

1 **Title: Consistency of hemodynamic and autonomic mechanisms underlying post-exercise**
2 **hypotension**

3

4 **Running Title: PEH mechanisms consistency**

5

6 Rafael Yokoyama Fecchio, MS^a; Leandro Brito, Ph.D^a; Tiago Peçanha, Ph.D^a; Cláudia Lucia de
7 Moraes Forjaz, Ph.D^a;

8

9 **Institutional Affiliation:**

10 ^a Exercise Hemodynamic Laboratory, School of Physical Education and Sport, University of São
11 Paulo, São Paulo, Brazil.

12

13 **Corresponding author:**

14 Cláudia Lucia de Moraes Forjaz, Ph.D

15 Email: cforjaz@usp.br

16

17 **ORCID of the authors:**

18 Rafael Yokoyama Fecchio: 0000-0003-3865-2349; Leandro Brito: 0000-0001-9902-7390; Tiago
19 Peçanha: 0000-0003-4968-5525; Cláudia Lucia de Moraes Forjaz: 0000-0001-7584-4265.

20

21

1 **DECLARATIONS**

2

3 **Funding**

4 This study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível
5 Superior – Brasil (CAPES/PROEX, code 001) and the Brazilian National Council for Scientific
6 and Technological Development (CNPQ, process 304436/2018-6).

7

8 **Conflict of interest**

9 The authors declare that they have no conflict of interest.

10

11 **Ethics Approval**

12 The current data was conducted in accordance with the principles of the Declaration of
13 Helsinki. This study is a part of a bigger study that was approved by the local Ethics Committee
14 (nº 2015/06) and included at Brazilian Clinical Trials register (www.ensaiosclinicos.gov.br-
15 [RBR-3nxxn34](https://ensaiosclinicos.gov.br/registro/registro/RBR-3nxxn34)).

16

17 **Consent to participate**

18 All participants provided informed consent before beginning their participation in the
19 study.

20

21

1 **Abstract**

2 Post-exercise hypotension (PEH) is a clinically relevant phenomenon, but its mechanisms vary
3 between different studies and between the participants within each study. Additionally, it is
4 possible that PEH mechanisms are not consistent in each individual (i.e. within-individual
5 variation), which has not been investigated yet. Thus, the aim of the current study was to assess
6 the within-individual consistency of PEH hemodynamic and autonomic mechanisms. For that, 30
7 subjects performed 4 sessions divided in 2 blocks (test and retest). In each block, an exercise
8 (cycling, 45min, 50%VO₂peak) and a control (seated rest, 45min) session was randomly
9 conducted. Blood pressure (BP) and its mechanisms were evaluated pre and post-interventions. In
10 each block, individual responses were calculated as post-exercise minus post-control, and a
11 response was considered present when its magnitude reached the typical error of the
12 measurement. Consistencies were evaluated by comparing test and retest responses through
13 kappa coefficient (k). PEH consistency was calculated using role sample, while mechanisms
14 consistency was evaluated in those with consistent PEH. Twenty-one (70%) participants showed
15 consistent PEH, 5 (17%) presented PEH in only test or retest and 4 (13%) had absent PEH
16 response, characterizing a good consistency (k= 0.510). Regarding mechanisms' responses, good
17 consistency was found for heart rate (k=0.456), sympathovagal balance (k=0.438) and baroreflex
18 sensitivity (k=0.458); while systemic vascular resistance (k=0.152), cardiac output (k=-0.400),
19 stroke volume (k=-0.055) and sympathetic vasomotor modulation (k=-0.096) presented marginal
20 consistencies. Thus, PEH is a highly consistent physiological phenomenon, although its
21 mechanisms present variable consistencies.

22 **Trial Registration Number:** RBR-3nrxn34 **Date of Registration:** 12 July 2016

23 **Keywords:** “blood pressure”; “aerobic exercise”; “reproducibility”; “within-individual
24 variation”.

What is known about topic

- Post-exercise hypotension (PEH) is a well-documented phenomenon with clinical relevance.
- Previous studies have demonstrated discrepant results regarding the hemodynamic and autonomic mechanisms of PEH, which has been related to differences in the characteristics of populations studied and exercise protocols employed.

What this study adds

- The divergent results found in PEH literature are also related to the within-individual variation of these responses.
- PEH presents good within-individual consistency, while the consistencies of its mechanisms are good for heart rate increase, sympathovagal balance increase and baroreflex sensitivity decrease, but only marginal for systemic vascular resistance decrease, cardiac output decrease, stroke volume decrease and sympathetic vasomotor modulation decrease.

1 **Introduction**

2
3 Post-exercise hypotension (PEH) is characterized by a decrease in blood pressure (BP)
4 observed after a single session of exercise when compared with control values obtained pre-
5 exercise or in a non-exercise day (1). PEH observed after aerobic exercise is accepted as
6 clinically relevant due to its significant magnitude and duration (2). Additionally, it has been
7 suggested as a tool to predict individual responsiveness to BP decrease after an aerobic training
8 period (3,4).

9 Several studies have focused on PEH mechanisms, but their results are very controversial.
10 Part of the studies have attributed PEH to a systemic vascular resistance (SVR) reduction (5–9)
11 mainly resulting from a decrease in peripheral sympathetic nervous activity (10) and/or
12 responsiveness (i.e. functional sympatholysis) (10) associated with a release of vasodilatory
13 substances (e.g. histamine) (10), both leading to a sustained post-exercise skeletal-muscle
14 vasodilation (11,12). In contrast, other studies reported PEH as determined by a cardiac output
15 (CO) decrease produced by a stroke volume (SV) reduction not offset despite the post-exercise
16 heart rate (HR) increase (13–15) mediated by an augmented cardiac sympathovagal balance (15).

17 The conflicting results regarding PEH mechanisms have been attributed to differences in
18 the populations and experimental protocols employed in the studies (16). PEH via CO reduction
19 has been mainly reported in overweight, hypertensive and elderly individuals as well as when
20 exercise was conducted in the morning or BP was assessed in the seated position; while the
21 decrease in SVR appears be the main mechanism of PEH in the absence of these specific
22 conditions (16). However, these factors do not fully explain the variation in PEH mechanisms,
23 since within a study employing a specific population and the same experimental protocol for all

1 subjects, 50% of them presented PEH due to a reduction in CO while the other 50% had a
2 decrease in SVR (17).

3 Another possible factor to explain the divergent results observed in literature and even
4 inside a specific study is an inconsistency of the mechanism of PEH. It is possible that these
5 mechanisms vary from day to day within the same subject even under similar conditions,
6 showing a large within-individual variation. However, to the best of our knowledge, the
7 consistency of PEH mechanisms has not been investigated yet. Along this line, a previous study
8 (18) showed that PEH is reproducible, but the consistency of its mechanisms was not determined.
9 Thus, the current study was designed to assess the within-individual consistency of PEH
10 hemodynamic and autonomic mechanisms, and the hypothesis is that this consistency is low,
11 explaining the large variability observed in literature.

12

13 **Methods**

14 **Participants**

15 Participants were included if they fulfilled the following criteria: 1) age between 20-60
16 years old; 2) absence of cardiovascular (except for hypertension), neurological, respiratory,
17 immunological, renal, endocrine or metabolic (except for diabetes, obesity and dyslipidemia)
18 diseases; 3) absence of resting and exercise electrocardiographic abnormalities suggesting
19 cardiovascular disease; 4) resting systolic (SBP) and diastolic (DBP) BPs below 160 and 105
20 mmHg, respectively; 5) not taking beta-blockers nor non-dihydropyridine calcium channel
21 blocker; and 6) not having limitations (e.g. orthopedic problems) that restrain exercise execution.

22 All participants provided written consent to participate. This study is part of a bigger
23 study that was approved by the local Ethics Committee (n^o 2015/06), included at Brazilian

1 Clinical Trials register (www.ensaiosclinicos.gov.br/RBR-3nxx34). Other findings from the
2 greater study have been previously published (18,19).

3

4 **Preliminary evaluation**

5 To check adherence to the study criteria, participants had three visits to the laboratory. In
6 the first visit, they were interviewed, and anthropometric and clinic BP measurements were
7 obtained. In the second visit, clinic BP was measured again, and in the third visit, the participants
8 underwent a maximal cardiopulmonary exercise test.

9 Clinical interview obtained information regarding personal data and known health status
10 (i.e presence of the diseases mentioned in the study criteria and current medication treatment).
11 Anthropometric data (body weight and height) were measured (Filizola S.A, Personal, Campo
12 Grande, Brazil), and body mass index was calculated. In each visit for BP assessment, BP was
13 measured in triplicate after 5 min of seated resting using the auscultatory method and a mercury
14 column sphygmomanometer (Unitec, São Paulo, Brazil). Measurements were taken in both arms
15 and SBP and DBP were determined, respectively, by the I and V phases of Korotkoff sounds.
16 The mean of the six measurements (2 visits x 3 measures) of each arm was calculated and the
17 higher mean was registered as the BP level of each participant. The cardiopulmonary maximal
18 test was performed on a cycle ergometer (Lode Medical Technology, Corival, Groningen,
19 Netherlands) employing a protocol with an initial load of 50W followed by increments of 30W
20 every 3 min until exhaustion that was determined as the impossibility to maintain pedalling at 60
21 rpm. A physician evaluated rest and exercise electrocardiogram (ECG) that was conducted to
22 identify abnormalities suggestive of cardiovascular disease. BP was measured at rest and at the
23 last min of each exercise stage. Oxygen consumption (VO_2) was continuously measured (CPX

1 Ultima, Medical Graphics Corporation) and analysed in means of 30s. Its highest value during
2 exercise was considered as VO_2 peak.

3

4 **Experimental Protocol**

5 The participants underwent four experimental sessions, being two exercise and two
6 control sessions performed in a randomized order. Firstly, experimental sessions were divided in
7 two blocks: test and retest. Each block was composed of one exercise and one control session.
8 These blocks were executed successively with sessions being randomized within each block.

9 For each experimental session, the participants were instructed to: 1) avoid intense
10 physical efforts for the previous 48h; 2) maintain habitual routine for the previous 24h; 3) avoid
11 alcohol consumption for the previous 24h; and 4) avoid smoking and consumption of caffeinated
12 foods or drinks on the session days. The participants who took regular medications were
13 instructed to take them according to the medical prescription, assuring the use at similar times on
14 the session days.

15 All experimental sessions were conducted by the same experienced evaluator in a
16 temperature-controlled laboratory (20–22°C). Each participant performed all the sessions at the
17 same time of day. The sessions were composed of three different periods: 1) pre-intervention; 2)
18 intervention (exercise or control); and 3) post-intervention.

19 In the pre-intervention period, the participants remained seated for 60 min. ECG,
20 respiratory movements and photoplethysmographic BP were continuously recorded from 10 to 20
21 min for cardiovascular autonomic evaluation. Then, from 20 to 35 min, auscultatory BP, HR and
22 CO were assessed in this sequence and in triplicates, and the mean value was calculated for
23 hemodynamic evaluation. During the intervention period, the participants followed the specific
24 protocol for each session. In exercise sessions, they exercised for 45 min on a cycle ergometer at

1 50% of VO_2 peak and VO_2 was measured from 15 to 35 min of exercise to check the intensity. In
2 the control sessions, they stayed seated on the cycle ergometer for 45 min without pedalling. In
3 the post-intervention period, the participants returned to the seated rest, and autonomic and
4 hemodynamic evaluations were performed, respectively, from 30 to 40 min and 40 to 55 min.

5

6 **Measurements**

7 Auscultatory BP was measured on the dominant arm using the auscultatory method and a
8 mercury column sphygmomanometer (Unitec, São Paulo, Brazil). Mean BP (MBP) was obtained
9 by: $\text{MBP} = (\text{SBP} + 2 \text{DBP}) / 3$. CO was estimated by the indirect Fick method (20), using the
10 CO_2 rebreathing technique and a metabolic cart (CPX Ultima, Medical Graphics Corporation).
11 Briefly, the participants spontaneously breathed ambient air until a steady CO_2 production was
12 achieved. At this moment, VCO_2 was determined and the arterial content of CO_2 (CaCO_2) was
13 estimated. Then, the participants performed a CO_2 rebreathing manoeuvre with a mixed gas
14 containing a high CO_2 concentration (8-10%) and 35% of O_2 until an equilibrium was achieved.
15 At this moment, venous content of CO_2 (CvCO_2) was determined. Thus, CO was estimated by
16 Fick formula: $\text{CO} = \text{VCO}_2 / (\text{CaCO}_2 - \text{CvCO}_2)$. SV and SVR were calculated as: $\text{SV} = \text{CO} / \text{HR}$
17 and $\text{SVR} = \text{MBP} / \text{CO}$.

