



# Acute effect of intensity and volume during strength training on sensation of pleasure, rating of perceived exertion, and pain in trained men

original paper

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DOI: <https://doi.org/10.5114/hm.2023.107245>

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## ABSTRACT

**Purpose.** The purposes of this study were: (a) to compare the sensation of pleasure, rating of perceived exertion (RPE), and pain in different volumes (volitional failure [VF] vs. fixed repetitions [FR]), equalizing the intensity; and (b) to compare the sensation of pleasure, RPE, and pain in different intensities (40%, 60%, and 80%) of one-repetition maximum (1RM), with equalization of training volume.

**Methods.** A total of 12 trained men (aged  $24.9 \pm 4.3$  years) performed 3 sets of seated row, leg press  $180^\circ$ , and chest press at 3 different intensities (40%, 60%, and 80% 1RM) for both training strategies (VF vs. FR).

**Results.** There was a decrease in pleasure and an increase in RPE and pain in VF training sessions at intensities of 40% and 60% 1RM compared with FR. However, no difference was observed for the intensity of 80% 1RM for pleasure. A dose-response effect was revealed in the comparison of intensities for pain and RPE. In turn, no effect was found for pleasure.

**Conclusions.** VF training sessions decreased responses regarding pleasure, as well as increased RPE and perceived pain for the intensities of 40% and 60% 1RM when compared with the same intensity in FR among trained men. Different intensities were not able to change the sensation of pleasure.

**Key words:** training, repetition failure, psychophysiological, discomfort, behaviour

## Introduction

Rating of perceived exertion (RPE) is a reliable and feasible measurement to assess training intensity [1]. High RPE scores are normally observed with increased intensity during aerobic exercise. However, RPE in strength training is influenced by one-repetition maximum percentage (1RM%) [2], and number of sets [3] and repetitions [4]. Therefore, RPE indicates central and peripheral changes due to psychological, pathological, or physiological factors [5, 6].

The relationship between RPE and other psychophysiological factors such as pleasure/displeasure has previously been observed [7]. The sensation of pleasure seems to decrease in high-intensity training [8]. However, this pleasure modulation pattern was only

revealed for continuous aerobic exercises [9]. Therefore, it is still not possible to establish a theoretical basis which explains the mechanisms presented in modulating this variable during strength training [10–12]. For example, Portugal et al. [12] investigated 3 intensities (40%, 60%, and 80% 1RM), equalizing volume in 8 fixed repetitions (FR) for all intensities. Moreover, a decrease in the sensation of pleasure was only observed when high intensity (80% 1RM) was compared with the control condition (without intervention) in trained men. The sensation of pleasure decreased in women in training performed at 70% 1RM when compared with 40% [11].

It is possible that the training configuration adopted in those studies (different 1RM% for a fixed number of repetitions) did not allow the investigated partici-

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Received: January 8, 2021

Accepted for publication: May 11, 2021

*Citation:* Vasconcelos GC, Damorim I, Santos T, Lima-Junior D, Fortes L. Acute effect of intensity and volume during strength training on sensation of pleasure, rating of perceived exertion, and pain in trained men. *Hum Mov.* 2023;24(1):104–113; doi: <https://doi.org/10.5114/hm.2023.107245>.

pants to experience different sensations during the training sessions, maintaining almost the same feeling of pleasure [3]. This might happen because low intensities and low training volume do not seem to influence pleasure modulation, keeping it positive [13]. For example, performing 8 repetitions at 80% 1RM is closer to exhaustion and highest in total work (resistance  $\times$  number of repetitions  $\times$  number of sets) than 40% 1RM to a similar repetition number [4]. In addition to presenting different metabolic, neuromuscular, and cardiovascular responses [14], this training configuration is in disagreement with the recommendations of the American College of Sports Medicine for trained men, which predict repetitions until concentric failure for a maximal strength percentage or repetition zones between 8 and 12 [15].

The use of performance sets to volitional failure (VF) during strength training sessions was popularized by the theory of achieving better results in muscle strength compared with submaximal training [16]. However, no difference was observed between conditions for increased strength compared with submaximal exercise [17]. Therefore, the comparison of different training strategies (VF vs. FR) allows different psychological responses, as seen in studies evaluating RPE [4]. In addition, the relationship between RPE and pain perception has been verified at different intensities [18]. It is thus possible to hypothesize that the training configuration cited in the previous studies did not clearly show the modulation of this variable for the population of trained men. Furthermore, the intensity management model outlines the use of tests that evaluate maximum dynamic force, which presents a limited practical application, and this kind of prescription is not part of the routine of strength training practitioners.

