculation reported in the Methods section was based on an anticipated effect size ($f = 0.35$) and indicated that 42 participants in total would be required after accounting for an expected 20% dropout rate. In contrast, using the effect size observed in the present pilot study ($f = 0.47$), a post hoc G*Power analysis estimated that 47 participants per training group would be needed to achieve a statistical power of 0.80 at an alpha level of 0.05. This updated estimate is intended to inform the design of a future confirmatory randomized controlled trial and should not be interpreted as replacing the original sample size calculation.

4. Discussion

The present pilot study examines both the acute and chronic effects of exercise

on inhibitory control in patients with CAD enrolled in a 12-week CR program. The results showed (1) an improvement in cardiorespiratory fitness, and (2) faster reaction times after exercise in all Stroop conditions (acute effect), with a chronic improvement detected only in the incongruent condition.

Cardiorespiratory fitness increased significantly after the intervention, confirming that the exercise program was effective in producing physiological adaptations. This improvement in VO_2peak is consistent with previous studies reporting that structured aerobic exercise enhances aerobic capacity in patients with cardiovascular disease (Tegegne et al., 2022). Increased cardiorespiratory fitness is clinically relevant, as it has been associated with a reduced risk of morbidity and mortality in this population (Keteyian et al., 2008).

Regarding cognitive accuracy, performance remained at ceiling levels (88–100%) at all time points, and no acute or chronic effects were detected. This suggests that accuracy may lack sensitivity to detect subtle cognitive changes in clinical populations, particularly when the task is not sufficiently demanding or when a ceiling effect is present. In such situations, reaction time provides a more informative index of cognitive efficiency (Willoughby et al., 2023).

Reaction time results revealed two key findings. First, acute exercise consistently improved reaction time across all Stroop conditions. This finding aligns with previous research showing that a single bout of aerobic exercise transiently enhances executive function and inhibitory control (Kamijo et al., 2009; McSween et al., 2019). The acute

facilitation observed after the CPET may be explained by rapid physiological responses that occur during and immediately after aerobic exercise. Increases in cerebral blood flow and oxygen delivery improve metabolic support to regions involved in inhibitory control, particularly the prefrontal cortex (Mekari et al., 2019). In parallel, acute exercise triggers the release of catecholamines (e.g., dopamine, norepinephrine), which modulate attention, working memory, and cognitive performance by increasing arousal and improving the signal-to-noise ratio at the cortical level (McMorris, 2016).

Additionally, transient elevations in lactate during high-intensity exercise have been shown to cross the blood–brain barrier and act as an energetic substrate for neurons, enhancing processing efficiency (Hashimoto et al., 2021). Acute exercise also increases brain-derived neurotrophic factor (BDNF), a key mediator of synaptic plasticity and short-term cognitive enhancement (Boyne et al., 2019; Fernández-Rodríguez et al., 2022; Müller et al., 2020). Collectively, these mechanisms create a temporary neurochemical and metabolic environment that facilitates faster information processing and improved inhibitory control immediately following exercise.

Second, a chronic improvement in reaction time was observed exclusively in the incongruent condition, the trial with the highest inhibitory demand. This selective adaptation suggests that sustained aerobic exercise may improve cognitive efficiency when executive control is challenged. The selective chronic improvement observed in the incongruent condition can be better understood by considering the cognitive

demands of this trial. Among the three Stroop conditions, the incongruent task imposes the greatest inhibitory load, as it requires suppressing the automatic tendency to read the word while selecting the font color instead. This form of inhibition is a core executive function supported by prefrontal mechanisms involved in conflict monitoring and top-down control. Prior evidence has shown that executive functioning, including inhibitory control, is the cognitive domain most sensitive to improvements in cardiorespiratory fitness and long-term aerobic exercise adaptations. Individuals with higher fitness levels demonstrate enhanced activation of prefrontal regions during executive versions of the Stroop task, suggesting that these networks may particularly benefit from sustained training (Dupuy et al., 2015).

In contrast, the congruent and neutral conditions place substantially lower demands on executive control and may therefore be less sensitive to training-related changes. These tasks can approach performance ceilings, particularly after familiarization, which reduces intra-individual variability and limits the potential to detect subtle improvements. As a result, chronic adaptations may only become evident in conditions where inhibitory demands are sufficiently high to engage the cognitive processes most influenced by long-term aerobic training. This pattern reinforces the specificity of exercise-induced benefits and supports the interpretation that improvements are most detectable when executive load is greatest.