18 For autonomic evaluation, HR was assessed by ECG (Cardioperfect, ST 2001 model,
19 Netherlands), respiratory movements by a thoracic piezoelectric belt (Pneumotrace 2, UFI, Morr
20 Bay, USA) and beat-to-beat BP by photoplethysmography (FMS – Finapres Measurement
21 System, Arnhem, Netherland). These signals were recorded for 10 min using a data acquisition
22 system (Windaq – DI-720, Akron, USA; 500 Hz/channel). Cardiovascular autonomic modulation
23 was evaluated by spectral analysis according to the recommendations of the “Task Force” (21)
24 and using Heart Scope II software (A.M.P.S. LLC, Version 1.3.0.3, New York, USA). The

1 temporal series of R-R intervals, respiration, SBP and DBP were obtained in stationary segments
2 of 250 ± 50 heart beats and were decomposed by the autoregressive method. For interpretation of
3 the results, cardiac sympathovagal balance was considered the ratio between the low- (LF = 0.04-
4 0.15 Hz) and high-frequency (HF = 0.15-0.4 Hz) components of R-R interval variability
5 (LF/HF_{R-R}). Sympathetic vasomotor modulation was considered the low-frequency component of
6 SBP variability (LF_{SBP}). Baroreflex sensitivity (BRS) was analysed by the maximum magnitude
7 of the transfer function between the R-R interval and the SBP variabilities at the low-frequency
8 band.

9

10 Data and statistical analysis

11 Box-plot graphs were employed to identify extreme values, and Shapiro-Wilk test (SPSS,
12 Illinois, USA) to check the normal data distribution. Non-normal variables were log-transformed
13 (i.e. natural logarithm - ln) to attend analysis of variance (ANOVA)'s statistical assumptions.

14 Similarity of pre-intervention values among the four experimental sessions were checked
15 by one-way ANOVA for repeated measures. To check whether responses to exercise were in
16 accordance with literature and were similar between the testing blocks, two-way ANOVAs for
17 repeated measures were performed comparing post-intervention values between the sessions (i.e.
18 post-exercise vs. post-control) and the blocks (test and retest). The Newman-Keuls post-hoc test
19 was planned to be applied if necessary.

20 For consistency analyses, initially, the typical error of measurement (TE) was calculated
21 for each variable (22) using pre-intervention values of the test and retest control sessions (i.e. pre-
22 control test and pre-control retest). These sessions were chosen to avoid any possible influence of
23 an anticipatory response to exercise (i.e. central command activation) on the cardiovascular
24 parameters (23). Afterwards, in each block (test and retest), the individual response to exercise

1 was calculated by the difference in the post-intervention values obtained in the exercise and
2 control sessions (i.e post-exercise – post-control). A change was considered present when the
3 difference was equal to or higher than previously calculated TE (24). Finally, consistency of the
4 response between test and retest was evaluated by Kappa coefficient (k - an agreement index for
5 categorical data: present vs. not-present) and considered as excellent for $k \geq 0.75$, good for k
6 between 0.40 and 0.75, and marginal for $k < 0.40$ (25). In addition, consistency results were also
7 shown by the relative frequencies of consistent response (i.e. response present at both test and
8 retest), inconsistent response (i.e. response present only in test or retest), and consistent absent
9 response (i.e. response not present in either test nor retest). For all analyses, $p \leq 0.05$ was
10 considered as significant.

11 Based on the main objective of the present study (consistency), the minimum number of
12 subjects required for PEH kappa analysis was calculated using the PASS software (version
13 19.0.3, NCSS, LCC, Kaysville, USA). Thus, considering a k of 0.60, an alpha error of 5%, a
14 statistical power of 80% and a PEH occurrence rate of 64% (26), the minimum sample size
15 required was 16 subjects. As the consistency of PEH mechanisms could only be evaluated with
16 subjects who show consistent PEH, the sample recruitment aimed to include more subjects.
17 Therefore, after data collection, ANOVA and consistency analyses of BP considered the entire
18 cohort (n=30), while analyses of PEH mechanisms were performed with the 21 participants who
19 presented consistent PEH in MBP. Analyses of LF_{SBP} and BRS included, respectively, 19 and 18
20 participants due to technical difficulties.

21

22 **Results**

1 Sample characteristics are detailed in Table 1. Participants comprised 24 males (80%) and
2 6 females (20%). Most of them with overweight (33%) or obesity (50%); with pre (27%) or
3 established hypertension (43%); and not taking medication (73%).

4 Pre-intervention values of MBP, SVR, CO, HR, SV, LF/HF_{R-R}, LF_{SBP} and BRS were
5 similar among the 4 experimental sessions (Table 2). Mean responses to exercise in test and retest
6 are demonstrated in Figure 1. For all variables, responses were similar in the test and retest (no
7 significant interaction in ANOVAs, all $p > 0.05$). Additionally, independently of the block (test or
8 retest), MBP, SVR, VS and BRS were significantly lower, while HR and LF/HF_{R-R} were
9 significantly higher after the exercise than the control session (significant session mean effect, all
10 $p < 0.05$). Independently of the session (control or exercise), BRS was significantly lower in the
11 test than in the retest. No significance was observed for LF_{SBP}.

12 TEs of all variables are presented in Table 3, and consistency of the responses are shown
13 in Figure 2. For MBP, 21 participants (70.0%) presented PEH in both test and retest, 5 (16.7%)
14 showed PEH only in test or retest, and 4 (13.3%) did not present PEH in neither test nor retest,
15 resulting in a good consistency ($k = 0.510$, $p = 0.005$). Regarding the mechanisms, consistency
16 was marginal for SVR ($k = 0.152$), CO ($k = -0.400$), SV ($k = -0.055$) and LF_{SBP} ($k = -0.096$), and
17 good for HR ($k = 0.456$), LF/HF_{R-R} ($k = 0.438$) and BRS ($k = 0.458$).

18 19 **Discussion**

20 The main findings of the current study are that PEH presented a good within-individual
21 consistency, while the consistencies of its mechanisms were good for HR, LF/HF_{R-R} and BRS,
22 but only marginal for SVR, CO, SV and LF_{SBP}.

23 Based on the mean responses (Figure 1), the proposed exercise was effective in promoting
24 PEH via SVR decrease, as commonly reported in literature (5–9). This response occurred in

1 absence of sympathetic vasomotor modulation changes (no alteration in LF_{SBP}), suggesting a
2 sustained vasodilation due to functional sympatholysis (6) and/or local release of vasodilatory
3 substances (27). Additionally, as also reported in literature, the exercise did not change CO since
4 the decrease in SV was compensated by the increase in HR mediated by the higher cardiac
5 sympathovagal balance (higher LF/HF_{R-R}) observed in the exercise session. Moreover, the post-
6 exercise tachycardia was not sufficient to abolish PEH, probably due to the reduced cardiac BRS
7 after the exercise. Therefore, the occurrence and mechanisms of PEH observed in the present
8 study are in accordance with previous literature (4,11,12).

9 As a novelty, for the best of our knowledge, this is the first study to show that mean post-
10 exercise responses are reproducible. All post-exercise hemodynamic and autonomic responses
11 were successfully replicated between the test and retest as all ANOVAs revealed no interaction
12 between session and block factors, indicating similar responses between the repeated tests (25).
13 Nevertheless, although group responses were reproducible, a recent paper about methodological
14 recommendations for PEH studies (28) highlighted that mean group responses do not necessary
15 reflect the individual responses, raising the necessity to examine these responses.

16 Along this line, the current data (Figure 2) showed a good within-individual consistency
17 of MBP decrease after exercise ($k=0.510$, i.e. between 0.40 and 0.75) as most of the participants
18 (70%) presented PEH in both blocks (test and retest). This result is in accordance with previous
19 studies that reported consistent BP responses to different physiological stimulus, such as mental
20 stress (29,30) and cold pressor test (30), and expands this consistency to physical stress.
21 Interestingly, differently from MBP response, the consistency of its components, SBP and DBP
22 responses ($k=0.379$ and $k=0.162$, data not shown) were only marginal, probably reflecting the
23 marginal consistency of their systemic hemodynamic determinants (i.e. CO and SVR) that are
24 discussed in the next paragraphs.

1 SVR response after exercise showed a marginal consistency that can be attributed, at least
2 in part, to the inconsistent effect of exercise on peripheral sympathetic modulation assessed by
3 BP variability, as $LF_{S_{BP}}$ response also showed a marginal consistency. In accordance, previous
4 studies also reported inconsistent responses of SVR (29) and muscle sympathetic activity (30) to
5 other physiological stresses (i.e. mental stress and cold pressor test). Additionally, the variable
6 response of SVR after exercise may also reflect an inconsistent effect of previous exercise on
7 other factors, such as local and hormonal vasomotor influences.

8 Regarding the cardiac responses to exercise, CO also had a high within-individual
9 variation that can be explained by the marginal consistency of SV responses, since SV is one of
10 the CO determinants (31). Although SV determinants are beyond the scope of this study, it is
11 possible to speculate that the inconsistent SV response after exercise might be related to the
12 inconsistent effect of exercise on cardiac afterload as shown by the marginal consistency of SVR
13 response. Alternatively, the inconsistent SV response might also reflect a variable effect of
14 previous exercise on cardiac pre-load, considering its importance in mediating post-exercise SV
15 decrease (32). On the other hand, post-exercise HR response showed good consistent between
16 test and retest, which is in accordance with its responses to other physiological manoeuvres, such
17 as mental stress and head-up tilt (29,30,33), and is coherent with the good consistency observed
18 for cardiac sympathovagal balance (i.e. LF/HF_{R-R}). Finally, BRS reduction after exercise also
19 showed a good consistency that might play an important role on the stability of MBP and HR
20 responses to exercise. The change in BRS after exercise is considered essential to allow for the
21 occurrence of PEH, since an unchanged baroreflex function would compensate for BP fall,
22 abolishing PEH (1). Thus, an inconsistent response of BRS would also result in inconsistent
23 responses of BP and HR after the exercise.

1 Given the exposed, it is possible to speculate that the marginal consistencies of both PEH
2 hemodynamic determinants (i.e. CO and SVR) are related to their interdependence. BP regulation
3 depends on the integrative responses of both cardiac and vascular factors (31). When CO
4 decreases, a compensatory increase on SRV is expected to maintain mean BP at an adequate level
5 for each occasion (31). Based on that, PEH occurrence requires a simultaneous effect of previous
6 exercise on both CO and SRV, decreasing one of them but also blunting the compensatory
7 increase of the other. The current study provided new insight on this topic by demonstrating that
8 PEH is a robust physiological response that occurs consistently after an exercise bout. However,
9 its hemodynamic determinant is inconsistent, and may vary each time the same exercise bout is
10 executed.

11 Although the current study focused on improving the comprehension about PEH
12 mechanisms, some clinical implications can be proposed. The between-individual cardiovascular
13 responses to different stresses have received emergent interest of the physiologists. Regarding
14 PEH, a previous study (17) reported it was due to a decrease in CO in 50% of the participants and
15 to a reduction in SVR in the other 50% (i.e. between-individual variation), suggesting the
16 possibility to identify the individuals who would present PEH via SVR which may be clinically
17 relevant for hypertensives who usually present an increase in SVR as the cause for BP increase
18 (34). However, the current result put this conjecture in check since it shows that each individual
19 may present PEH by a different hemodynamic mechanism after each bout of the same exercise
20 (high within-individual variation). Thus, future studies should evaluate how experimental design
21 characteristics can be manipulated to attenuate the within-individual variability of PEH
22 hemodynamic and autonomic mechanisms.

23 Lastly, it is important to mention that the current results are limited to aerobic exercise
24 protocols since the mechanisms (12) of PEH are different after other types of exercise, such as

1 dynamic resistance exercise. Moreover, the marginal consistencies of PEH hemodynamic
2 determinant were mainly observed for SV, CO and SVR that can be influenced by pre-exercise
3 plasma volume and hydration status that were not checked in the current study. Although this
4 lack of control could initially be interpreted as a relevant limitation, it is important to highlight
5 that the current study emulates most of the PEH studies' designs that do not control hydration
6 status, and that a recent study using a similar protocol reported no difference in plasma volume
7 and hydration status before different exercise and control sessions (35). Finally, as a first study
8 on PEH consistency, this study involved a comprehensive sample composed by individuals of
9 both sexes, at different age groups, and with a large variation in BMI and BP status. Within-
10 individual PEH consistency may be different in each of these specific populations, and future
11 studies should address this issue. However, specifically for sex, we performed complementary
12 analyses excluding the women (n=6) and they did not reveal any difference in consistency results
13 for PEH or its mechanisms (data not shown). Additionally, anti-hypertensive medication use
14 (class and dose) may affect PEH magnitude and mechanisms (36,37). However, despite these
15 possible influences on the response to exercise, it is improbable that medication use changes PEH
16 variation between different days (within-individual consistency) if the subjects receive the same
17 dose of medication at the same time of day before the exercise sessions as done in the present
18 study. In additional analyses, consistency results remained the same (data not shown) for all
19 variables when individuals taking anti-hypertensive medication (n=8) were excluded. Future
20 studies, however, may investigated PEH consistency with medication took at different times to
21 evaluate any possible impact.