Therefore, it is possible that the VF strategy might generate different responses regarding pleasure in trained men compared with FR. In this sense, it seems interesting to compare VF vs. FR in order to better understand affective responses. The relevance of this research is also supported by the intention to incorporate an understanding of modulating pleasure in the strength training prescription guidelines [19]. Therefore, the objectives of the present study are: (a) to compare the sensation of pleasure, RPE, and pain in different volumes (VF vs. FR), equalizing the intensity; and (b) to compare the sensation of pleasure, RPE, and pain at different intensities (40%, 60%, and 80% 1RM), with training volume equalization. The hypotheses of the study are that pleasure will decrease in VF, as RPE and perception of pain will increase; when compared with intensities (40% vs. 60% vs. 80% 1RM),

pleasure would not decrease and RPE would have a dose-response effect.

## Material and methods

### Participants

A total of 18 participants were non-probabilistically selected. Nevertheless, only 12 trained men completed all steps of the study. Everyone had strength training experience of at least 6 months. The subjects were recruited through invitations made by word-of-mouth at the university and through advertisements published on social media. We included individuals who did not present a history of musculoskeletal injuries and did not use psychoactive or ergogenic nutritional drugs which could interfere in the study. The data were collected from an anamnesis. Participants who did not carry out all the visits were excluded. The subjects were instructed to maintain their usual activities, as well as not to alter their diet during the tests.

### Experimental design

The cross-over study required 9 visits. The participants were informed about the procedures in the first visit. Next, they were familiarized with the perceptive scales: effort, sensation, pain, and the 10-repetition maximum (10RM) tests. The 10RM test was replicated on the second and third visits to establish its reproducibility. Thus, we minimized any prescription error of 10RM. Then, the acute effects of 3 intensities (40%, 60%, and 80% 1RM) were investigated between the fourth and ninth visits, adopting VF or FR. There were 2–7-day intervals between the visits. The dependent variables were evaluated before, after the end of each set (not exceeding 10 s), and after 15 minutes and 30 minutes of the training session. The main outcomes of this study were RPE, perception of pain, and sensation of pleasure during strength training.

### Measures

#### *Anthropometry and body composition*

The anthropometric measures followed the recommendations of the International Society for the Advancement of Kinanthropometry [20] for body mass (portable scales PL 200, Filizola SA, São Paulo, Brazil, precision of 0.1 kg), height (professional stadiometer Sanny, São Paulo, Brazil, 0.1 cm precision), 3 skinfolds [21], and fat percentage by the Siri equation [22].

*10-repetition maximum test*

The 10RM test was used to detect muscle strength. The exercises performed were: seated row, leg press 180°, and chest press (Matrix®). The test was carried out in 3 visits, with intervals of 48 hours in an attempt to reduce learning effects of motor gestures. Up to 3 attempts were made for each exercise to stipulate 10RM in a circuit design with a 15-minute interval between trials of the same exercise and a 5-minute interval for the different exercises. The following strategies were adopted to minimize the margin of error: (a) standardization of exercise technique and data collection; (b) specific warm-up at 50% 1RM, in accordance with the value indicated by the individual; (c) corrections made on the technique; and (d) verbal encouragement to all participants. The individuals performed each exercise until they were unable to accomplish the movement as described by the evaluator. The equation used to predict 1RM for lower limbs was as follows [23]:

$$1RM = (0.0333 \times \text{repetitions}) \times \text{submaximal load} + \text{submaximal load}$$

For upper limbs, we used the equation by Adams [24], in accordance with the findings by Meneses et al. [25]:

$$1RM = \text{submaximal load} / [100 - (2 \times \text{repetitions})] \times 100$$

*Psychometric scales*

The sensation of pleasure was quantified by a feeling scale [26] used to register the affective valence (pleasure and displeasure), consisting of 11 points with single items, with the polarity ranging from +5 (very good) to -5 (too bad). The perception of pain was quantified with a pain scale of 10 items [27]. The 10-point Borg Category-Ratio (CR10) Scale [28] was used to measure RPE. This instrument is composed of 11 points, with anchors varying from 0 (minimum effort) to 10 (maximum effort), and is a potentially effective scale for monitoring exercise intensity. After 30 minutes of session training, we asked each subject: 'How would you rate your effort?' [29].

*Strength training protocol*

The strength training protocol was composed of 3 exercises (seated row, leg press 180°, and chest press), always in the same order, with 3 sets for each exercise.