These findings are consistent with studies reporting that chronic exercise induces long-term improvements in

executive function in cardiac patients (Alagiakrishnan et al., 2018). Several physiological mechanisms may contribute to this chronic benefit. Improvements in cardiorespiratory fitness, as reflected by the significant increase in VO_2peak , are known to enhance cerebral oxygenation and facilitate neurovascular coupling during cognitive task performance, thereby reducing the metabolic cost associated with executive processing (Dupuy et al., 2015; Mekari et al., 2019). Moreover, regular aerobic exercise promotes angiogenesis, mitochondrial biogenesis, and an increase in neurotrophic molecules such as BDNF, all of which support synaptic plasticity and prefrontal cortex efficiency—processes that are particularly relevant for inhibitory control and executive function (Boyne et al., 2019; Müller et al., 2020). Together, these adaptations may contribute to the improved cognitive efficiency observed after training, especially under conditions that require higher executive demand.

Beyond the observed improvements in inhibitory control, these findings may hold broader implications for cognitive health. Reaction time is considered a sensitive marker of biological and cognitive aging, with normative data indicating that simple reaction time slows by approximately 1–2% every five years in middle-aged and older adults (Woods et al., 2015). In this context, the $\approx 10\%$ reduction in reaction time observed in our participants represents a magnitude of change that exceeds what would be expected from normal age-related trajectories, suggesting a possible shift toward more efficient neural processing. Although causality cannot be inferred in this pilot study, such improvements may reflect early

functional gains that align with mechanisms typically linked to cognitive reserve, including enhanced processing efficiency and maintained cognitive performance despite advancing age. This interpretation is consistent with evidence showing that higher levels of physical activity are associated with slower cognitive decline, reduced dementia risk, and improved neural efficiency in older adults. Although interaction effects were not statistically significant in any Stroop condition, the magnitude of the effect sizes suggests changes of potential functional significance, particularly in the context of executive efficiency. All η^2p values for the acute effect exceeded 0.10 (moderate – large effects), indicating that exercise consistently explained more than 10% of the variance in reaction time—considered clinically relevant in exercise-based interventions (Lakens, 2013; Richardson, 2011). For the chronic effect, a trend toward improvement was observed in the incongruent condition, with a mean reduction in reaction time of 139 ms at rest from pre- to post-intervention (95% CI = -282 to 4; $p = .055$). Given the pilot nature of this study, effect sizes and confidence intervals provide a more informative interpretation of the findings than p -values alone, enabling a more accurate assessment of their potential clinical relevance.

This pilot study also demonstrates the feasibility and safety of the proposed protocol, which includes the use of a computerized Stroop task and an individualized exercise prescription based on ventilatory thresholds within an isocaloric framework. The analytic approach allowed for capturing both acute and chronic cognitive responses to exercise, providing

effect sizes that are useful for planning a larger trial.

Several limitations must be considered. The small sample size restricts generalizability and limits the ability to detect between-group effects. In addition, the absence of neurobiological measures (e.g., lactate, BDNF) prevents the identification of the physiological mechanisms behind cognitive changes. Future research should incorporate such biomarkers, expand the cognitive test battery, and evaluate other moderators such as sex differences and genetic polymorphisms (e.g., BDNF Val66Met). Moreover, forthcoming research will evaluate potential sex-related differences and implement longitudinal follow-ups to determine the persistence and trajectory of cognitive adaptations over time.

5. Conclusions

This pilot study suggests that aerobic exercise within a cardiac rehabilitation program may acutely and chronically enhance inhibitory control in patients with coronary artery disease. These findings should not be interpreted as evidence of cognitive rehabilitation in a strict clinical sense, but rather as preliminary indicators of exercise-related modulation of executive efficiency. Acute exercise was associated with consistent improvements in reaction time across all Stroop conditions, while the 12-week training program elicited an additional improvement under conditions of high inhibitory demand. Collectively, these results support the potential role of exercise in modulating executive functioning in cardiac patients and provide a rationale for the ongoing continuation of this study, in which the sample size is being expanded to

allow a more robust evaluation of these effects and a clearer characterization of the underlying physiological mechanisms.

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