22

23 **Conclusion**

1 PEH is a highly consistent phenomenon that presents low within-individual variation.
2 However, the within-individual consistency of PEH hemodynamic and autonomic mechanisms
3 varies depending on the considered mechanism, with HR, LF/HF_{R-R} and BRS post-exercise
4 responses having good consistencies, while CO, SV, SVR and LF_{SBP} responses present marginal
5 consistency.

6

7 **Acknowledgements**

8 The authors want to acknowledge the volunteers of the current study.

9

10 **Funding**

11 This study received financial support from CNPq (304436/2018-6) and CAPES (0001).

12

13 **Conflict of interest**

14 The authors declare that they have no conflict of interest.

15

16 **REFERENCES**

- 17 1. Kenney MJ, Seals DR. Postexercise hypotension. Key features, mechanisms, and clinical
18 significance. *Hypertens (Dallas, Tex 1979)*. 1993;22(5):653–64.
- 19 2. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. Exercise and
20 hypertension. *Med Sci Sport Exerc*. 2004;36(3):533–53.
- 21 3. Luttrell MJ, Halliwill JR. Recovery from exercise: vulnerable state, window of
22 opportunity, or crystal ball? *Front Physiol [Internet]*. 2015;6:204.
- 23 4. Brito LC, Fecchio RY, Peçanha T, Andrade-Lima A, Halliwill JR, Forjaz CLM.
24 Postexercise hypotension as a clinical tool: a “single brick” in the wall. *J Am Soc*

- 1 Hypertens [Internet]. 2018;12(12):e59–64.
- 2 5. Cucato GG rizzo, Chehuen M da R, Ritti-Dias RM, Carvalho CRF, Wolosker N, Saxton
3 JM, et al. Post-walking exercise hypotension in patients with intermittent claudication.
4 Med Sci Sports Exerc. 2015;47(3):460–7.
- 5 6. Halliwill JR, Taylor JA, Eckberg DL. Impaired sympathetic vascular regulation in humans
6 after acute dynamic exercise. J Physiol. 1996;495 (Pt 1):279–88.
- 7 7. Cléroux J, Kouamé N, Nadeau A, Coulombe D, Lacourcière Y. Aftereffects of exercise on
8 regional and systemic hemodynamics in hypertension. Hypertension [Internet].
9 1992;19(2):183–91.
- 10 8. Jones H, George K, Edwards B, Atkinson G. Is the magnitude of acute post-exercise
11 hypotension mediated by exercise intensity or total work done? Eur J Appl Physiol.
12 2007;102(1):33–40.
- 13 9. Harvey PJ, Morris BL, Kubo T, Picton PE, Su WS, Notarius CF, et al. Hemodynamic
14 after-effects of acute dynamic exercise in sedentary normotensive postmenopausal women.
15 J Hypertens [Internet]. 2005;23(2):285–92.
- 16 10. Bisquolo VAF, Cardoso CG, Ortega KC, Gusmão JL, Tinucci T, Negrão CE, et al.
17 Previous exercise attenuates muscle sympathetic activity and increases blood flow during
18 acute euglycemic hyperinsulinemia. J Appl Physiol. 2005;98(3):866–71.
- 19 11. Halliwill JR, Buck TM, Lacewell AN, Romero SA. Postexercise hypotension and
20 sustained postexercise vasodilatation: what happens after we exercise? Exp Physiol.
21 2013;981(1):7–18.
- 22 12. Romero SA, Minson CT, Halliwill JR. The cardiovascular system after exercise. J Appl
23 Physiol [Internet]. 2017;122(4):925–32.
- 24 13. Dujčić Ž, Ivančev V, Valic Z, Baković D, Marinović-Terzić I, Eterović D, et al.

- 1 Postexercise hypotension in moderately trained athletes after maximal exercise. *Med Sci*
2 *Sports Exerc.* 2006;38(2):318–22.
- 3 14. Hamer M, Boutcher SH. Impact of moderate overweight and body composition on
4 postexercise hemodynamic responses in healthy men. *J Hum Hypertens.* 2006;20(8):612–
5 7.
- 6 15. de Brito L, Rezende RA, Da Silva ND, Tinucci T, Casarini DE, Cipolla-Neto J, et al. Post-
7 exercise hypotension and its mechanisms differ after morning and evening exercise: A
8 randomized crossover study. *PLoS One [Internet].* 2015;10(7):e0132458.
- 9 16. Brito LC, Queiroz ACC, Forjaz CLM. Influence of population and exercise protocol
10 characteristics on hemodynamic determinants of post-aerobic exercise hypotension.
11 *Brazilian J Med Biol Res.* 2014;47(8):626–36.
- 12 17. Forjaz C, Cardoso C, Rezk C, Santaella D, Tinucci T. Postexercise hypotension and
13 hemodynamics: The role of exercise intensity. *J Sports Med Phys Fitness.* 2004;44(1):54–
14 62.
- 15 18. Fecchio RY, Chehuen M, Brito LC, Peçanha T, Queiroz ACC, de Moraes Forjaz CL.
16 Reproducibility (Reliability and Agreement) of Post-exercise Hypotension. *Int J Sports*
17 *Med.* 2017;
- 18 19. Fecchio RY, Brito LC de, Peçanha T, Forjaz CL de M. Post-exercise hypotension and its
19 hemodynamic determinants depend on the calculation approach. *J Hum Hypertens*
20 *[Internet].* 2020;17–21.
- 21 20. Jones N, Campbell E, McHardy G, Higgs B, Clode M. The estimation of carbon dioxide
22 pressure of mixed venous blood during exercise. *Clin Sci.* 1967;32(2):311–27.
- 23 21. European Society of Cardiology; North American Society of Pacing and
24 Electrophysiology. Heart rate variability. Standards of measurement, physiological

- 1 interpretation, and clinical use. Task Force of the European Society of Cardiology and the
2 North American Society of Pacing and Electrophysiology. *Eur Heart J* [Internet].
3 1996;17:354–81.
- 4 22. Hopkins WG. Measures of reliability in sports medicine and science. *Sport Med*.
5 2000;30(1):1–15.
- 6 23. Williamson JW. The relevance of central command for the neural cardiovascular control of
7 exercise. *Exp Physiol*. 2010;
- 8 24. Swinton PA, Hemingway BS, Saunders B, Gualano B, Dolan E. A Statistical Framework
9 to Interpret Individual Response to Intervention: Paving the way for personalised nutrition
10 and exercise prescription. *Front Nutr* [Internet]. 2018;5(May):41.
- 11 25. Rosner B. *Fundamentals of Biostatistics*. 7th ed. Brooks/Cole CL, editor. Boston:
12 Brooks/Cole, Cengage Learning; 2011. 568–571 p.
- 13 26. Costa EC, Dantas TCB, Junior LF de F, Frazão DT, Prestes J, Moreira SR, et al. Inter- and
14 Intra-Individual Analysis of Post-Exercise Hypotension Following a Single Bout of High-
15 Intensity Interval Exercise and Continuous Exercise: A Pilot Study. *Int J Sports Med*.
16 2016;37(13):1038–43.
- 17 27. Lockwood JM, Wilkins BW, Halliwill JR. H1 receptor-mediated vasodilatation contributes
18 to postexercise hypotension. *J Physiol*. 2005;
- 19 28. De Brito LC, Fecchio RY, Peçanha T, Lima A, Halliwill J, Forjaz CLDM.
20 Recommendations in Post-exercise Hypotension: Concerns, Best Practices and
21 Interpretation. *Int J Sports Med*. 2019;40(8).
- 22 29. Liu X, Iwanaga K, Shimomura Y, Katsuura T. The Reproducibility of Cardiovascular
23 Response to a Mental Task. *J Physiol Anthropol*. 2010;29(1):35–41.
- 24 30. Fonkoue IT, Carter JR. Sympathetic neural reactivity to mental stress in humans: test-

- 1 retest reproducibility. *Am J Physiol Regul Integr Comp Physiol* [Internet].
2 2015;309(11):R1380-6.
- 3 31. Pappano AJ, Wier WG. *Cardiovascular Physiology, Tenth Edition*. Elsevier, editor.
4 *Cardiovascular Physiology, Tenth Edition*. 2012.
- 5 32. Rondon M, Alves M, Braga A, Teixeira O, Barretto A, Krieger E, et al. Postexercise Blood
6 Pressure Reduction in Elderly Hypertensive Patients. *J Am Coll Cardiol*. 2002;39(4):676–
7 82.
- 8 33. Youde J, Panerai R, Gillies C, Potter J. Reproducibility of circulatory changes to head-up
9 tilt in healthy elderly subjects. *Age Ageing*. 2003;32(4):375–81.
- 10 34. Beevers G, Lip GY, O'Brien E. The pathophysiology of hypertension. *BMJ Br Med J / Br*
11 *Med Assoc*. 2001;322(7291):912–6.
- 12 35. Lobo FS, Queiroz AC, Silva Junior ND, Medina FL, Costa LA, Tinucci T, et al. Hydration
13 Does Not Change Postexercise Hypotension and Its Mechanisms. *J Phys Act Heal*.
14 2020;17(5):533–9.
- 15 36. Brito LC, Azevêdo L, Peçanha T, Fecchio RY, Rezende RA, da Silva GV, et al. Effects of
16 ACEi and ARB on post-exercise hypotension induced by exercises conducted at different
17 times of day in hypertensive men. *Clin Exp Hypertens*. 2020;
- 18 37. Ramirez-Jimenez M, Morales-Palomo F, Ortega JF, Mora-Rodriguez R. Post-exercise
19 Hypotension Produced by Supramaximal Interval Exercise is Potentiated by Angiotensin
20 Receptor Blockers. *Int J Sports Med*. 2019;