The subjects underwent a standardized warm-up of 10–15 repetitions before each exercise. In the VF training, a maximum number of repetitions were performed for the intensities of 40%, 60%, and 80% 1RM. The FR training was implemented in a number of 8 repetitions for the intensities of 40%, 60%, and 80% 1RM. Two minutes of passive interval between the sets and exercises were assumed in both strategies. The number of repetitions for each set in the training sessions lasted until the concentric failure in each visit. The exercise was conducted until the concentric failure, and the correct way to perform the exercises was stipulated for everyone, although the execution time was not determined. The sensation of pleasure, pain, and RPE were measured 15 s before and after each set. The total work was quantified as resistance  $\times$  sets  $\times$  repetitions.

*Data analysis*

Participant characterization data were reported as average and standard deviation. The Shapiro-Wilk test was performed to evaluate normality. Levene's test assessed homoscedasticity, and data sphericity was verified by Mauchly's test. A two-way repeated measures ANOVA test was used to compare the mean responses of the final of each set in the variables: sensation of pleasure, pain, and RPE: (a) to analyse the differences between strategy and moment [(VF vs. FR) vs. (before the experiment, between all sets, and after the experiment)] at each investigated intensity (40%, 60%, and 80% 1RM), with intensity equalization followed by post-hoc Newman-Keuls test; (b) to analyse the differences between intensity vs. moments [(40%, 60%, and 80% 1RM) vs. (before the experiment, between all sets, and after the exercises)], with volume equalization (8 FR) followed by post-hoc Newman-Keuls test; and (c) to analyse the number of repetitions for sets and exercises. In addition, a one-way ANOVA was conducted to compare differences between total work for the strategies (VF vs. FR). The effect size (*ES*) was used to point out differences from the practical point of view. The following criteria were adopted, in accordance with Rhea [30]:  $d < 0.35$ : trivial *ES*,  $0.35 \leq d < 0.8$ : low *ES*,  $0.8 \leq d < 1.5$ : moderate *ES*, and  $d \geq 1.5$ : large *ES*. Intraclass correlation coefficients and percentage coefficients of variation were used to determine relative and absolute test-retest reliability for 10RM. All data were processed with the Statistica 7.0 software. A significance level of 5% was adopted.

### Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the Ethics Committee of the Health Sciences Centre of the Federal University of Pernambuco (CAAE 63080616.8.0000.5208).

### Informed consent

Informed consent has been obtained from all individuals included in this study.

### Results

A total of 12 trained men of the 18 individuals recruited (age:  $24.9 \pm 4.3$  years, body mass:  $72.2 \pm 3.5$  kg, and fat:  $18 \pm 6.4\%$ ) completed all visits, performing the 10RM test (seated row:  $71.3 \pm 4.3$ , leg press  $180^\circ$ :  $74.5 \pm 3.5$ , and chest press:  $77.3 \pm 8.5$ ). Table 1 shows the results analysed by two-way ANOVA of the number of repetitions for sets and exercises (seated row, leg press  $180^\circ$ , and chest press) at the intensities of 40%, 60%, and 80% of 1RM for the VF strategy. Table 2 presents the total work for each exercise in the 2 con-

Table 1. Number of repetitions (mean  $\pm$  standard deviation) per set and exercise

Intensity and exercise	Volitional failure			<i>p</i> Moment
	Set 1	Set 2	Set 3	
40% of 1RM				
Seated row	36.0 $\pm$ 6.1	25.5 <sup>a</sup> $\pm$ 3.9	21.2 <sup>b</sup> $\pm$ 2.6	< 0.001
Leg press	28.9 $\pm$ 5.0	18.2 <sup>a</sup> $\pm$ 4.2	15.9 <sup>b</sup> $\pm$ 1.9	< 0.001
Chest press	35.9 $\pm$ 7.6	19.5 <sup>a</sup> $\pm$ 4.5	16.4 <sup>a</sup> $\pm$ 4.6	< 0.001
60% of 1RM				
Seated row	20.7 $\pm$ 2.7	14.6 <sup>a</sup> $\pm$ 2.3	11.8 <sup>b</sup> $\pm$ 1.7	< 0.001
Leg press	20.1 $\pm$ 4.3	13.3 <sup>a</sup> $\pm$ 2.7	11.3 <sup>a</sup> $\pm$ 2.7	< 0.001
Chest press	20.8 $\pm$ 5.9	11.5 <sup>a</sup> $\pm$ 3.0	7.6 <sup>b</sup> $\pm$ 1.4	< 0.001
80% of 1RM				
Seated row	10.3 $\pm$ 2.1	8.8 <sup>a</sup> $\pm$ 1.4	7.5 <sup>b</sup> $\pm$ 1.4	< 0.001
Leg press	8.9 $\pm$ 1.8	6.9 <sup>a</sup> $\pm$ 1.5	6.6 <sup>a</sup> $\pm$ 1.3	< 0.001
Chest press	9.3 $\pm$ 1.9	8.3 <sup>a</sup> $\pm$ 1.6	6.1 <sup>b</sup> $\pm$ 1.3	< 0.001

The mean number of repetitions was not included for the fixed repetition strategy because there was no variation. 1RM – one-repetition maximum

<sup>a</sup>  $p < 0.05$  in relation to set 1, <sup>b</sup>  $p < 0.05$  in relation to set 2

Table 2. Descriptive values of total work (mean  $\pm$  standard deviation) per exercise

Intensity and exercise	Total work		<i>p</i> Group
	Volitional failure	Fixed repetition	
40% of 1RM			
Seated row	2872.3 $\pm$ 484.3	836.0* $\pm$ 111.2	< 0.001
Leg press	3144.9 $\pm$ 834.7	1173.8* $\pm$ 284.7	< 0.001
Chest press	2815.8 $\pm$ 713.5	912.3* $\pm$ 105.2	< 0.001
60% of 1RM			
Seated row	2452.1 $\pm$ 516.8	1254.6* $\pm$ 172.0	< 0.001
Leg press	2983.8 $\pm$ 633.2	1695.2* $\pm$ 462.0	< 0.001
Chest press	2211.8 $\pm$ 428.28	1354.1* $\pm$ 199.4	< 0.001
80% of 1RM			
Seated row	1823.9 $\pm$ 272.4	1718.2* $\pm$ 216.3	< 0.001
Leg press	2074.5 $\pm$ 457.6	2263.1 $\pm$ 563.0	0.380
Chest press	1729.6 $\pm$ 225.9	1822.1 $\pm$ 240.3	0.522

1RM – one-repetition maximum

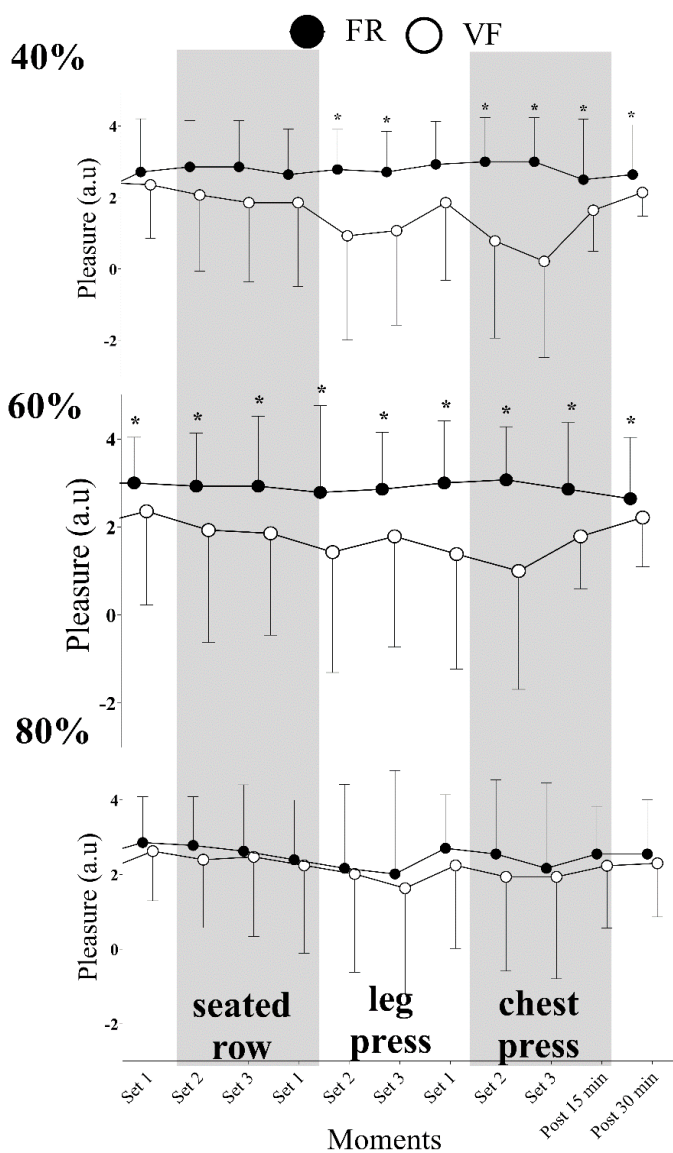
\*  $p < 0.05$

ditions (VF vs. FR). The intraclass correlation coefficient and coefficient of variation for 10RM were 0.99 and 0.3, respectively.