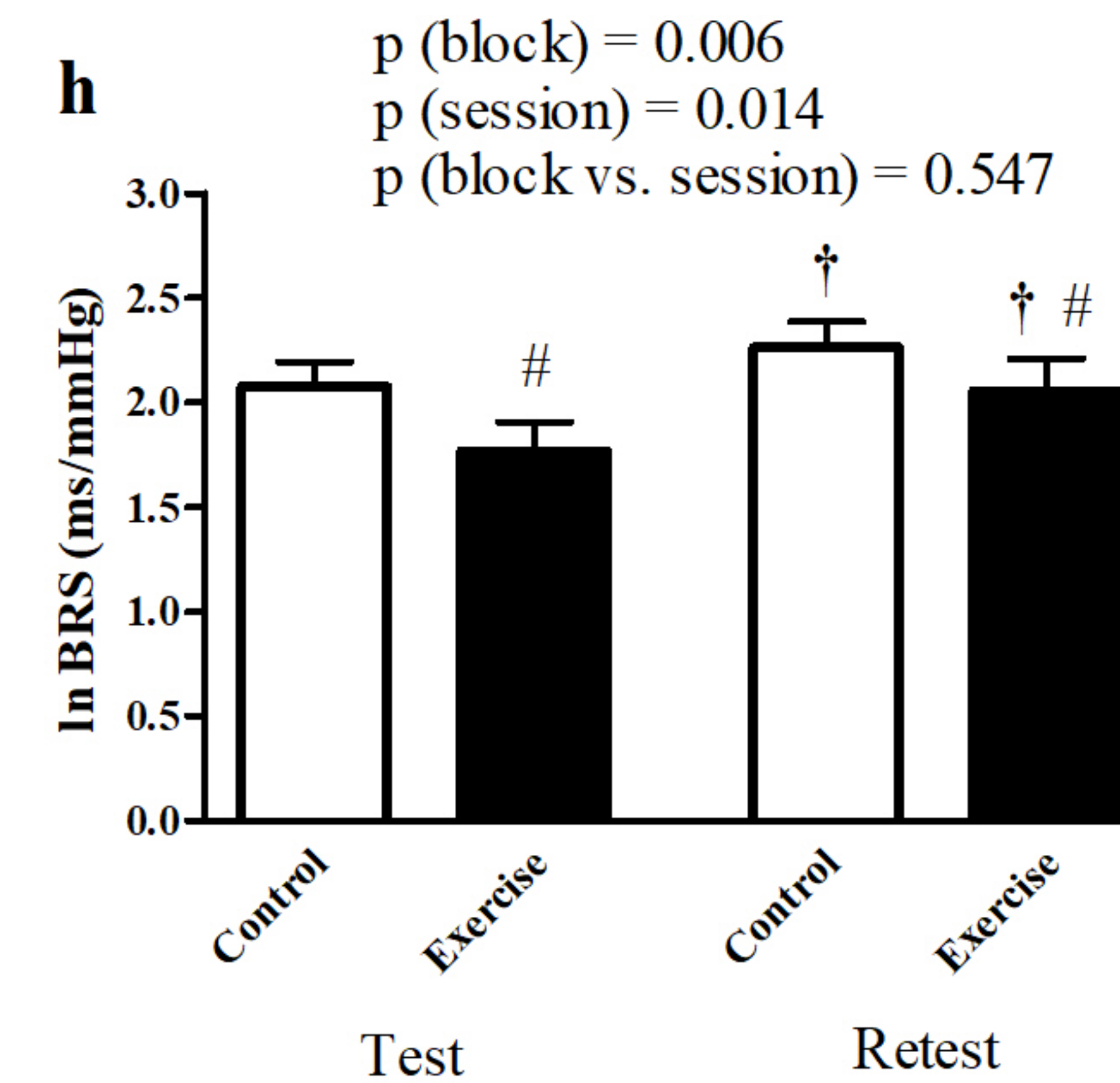
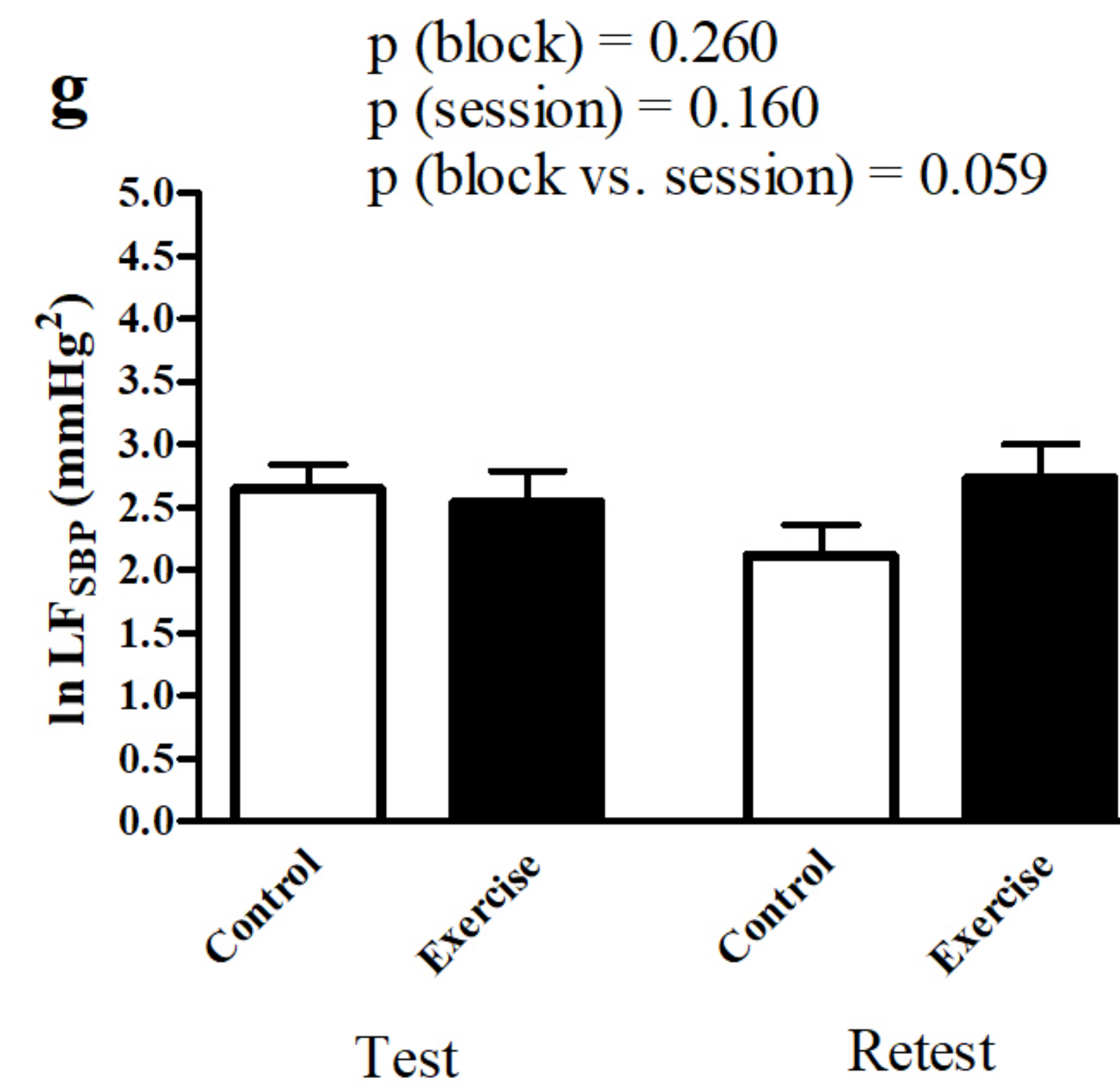
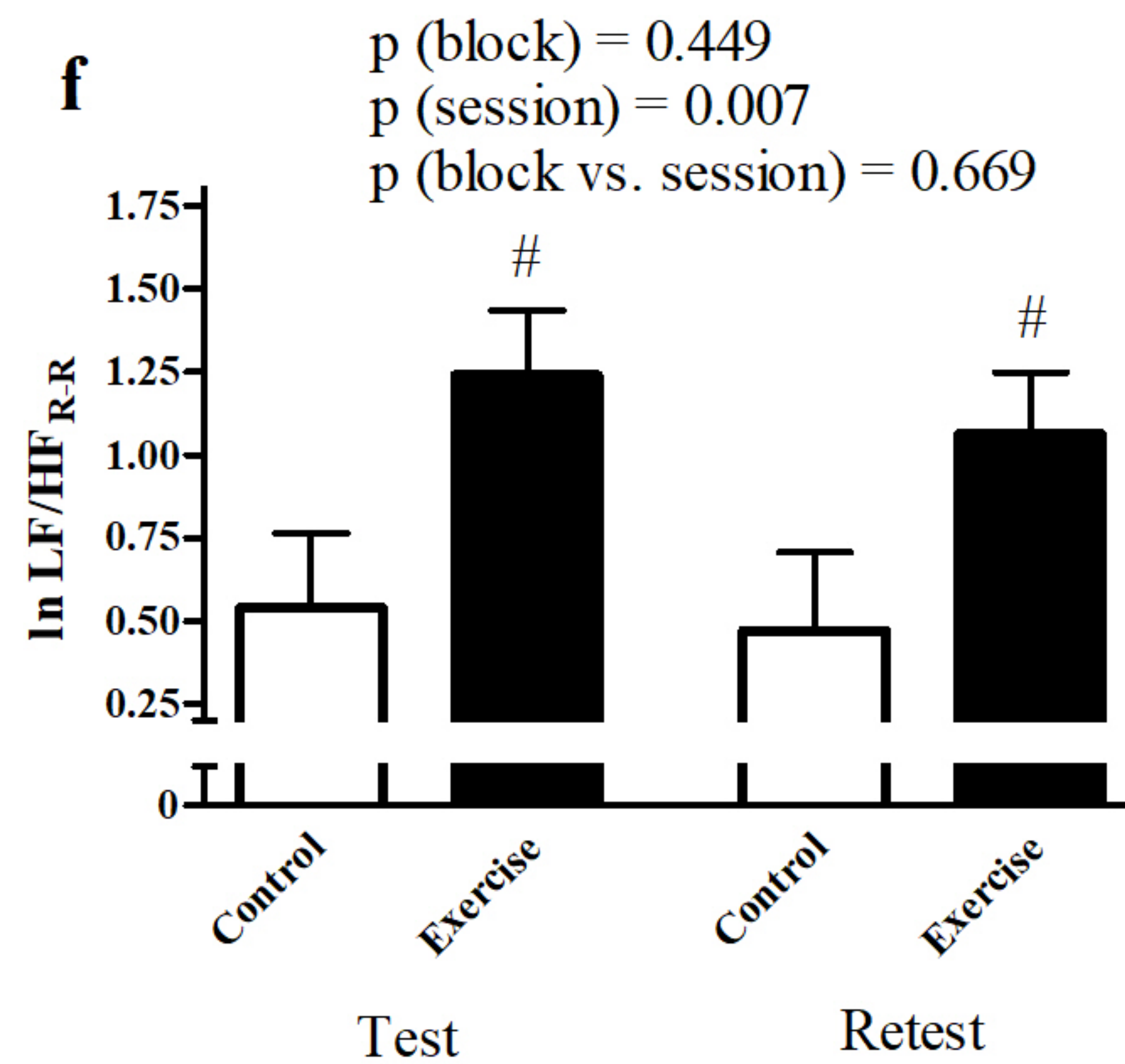
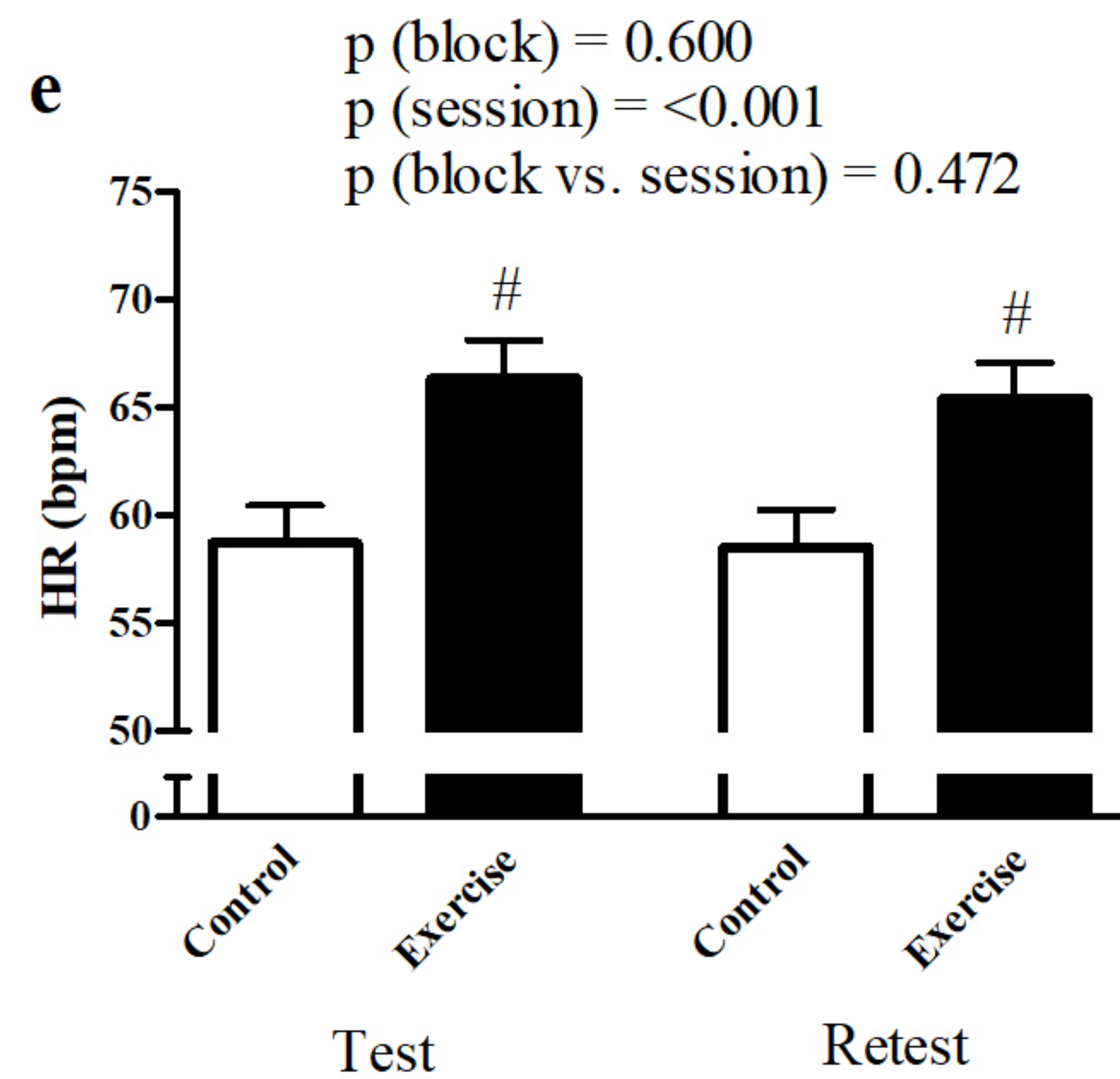