Volitional failure × fixed repetition

*Sensation of pleasure*

Figure 1 shows the results analysed by two-way repeated measures ANOVA for each intensity (40%, 60%, and 80% 1RM). An interaction between strategy (VF vs. FR) vs. moment (before the experiment, between all sets, and after the experiment) ( $F_{(11, 143)} = 2.12, p = 0.022,$



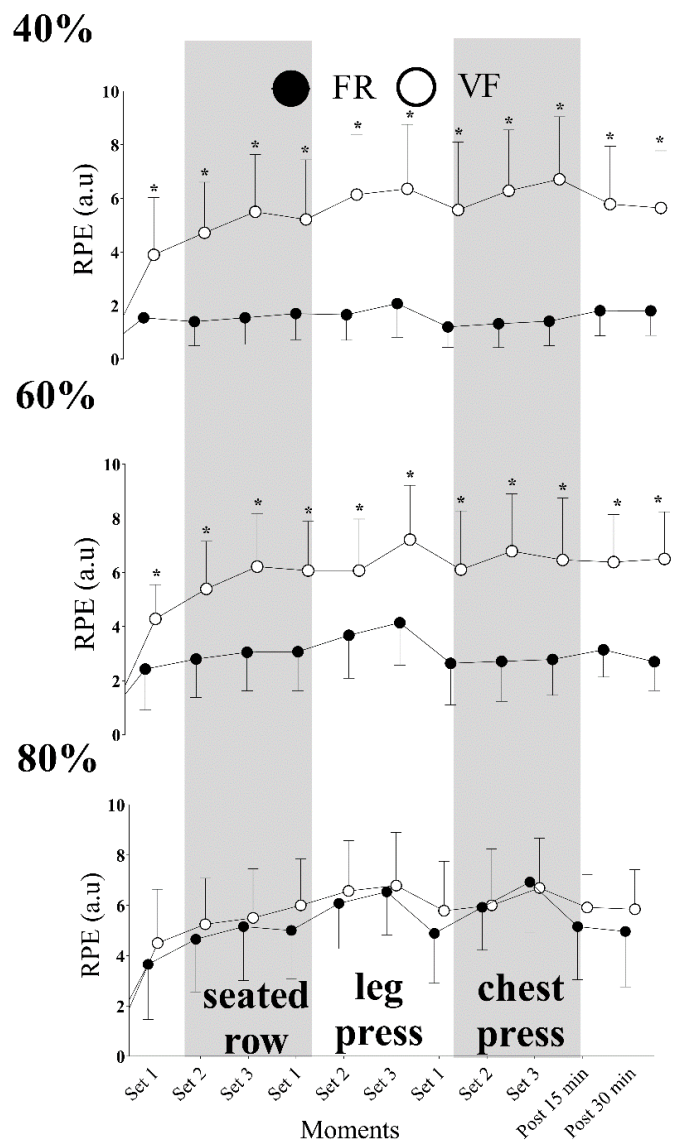
FR – fixed repetition, VF – volitional failure, a.u. – arbitrary unit  
 \* The moment between strategies was significantly different ( $p < 0.05$ )

Figure 1. Comparison of pleasure in VF vs. FR strategies at the intensity of 40%, 60%, and 80% of one-repetition maximum

$ES = 2.25$  – large) was observed for 40% 1RM. An interaction effect was also revealed for the 60% 1RM intensity ( $F_{(11, 132)} = 3.34, p = 0.001, ES = 1.72$  – large). Both analyses demonstrated that the sensation of pleasure was reduced in the VF strategy, whereas we did not find any difference for the 80% 1RM intensity ( $F_{(11, 143)} = 0.220, p = 0.995, ES = 0.10$  – trivial).

*Rating of perceived exertion*

Figure 2 shows the results analysed by two-way repeated measures ANOVA for each intensity investigated (40%, 60%, and 80% 1RM). An interaction effect