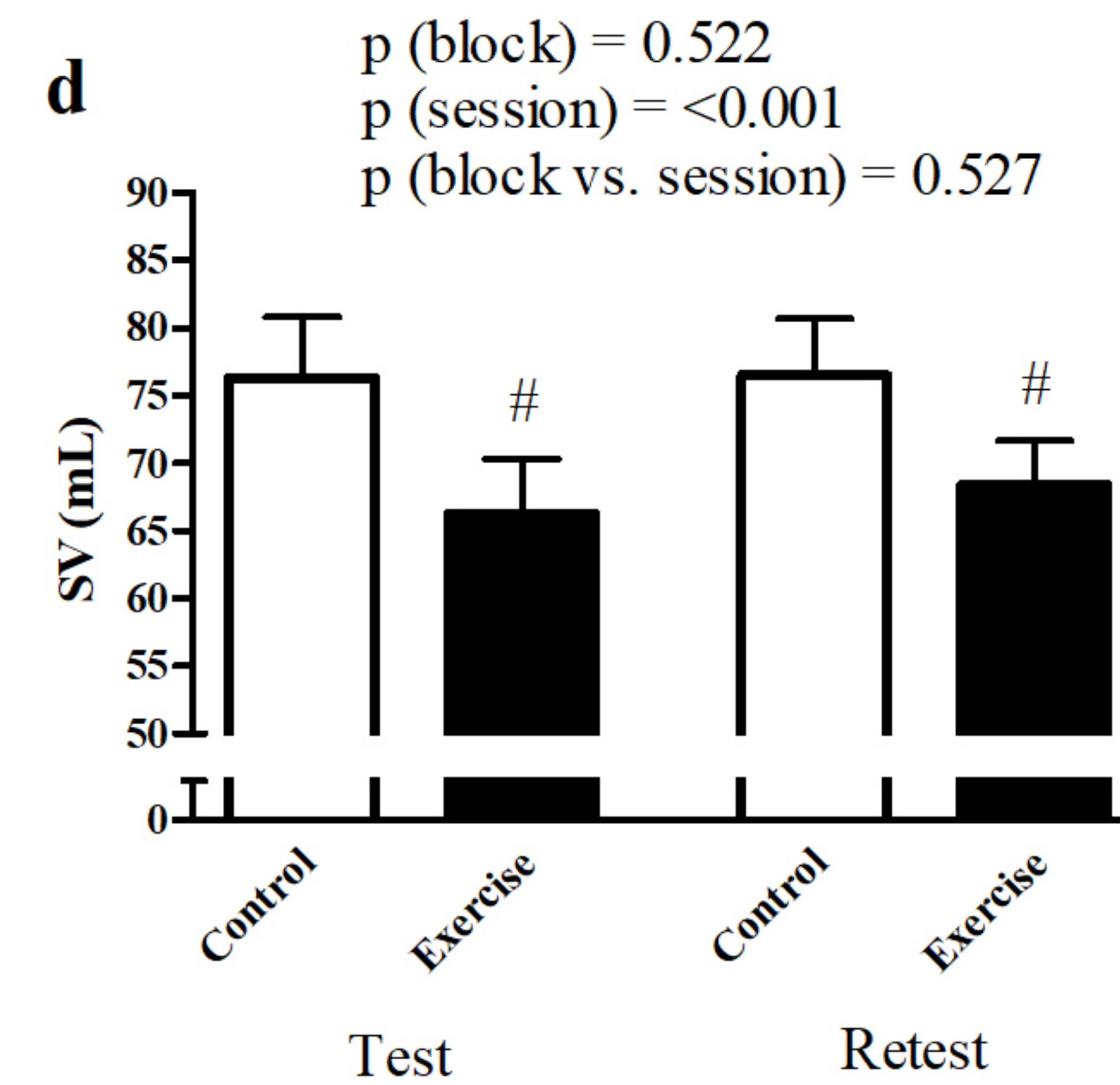
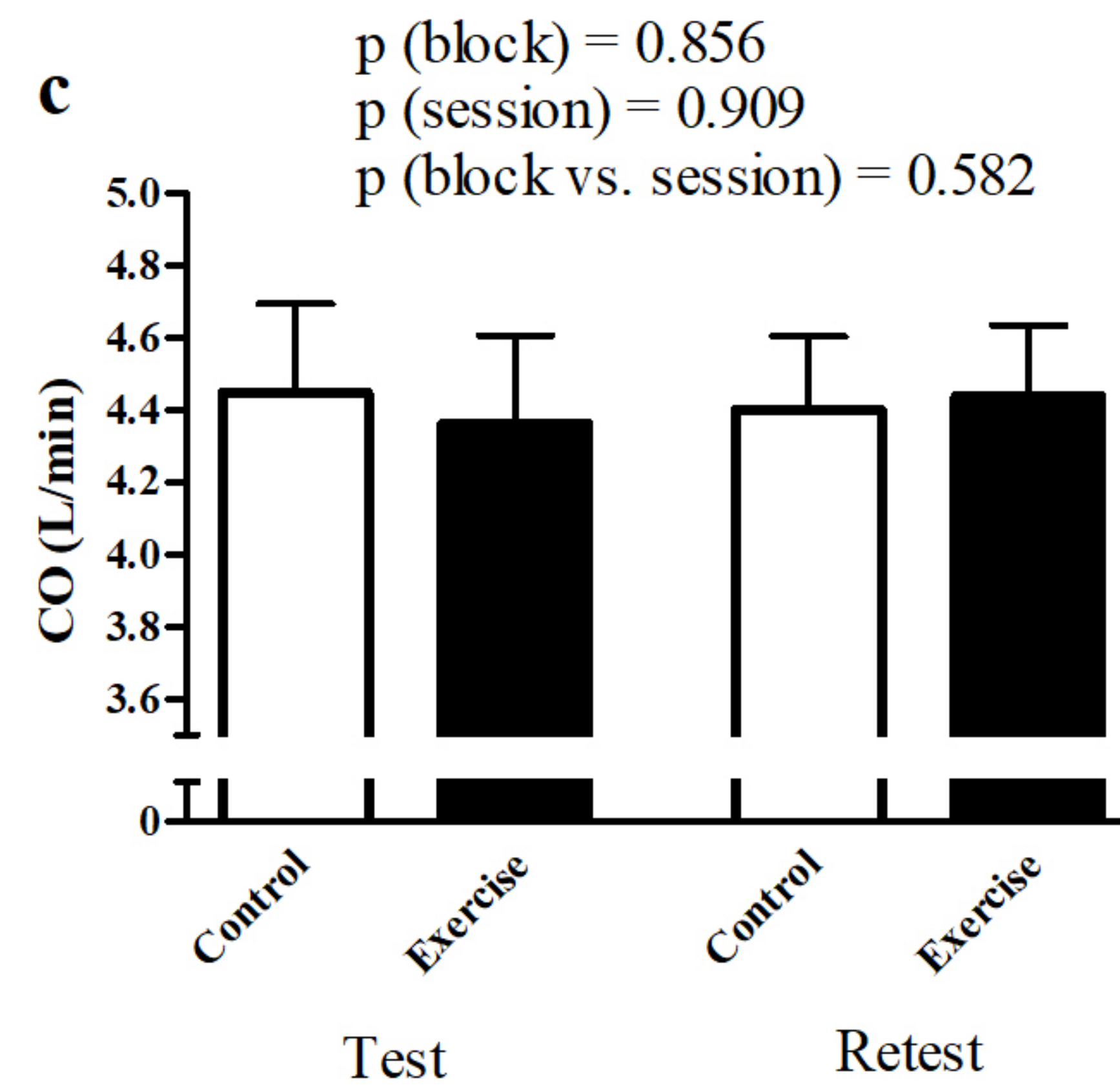
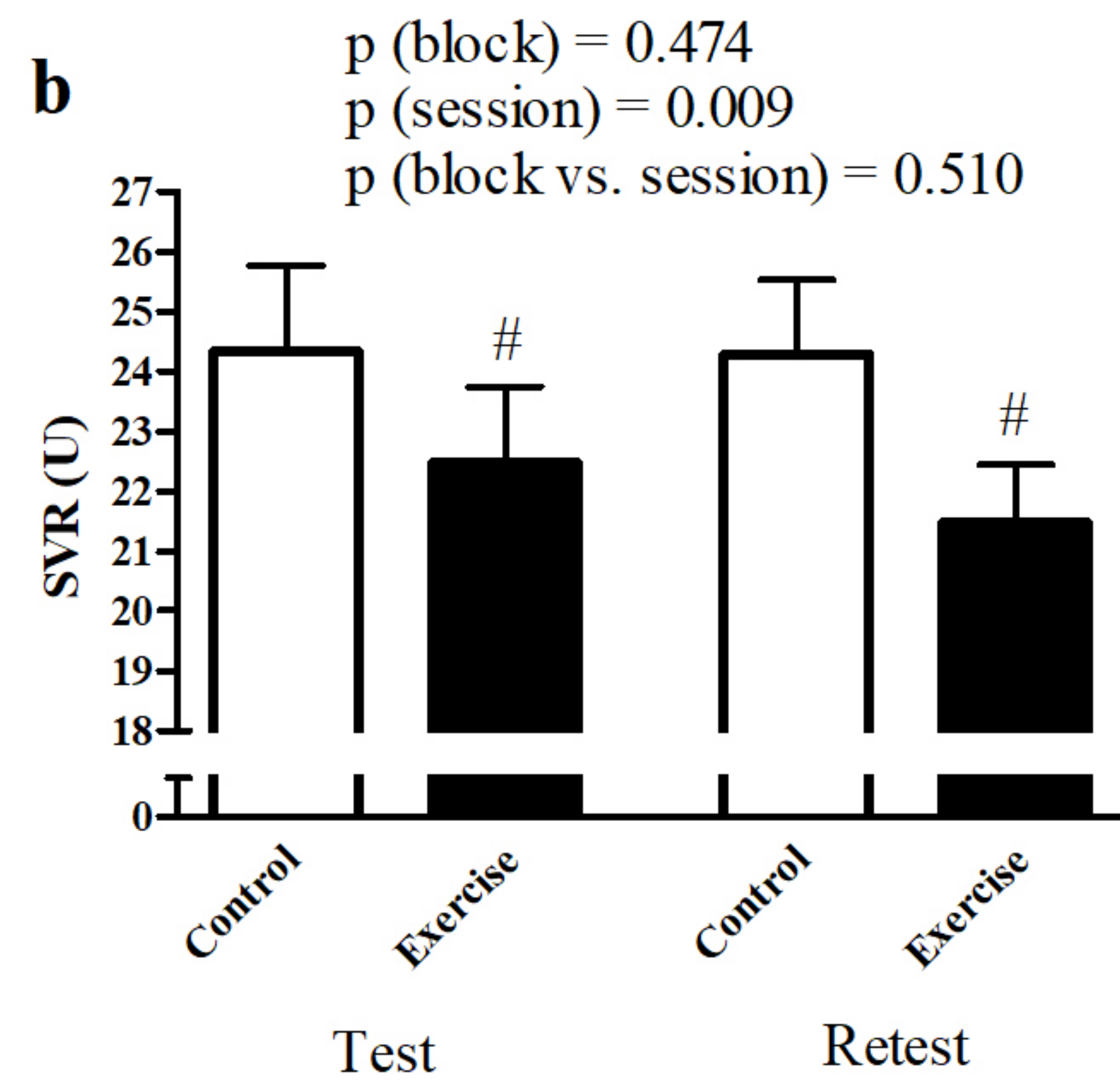
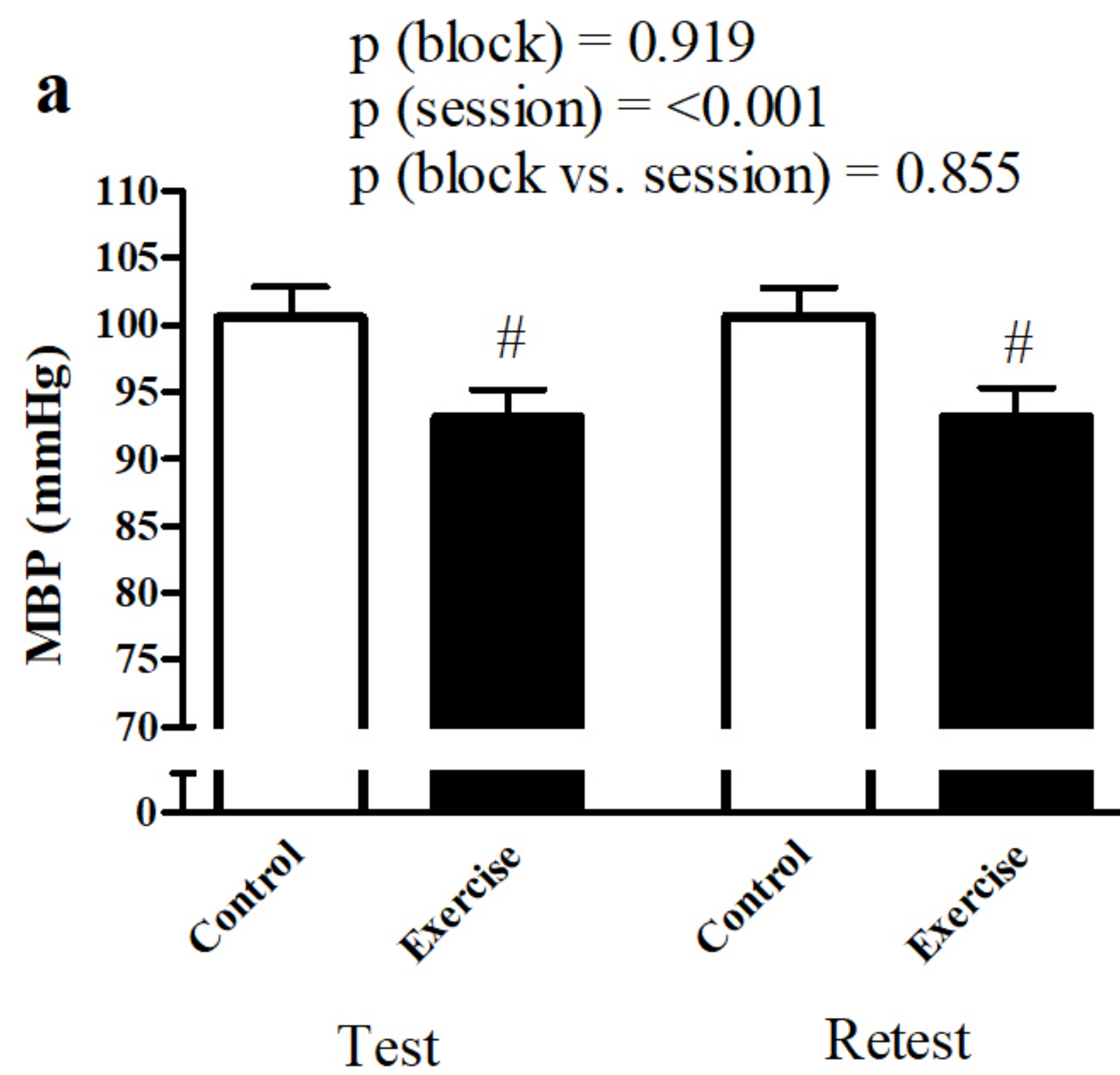
21