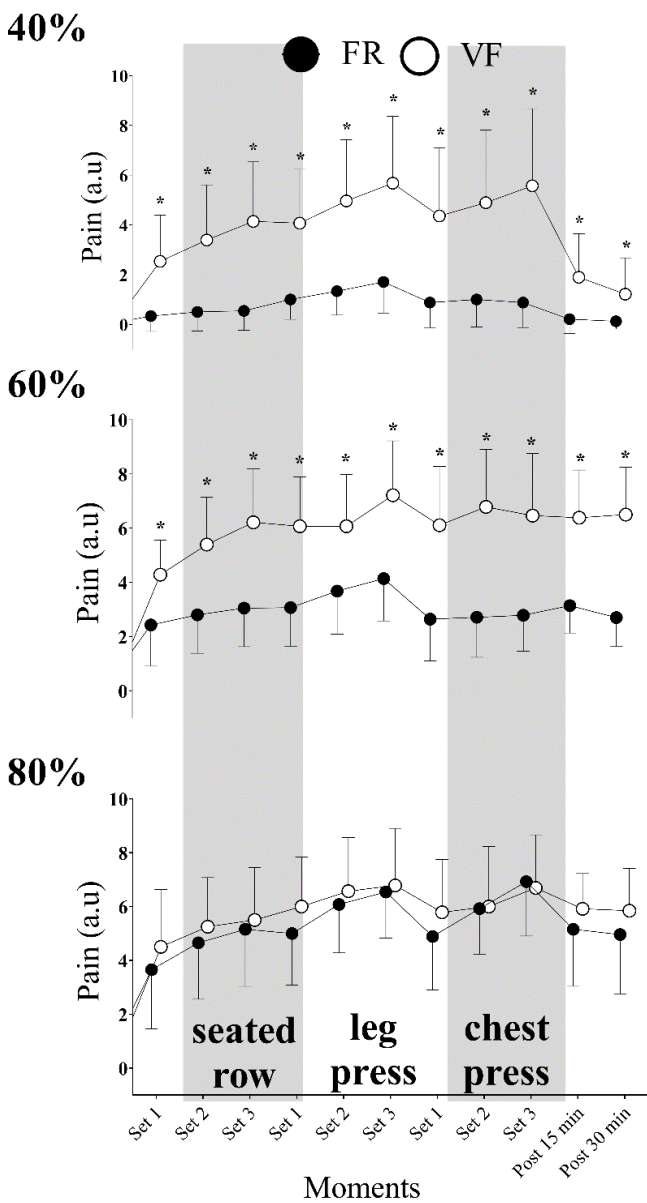
FR – fixed repetition, VF – volitional failure, RPE – rating of perceived exertion, a.u. – arbitrary unit  
 \* The moment between strategies was significantly different ( $p < 0.05$ )

Figure 2. Comparison of RPE in VF vs. FR strategies at the intensity of 40%, 60% and 80% of one-repetition maximum

for strategy (VF vs. FR) vs. moment (before the experiment, between all sets, and after the experiment) ( $F_{(11, 143)} = 17.79, p = 0.001, ES = 5.80$  – large) was observed for 40% 1RM. An interaction was also revealed for 60% 1RM ( $F_{(11, 132)} = 7.74, p = 0.001, ES = 2.77$  – large), and RPE was increased in the VF strategy in both analyses. However, the results did not indicate an interaction for 80% 1RM ( $F_{(11, 121)} = 1.680, p = 0.059, ES = 0.24$  – trivial).

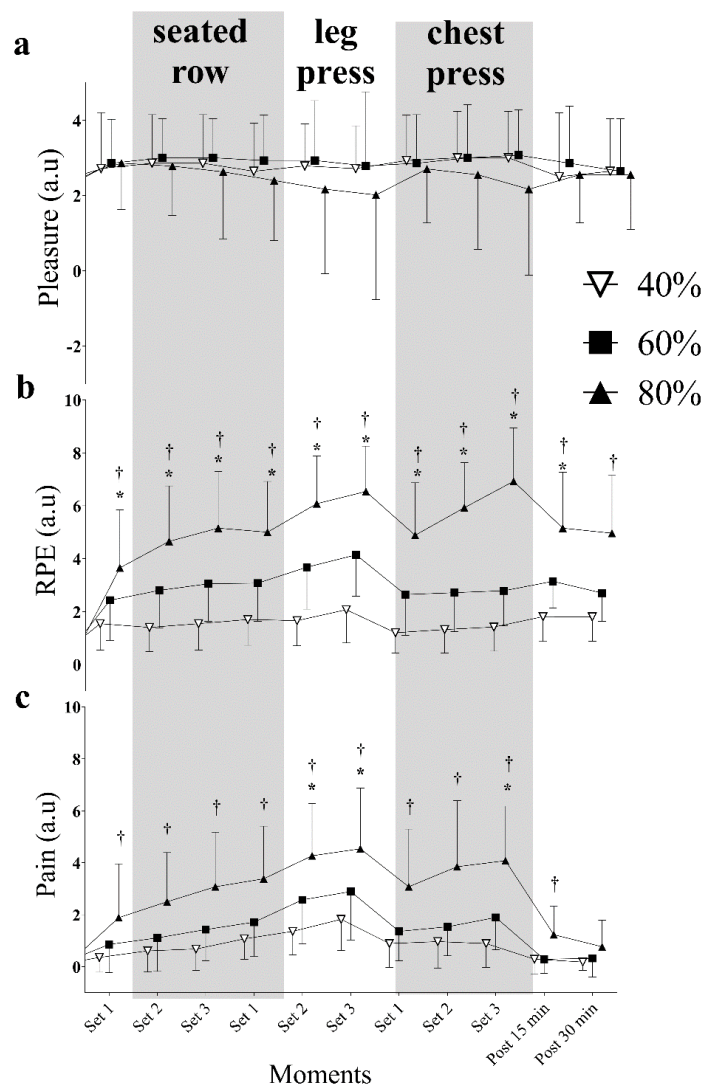
Pain

Figure 3 shows the results analysed by two-way repeated measures ANOVA for each intensity investigated (40%, 60%, and 80% 1RM). An interaction effect for strategy (VF vs. FR) vs. moment (before the experiment, between all sets, and after the experiment) ( $F_{(11, 132)} = 18.447, p = 0.001, ES = 1.03$  – moderate) was observed for 40% 1RM. Furthermore, an interaction between strategy vs. moment ( $F_{(11, 121)} = 4.88, p = 0.001, ES = 0.77$  – low) was found for 60% 1RM.



FR – fixed repetition, VF – volitional failure, a.u. – arbitrary unit  
 \* The moment between strategies was significantly different ( $p < 0.05$ )

Figure 3. Comparison of perceived pain in VF vs. FR strategies at the intensity of 40%, 60%, and 80% of one-repetition maximum



a.u. – arbitrary unit, RPE – rating of perceived exertion  
 \*  $p < 0.05$ , 60% one-repetition maximum in relation to 40% one-repetition maximum, †  $p < 0.05$ , 80% one-repetition maximum in relation to 40% one-repetition maximum

Figure 4. Comparison of 40% vs. 60% vs. 80% one-repetition maximum intensities for (a) pleasure, (b) RPE, and (c) pain

An increase in pain for the VF strategy was revealed for both analyses in the comparisons of training strategies. No significant difference was found for 80% 1RM ( $p > 0.05$ ).

#### Intensities (40% vs. 60% vs. 80% 1RM)

The volume regarding intensity comparison (40% vs. 60% vs. 80% 1RM) was equalized. We found an interaction intensity vs. moment for RPE and pain, which increased at the 80% intensity ( $F_{(22, 264)} = 10.837$ ,  $p = 0.001$ ) and 60% 1RM ( $F_{(22, 264)} = 7.286$ ,  $p = 0.001$ ) compared with 40% 1RM (Figure 4). On the other hand, no interaction effect was observed between intensity vs. moment in the pleasure evaluation ( $F_{(22, 286)} = 1.632$ ,  $p = 0.388$ ).

### Discussion

The present study aimed to compare the sensation of pleasure, RPE, and pain in different volumes (VF vs. FR) at the intensities of 40%, 60%, and 80% 1RM with equalized volume. The main findings of the study confirmed its hypotheses, namely: (a) the sensation of pleasure responses significantly decreased in VF training performed at the intensities of 40% and 60% 1RM when compared with FR for the same intensity; (b) an increase in RPE and pain perception in VF training at the intensities of 40% and 60% 1RM was observed when compared with FR at the same intensities, although this finding was not replicated at the intensity of 80% 1RM; and (c) the sensation of pleasure did not change when intensities of 40% vs. 60% vs. 80% 1RM were compared for FR (equalized volume). These results indicate that the sensation of pleasure was decreased, while RPE and pain perception increased in training with 40% and 60% 1RM performed in VF when compared with FR.

Strength training studies on pleasure are still inconclusive [7, 11, 12, 31, 32]. In a study involving trained men, Portugal et al. [12] observed a decrease in pleasure only when the high-intensity (80% 1RM) group was compared with the control group (without exercise). In contrast, a difference in pleasure modulation was revealed in the intensity comparisons (40% vs. 60% vs. 80% 1RM) for FR. Altogether, these results corroborate the present study. In contrast, a dose-response effect of the sensation of pleasure after physical exercise for different intensities with a greater sensation of pleasure at moderate intensity has already been observed [10]. A decrease in the sensation of pleasure was demonstrated in women trained at high intensity

(70% 1RM) compared with low intensity (40% 1RM) [11]. The volunteers in the aforementioned studies performed a fixed number of repetitions, and perhaps this training configuration allowed modulating sensations such as discomfort and displeasure, even if administered at different intensities. Another point to be highlighted is that, according to the theory of behaviour, low intensities maintain positive responses of the sensation of pleasure [33].