22

1 **Figure legends**
2

3 **Fig. 1** Mean blood pressure (MBP - panel a), systemic vascular resistance (SVR – panel b),
4 cardiac output (CO – panel c), stroke volume (SV – panel d), heart rate (HR – panel e),
5 natural logarithm of the ratio between low and high frequency components of R-R interval
6 ($\ln LF/HF_{R-R}$ – panel f), low frequency band of systolic blood pressure ($\ln LF_{SBP}$ – panel g),
7 and natural logarithm baroreflex sensitivity ($\ln BRS$ – panel h) measured after exercise and
8 control sessions conducted in the test and retest blocks of experiments; data are expressed
9 as mean \pm standard error; † significantly different from control – session main effect in
10 ANOVA ($p < 0.05$). * significantly different from test – block main effect in ANOVA
11 ($p < 0.05$)
12

13 **Fig. 2** Within-individual consistency in responses of mean blood pressure (MBP - panel a),
14 systemic vascular resistance (SVR – panel b), cardiac output (CO – panel c), stroke
15 volume (SV – panel d), heart rate (HR – panel e), ratio between low and high frequency
16 components of R-R interval (LF/HF_{R-R} – panel f), low frequency component of systolic
17 blood pressure (LF_{SBP} – panel g), baroreflex sensitivity (BRS – panel h) to exercise
18 evaluated by kappa coefficient (k). * statistically significant ($p < 0.05$)
19
20
21



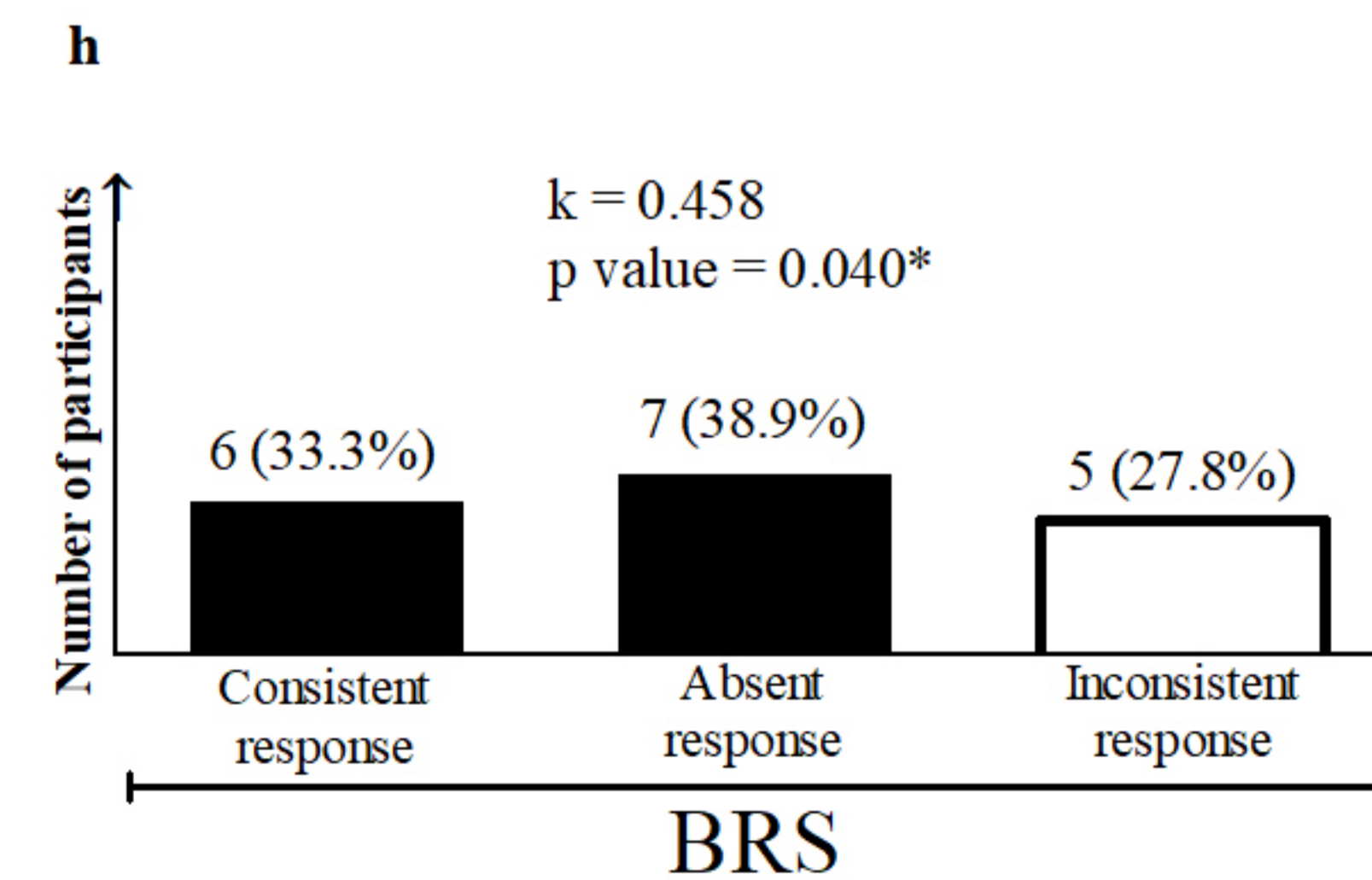
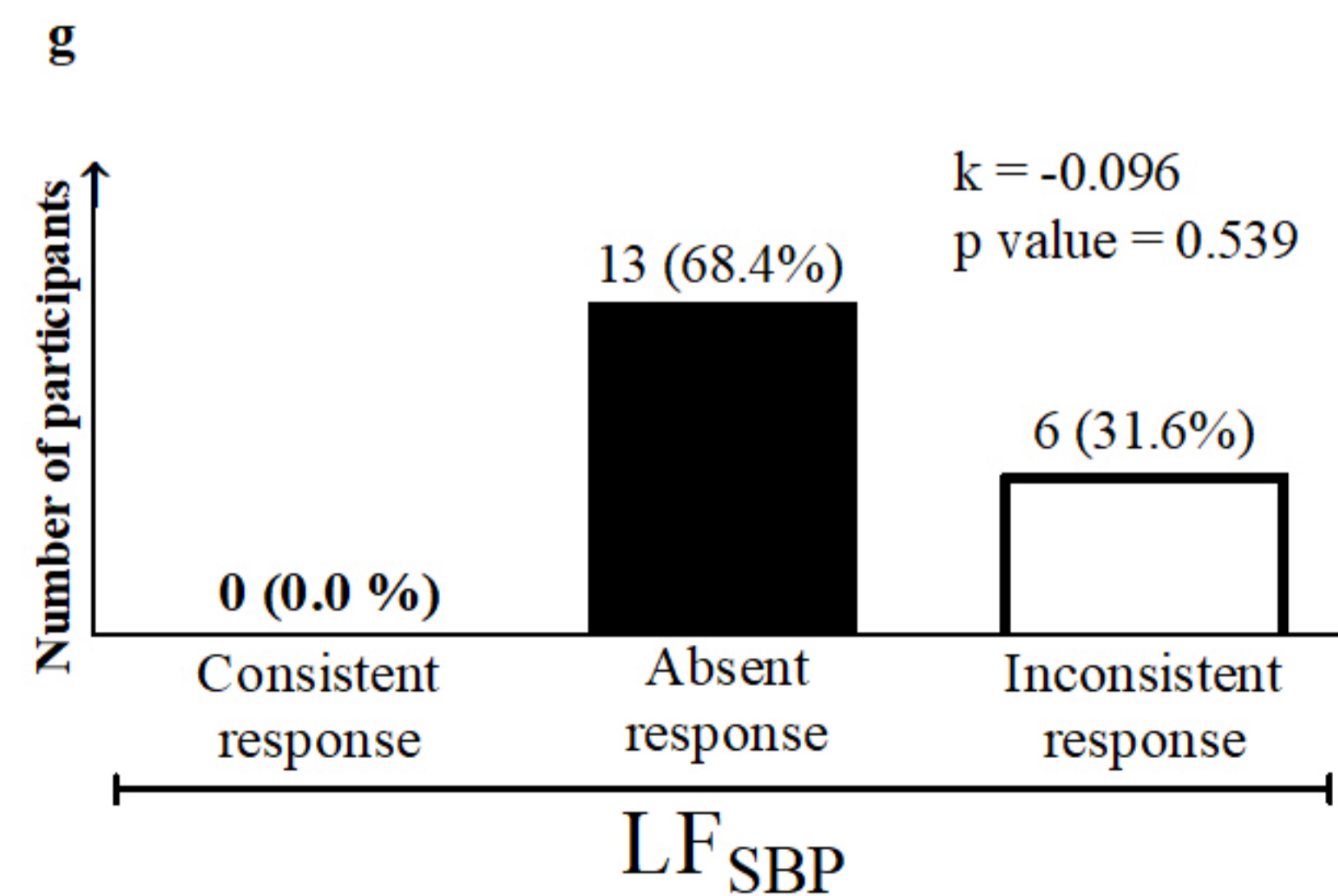
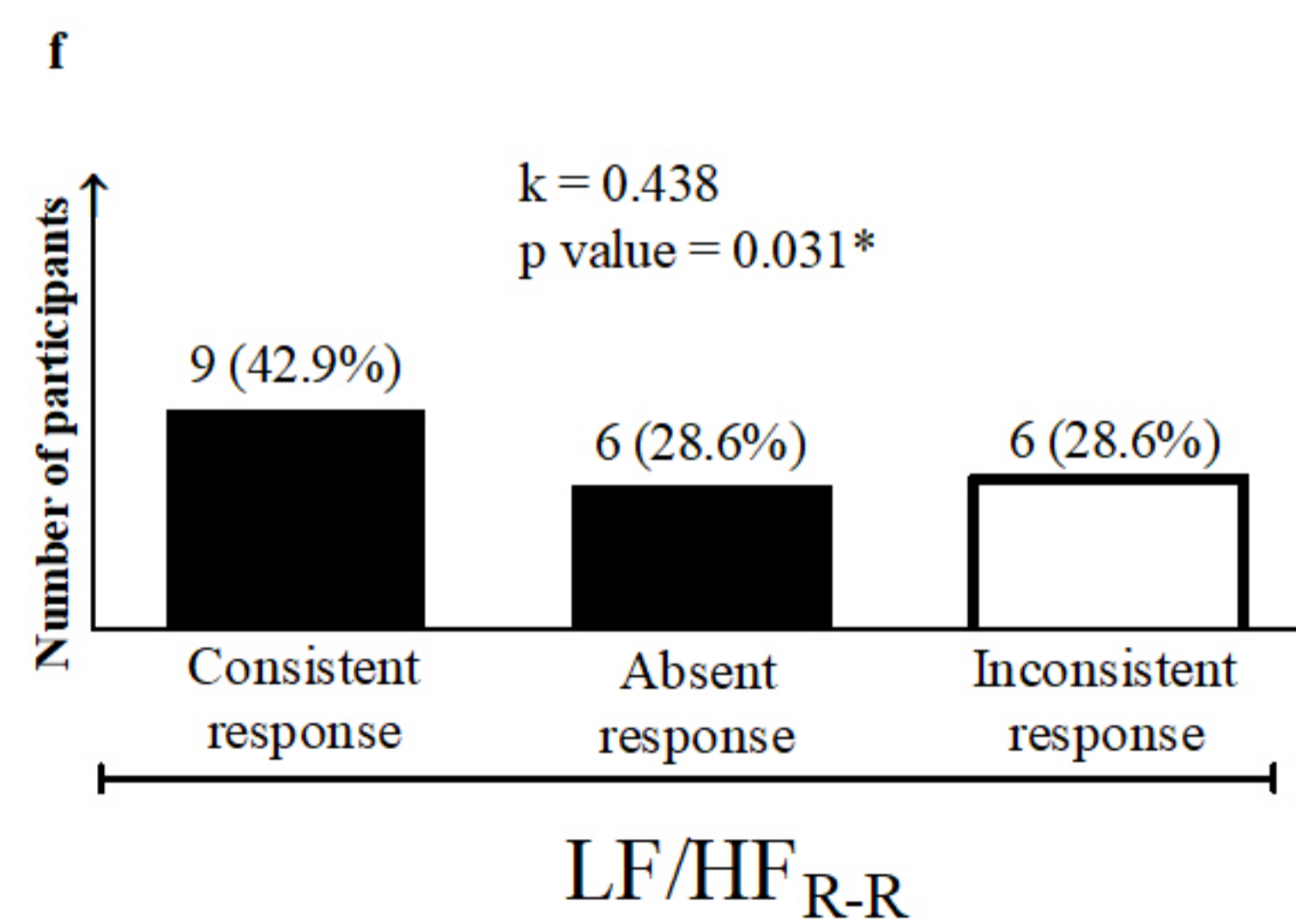
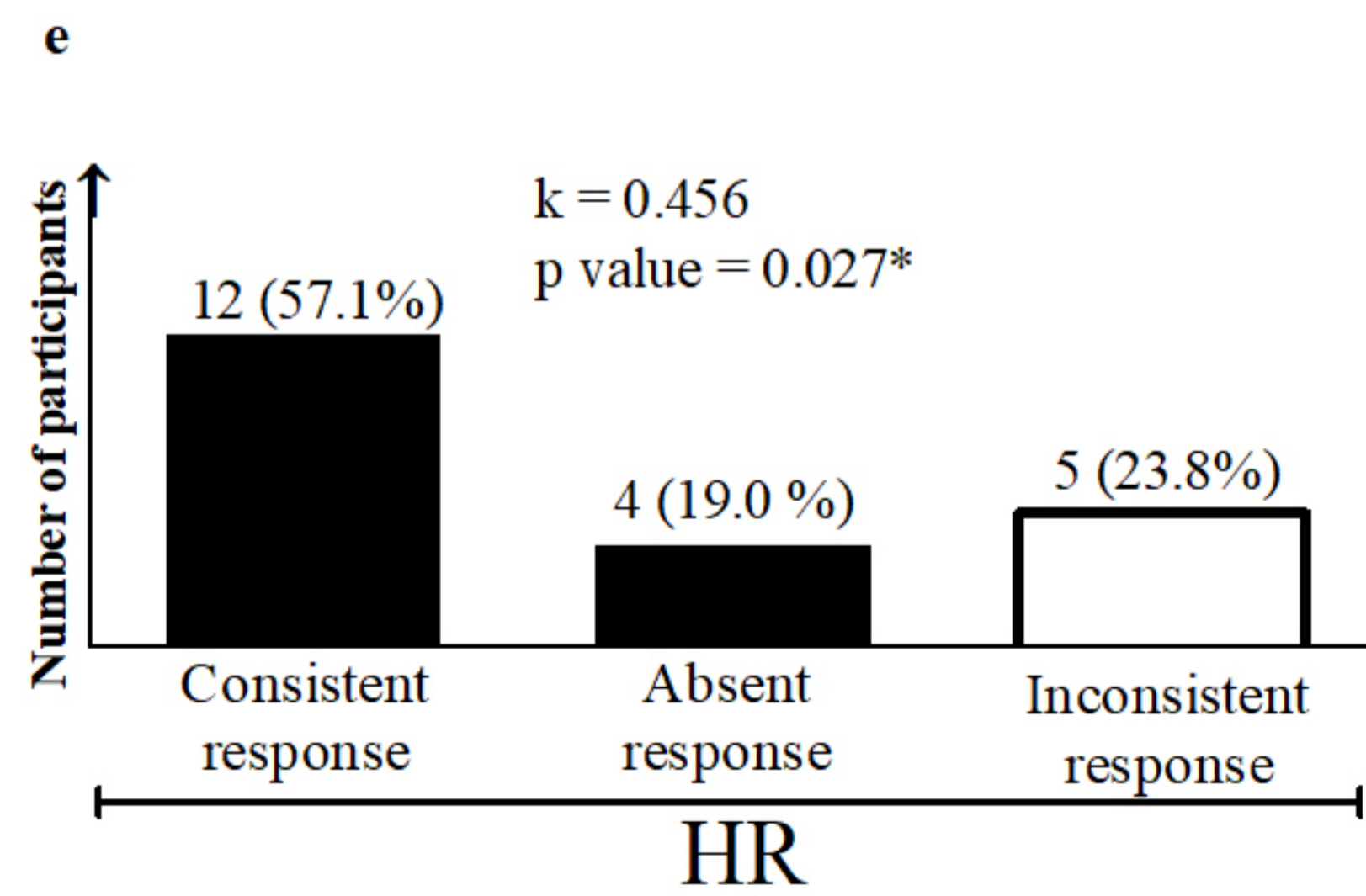
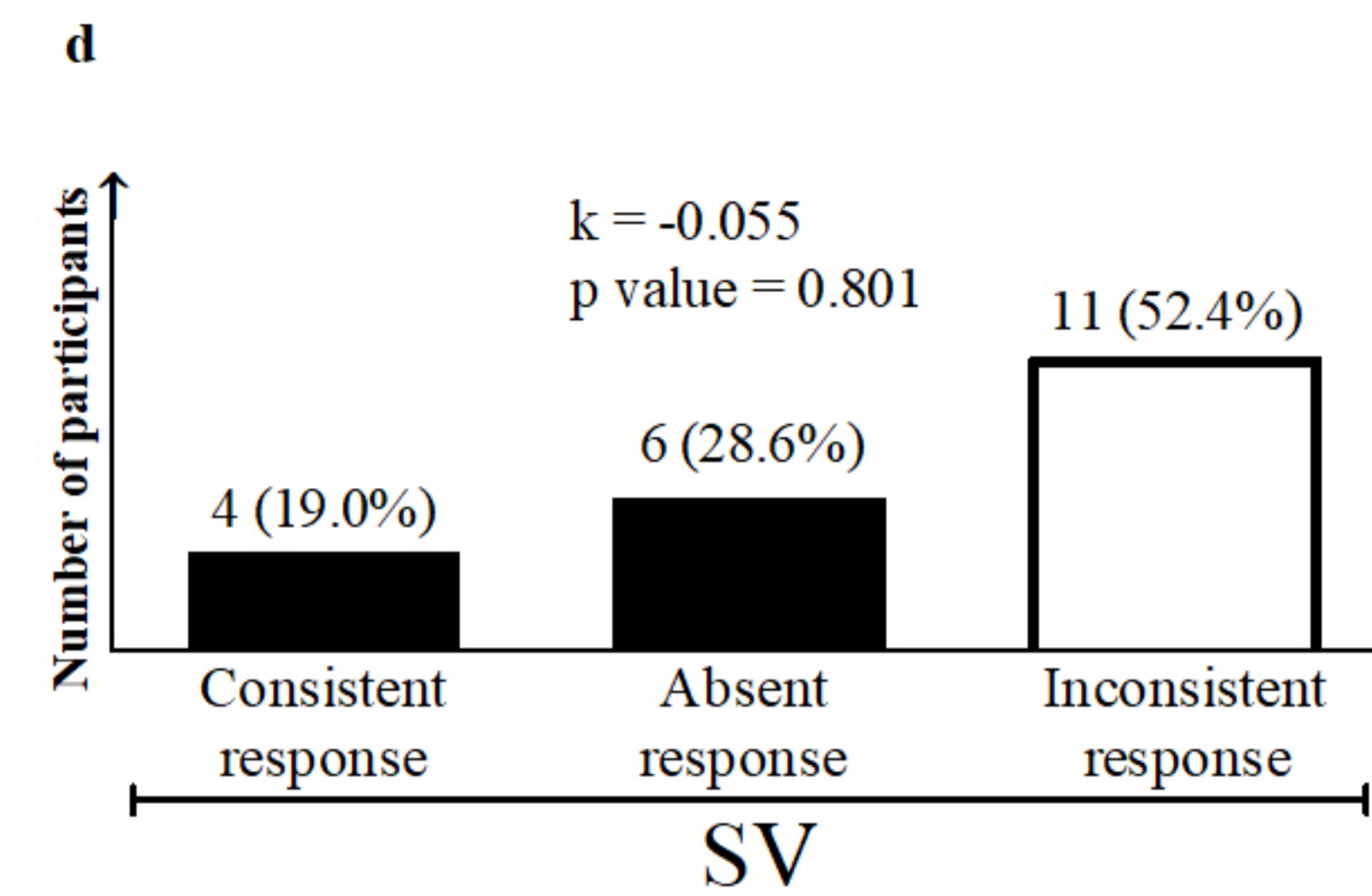
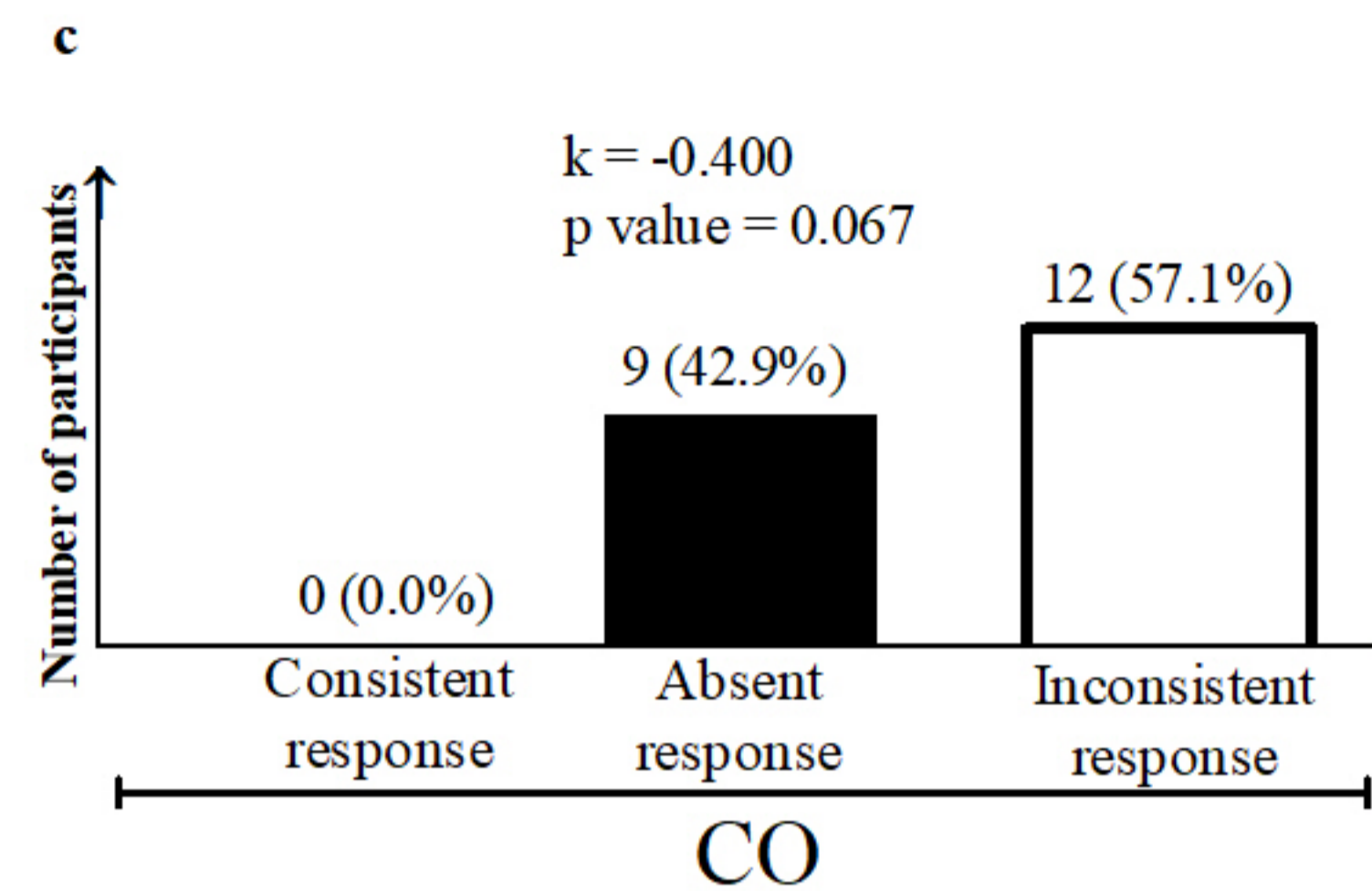
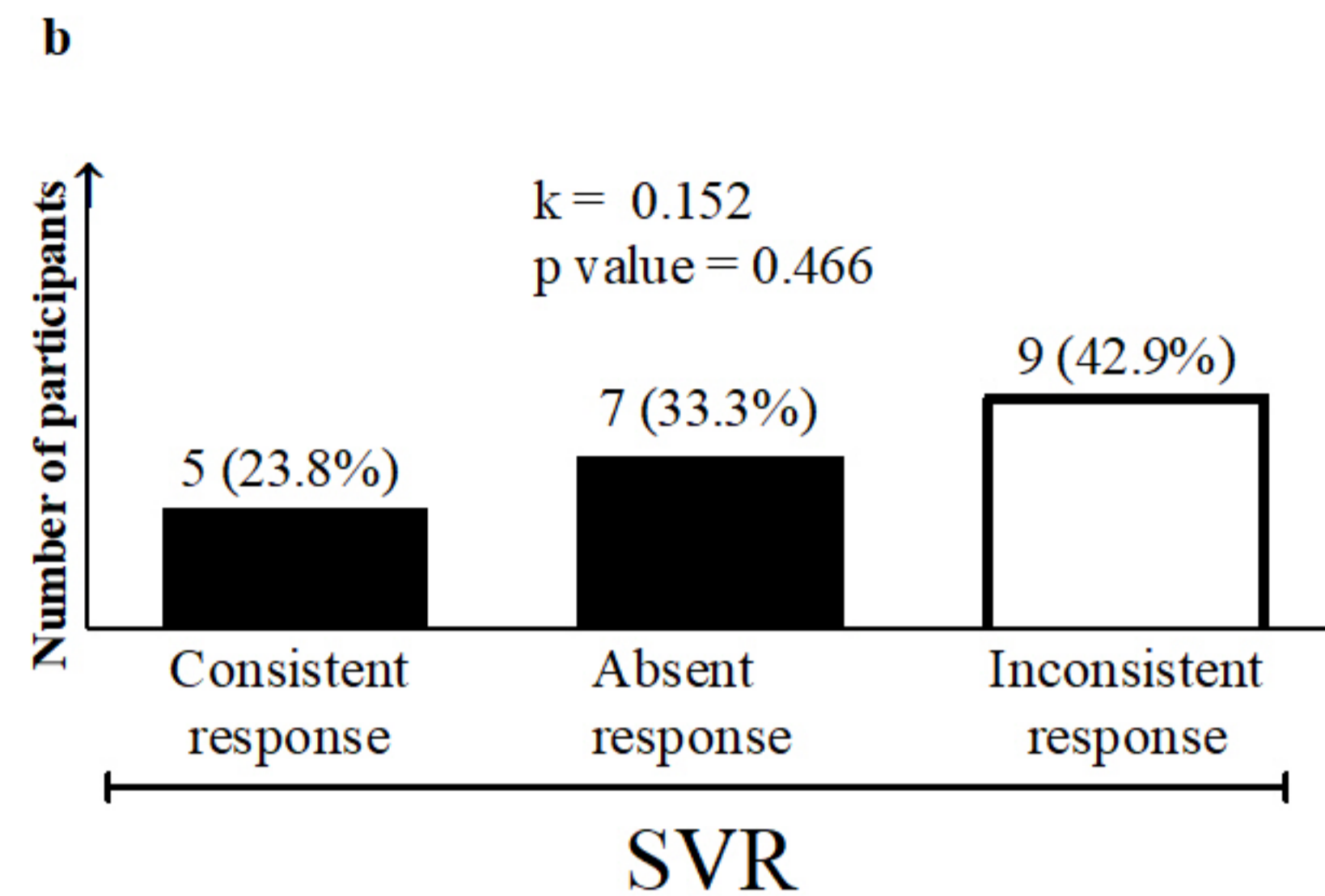
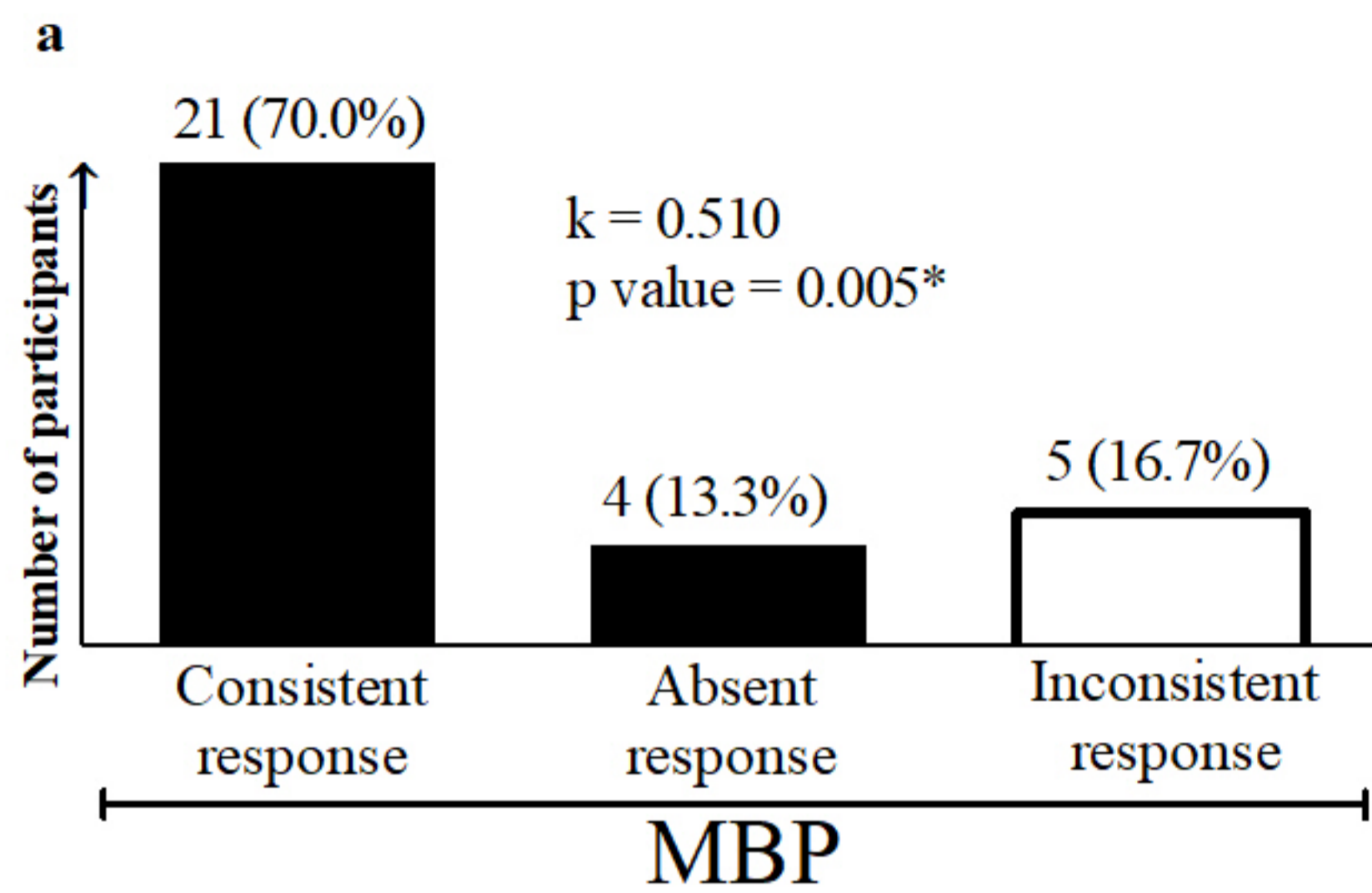