However, VF training generates greater discomfort compared with training that does not lead to maximum effort [17]. Thus, the training configuration performed in previous studies may have decreased the sensation of pleasure during the higher intensities because it led participants to the maximum effort compared with the low-intensity and low-volume training. It is also noteworthy that the prescribed RM training is well used by trained males in fitness centres. Moreover, VF might contribute to changes in the perception of pain and effort, consequently decreasing the sensation of pleasure. Thus, we observed a necessity to evaluate the affective responses in VF in different percentages of 1RM.

In fact, the present study is the first to compare the effects of different VF fractions on the sensation of pleasure. The results of this study, comparing intensities (40%, 60%, and 80% 1RM) and using different strategies (VF vs. FR), revealed a significant decrease in the sensation of pleasure in VF compared with FR at the intensities of 40% and 60% 1RM. In this case, the rationale given is that intensity does not modulate the feeling of pleasure in trained men [12]. However, different training configurations should be considered when administered in strength training. These results demonstrate that the sensation of pleasure in strength training is not solely modulated by intensity, but by a high training volume performed in VF. This can be justified by the different neuromuscular, cardiovascular, and biochemical responses to this training strategy when compared with submaximal exercise [14].

The scientific literature points out a relationship between the fraction of 1RM and RPE responses when the number of repetitions is predetermined [2]. These results are in accordance with the present study, in which a dose-response effect was observed for RPE when compared with intensities 40% vs. 60% vs. 80% 1RM in FR. It is suggested that these results are exclusively related to raised external resistance. However, increased RPE is also observed when the same fraction of 1RM is prescribed for more than 1 set or in different training configurations [3]. Studies have

shown that training with a low 1RM percentage in VF potentiates RPE increase compared with a high 1RM% in VF [4, 34]. Parallel to the aforementioned studies, our paper shows an increase in RPE in VF training at the intensities of 40% and 60% 1RM when compared with FR. There is possibly a contribution of accumulated metabolites and muscle fatigue due to the training configuration adopted to increase RPE.

Similar to the RPE results, pain perception also increased at the intensities of 40% and 60% 1RM in VF when compared with FR. Previous studies point to a relationship between pain perception and RPE [27, 35] and an increase in pain perception scores with an increase in the number of sets [36, 37]. All the results presented reinforce the idea that the metabolic disturbance has a strong influence on the perceptual responses during strength training owing to the training configuration.

In fact, training sessions administered at the highest 1RM%, whether applying a maximum number of repetitions or not, did not influence the sensation of pleasure in the trained men. In addition, lower intensities in VF significantly worsened the sensation of pleasure and increased the perception of pain and RPE. Displeasure is apparently not adequate, and this scenario might negatively influence an individual's performance to achieve their goals [38]. According to behaviour theories, it is postulated that there is a decrease in the frequency of the type of training or even demotivation of the practice [33].

Because of the lack of instruments, it was not possible to directly evaluate the concentration of metabolites which could serve as a basis to improve the results and discuss the different training strategies with regard to the sensation of pleasure, pain, and RPE. However, it has been reported that an increase in metabolite concentration influences an increase in pain perception and effort responses [39]. The description of the number of repetitions and the affection responses presented in the study can aid coaches and researchers in programming strength training variables in a practical way. In other words, some people may not like performing at low intensities with high numbers of repetitions, and this type of prescription might keep them from training. However, it is important to note that the sensation of pleasure scale used in the present study is still in the process of cross-cultural validation. Nevertheless, these scales are accepted by researchers in the area to evaluate affective responses.

## Conclusions

This study is the first to empirically demonstrate that VF training sessions at the intensities of 40% and 60% 1RM decrease affect and significantly increase RPE and perceived pain when compared with the same intensity in FR among trained men. However, the intensity of 80% 1RM, regardless of the adopted strategy, maintained a similar affect, probably owing to the equivalence of total work in intensity between the training strategies. Moreover, different intensities were not able to change the affect. Thus, unlike what is seen in aerobic exercise, it seems that the sensation of pleasure in strength training is not related to intensity.

## Acknowledgments

The authors would like to acknowledge the students Amanda Machado Nunes, Luanna Karina Pereira da Silva, Igor Nunes Miranda, and Danielly Marques Ferreira for providing assistance in data collection.

## Disclosure statement

No author has any financial interest or received any financial benefit from this research.

## Conflict of interest

The authors state no conflict of interest.

## Funding

This research was funded by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

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