Table 1. Characteristics of the participants (n=30; 24 males and 6 females).

Age (ys)	42 ± 11
Height (m)	1.73 ± 0.06
Weight (kg)	90.5 ± 18.5
Body Mass Index (kg/m ²)	30.1 ± 5.1
Systolic BP (mmHg)	123 ± 13
Diastolic BP (mmHg)	83 ± 11
Mean BP (mmHg)	97 ± 11
Blood pressure diagnosis	
Normotensive, n (%)	9 (30)
Pre-hypertensive, n (%)	8 (27)
Hypertensive, n (%)	13 (43)
Anti-hypertensive Drug therapy	
No medication, n (%)	22 (73)
AT1 receptor blocker, n (%)	4 (13)
Angiotensin-converting enzyme inhibitor, n (%)	2 (7)
Diuretic, n (%)	1 (3)
AT1 receptor blocker + diuretic + dihydropyridine calcium channel blocker, n (%)	1 (3)

Continuous values are expressed as mean ± standard deviation. BP = blood pressure. Normotension was defined as systolic and diastolic blood pressure < 130 and 85 mmHg, respectively. Pre-hypertension was defined as systolic and/or diastolic blood pressure between 130-139 and/or 85-89 mmHg, respectively. Hypertension was defined as systolic and/or diastolic blood pressure ≥ 140 and/or 90 mmHg or the use of anti-hypertensive medications.

Table 2. Mean blood pressure (MBP) and its hemodynamic and autonomic mechanisms measured in the pre-intervention periods of the exercise and control sessions of the test and retest evaluations.

	TEST			RETEST		p
	N	Exercise	Control	Exercise	Control	
MBP (mmHg)	30	94 ± 12	95 ± 11	95 ± 11	93 ± 10	0.647
CO (mL/min)	21	4921 ± 1254	4837 ± 1111	5095 ± 1075	4763 ± 936	0.269
SVR (U)	21	20 ± 5	21 ± 5	19 ± 4	21 ± 5	0.138
SV (mL)	21	75 ± 22	77 ± 20	81 ± 23	74 ± 19	0.164
HR (bpm)	21	67 ± 9	64 ± 8	64 ± 8	66 ± 8	0.148
lnLF/HF_{R-R}	21	0.59 ± 1.10	0.54 ± 1.04	0.55 ± 0.81	0.64 ± 1.02	0.973
lnLF_{SBP} (mmHg²)	19	2.28 ± 0.86	2.33 ± 1.16	2.09 ± 1.04	2.39 ± 1.05	0.649
lnBRS(ms/mmHg)	18	1.79 ± 0.54	1.76 ± 0.65	1.87 ± 0.49	1.86 ± 0.49	0.717

Data are expressed as mean ± standard deviation. CO = cardiac output; SVR = systemic vascular resistance; SV = stroke volume; HR = heart rate; LF/HF_{R-R} = ratio between low and high frequency bands of R-R interval variability; LF_{SBP} = low frequency band of systolic blood pressure; BRS = baroreflex sensitivity; ln = natural logarithm.

Table 3. Typical error of measurement calculated using the pre-intervention values of the control sessions conducted in the test and retest blocks expressed in their actual units of measurement (TE) and in percentage of the mean test and retest values (TE%).

	TE	TE%
MBP (mmHg)	2.9	3.1
SVR (U)	2.8	13.7
CO (L/min)	0.487	10.0
SV (mL)	8.3	11.1
HR (bpm)	4.3	6.4
ln LF/HF_{R-R}	0.66	94.5
ln LF_{SBP} (mmHg²)	0.64	28.2
ln BRS (ms/mmHg)	0.28	15.0

MBP = mean blood pressure; SVR = systemic vascular resistance; CO = cardiac output; SV = stroke volume; HR = heart rate; ln LF/HF_{R-R} = natural logarithm of the ratio between low and high frequency bands of R-R interval; ln LF_{SBP} = natural logarithm of the low frequency component of systolic blood pressure; ln BRS = natural logarithm of baroreflex sensitivity.